Agile BioFoundry

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

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DBTL Host: *Rhodosporidium toruloides*

John Gladden, Jon Magnuson, Nathan Hillson, Gregg Beckham, Phil Laible, Hector Garcia-Martin

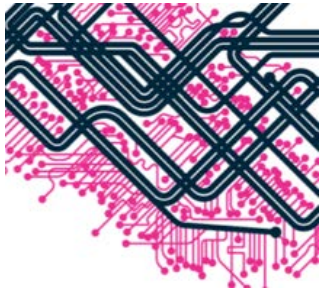
BETO Peer Review 2019
Technology Session Review Area: Agile BioFoundry
March 7, 2019

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.



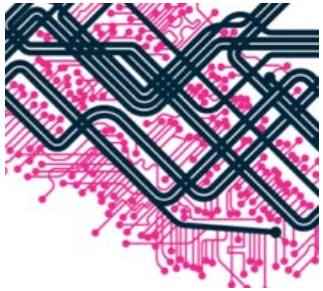
Target-Host Pair Goal Statement

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 *Rhodosporidium toruloides IFO0880*
- Target 1: Terpenes: cineole, bisabolene, farnesene, kaurene
- Target 2: C16-18 fatty alcohols

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 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

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	$20k	$0.9MM	$1.8MM	$2.2MM
Partners: LBNL (11%); PNNL (16%); SNL (73%)				

Barriers

Ct-L. Decreasing Development Time for Industrially Relevant Microorganisms

- Developing an industrially-relevant host, *R. toruloides*, 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 *R. toruloides* enabled by the DBTL cycle

End-of-project goal:

Assess production in 10 L bioreactors of the top 3 target molecules, with target titers of at least 10 g/L, rate of 100 mg/L/h, and 40% theoretical yield in DMR-EH hydrolysate.

1- Project Overview

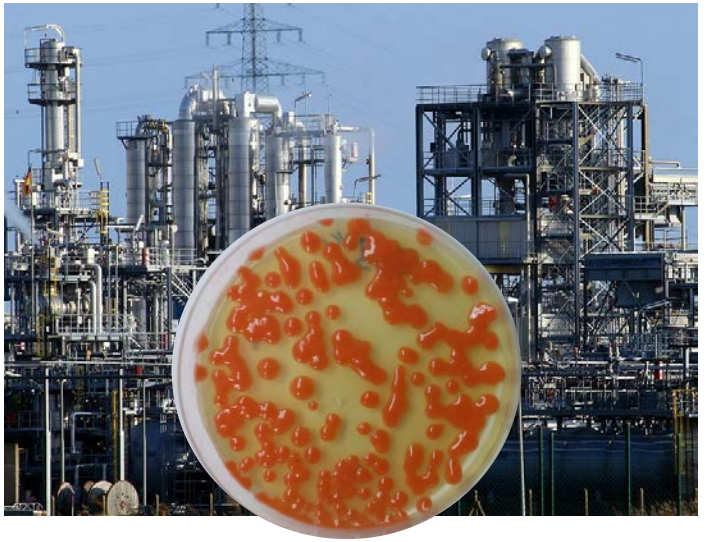
Project Overview

History: Task initiated at the beginning of the Agile BioFoundry

- *Rhodosporidium toruloides* is a new host introduced in FY17
- Heterologous terpene production had just been demonstrated prior

Context: *R. toruloides* offers a robust host for producing terpene and lipid-derived compounds

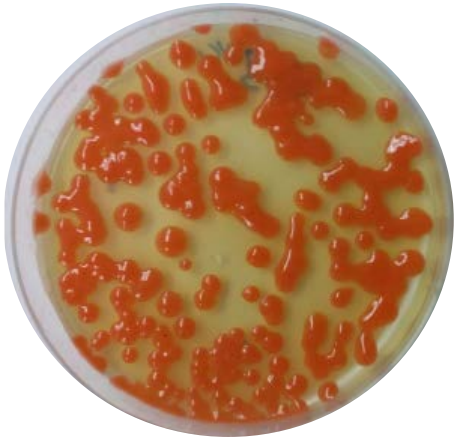
- Naturally consumes lignocellulose: pentose, hexose, aromatics
- High natural flux in terpene and lipid pathways

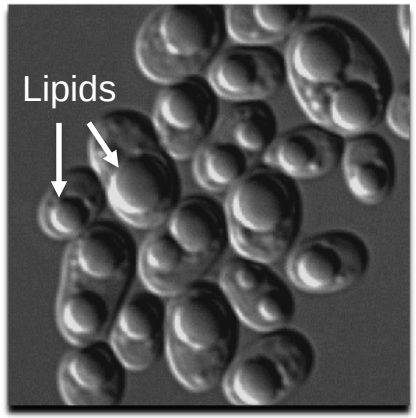


Project goals:

- Employ the ABF DBTL to produce two targets: terpenes and fatty alcohols.
- Expand knowledgebase and engineering tools/strategies
- Use T/H pairs to identify areas to improve DBTL cycle efficiency

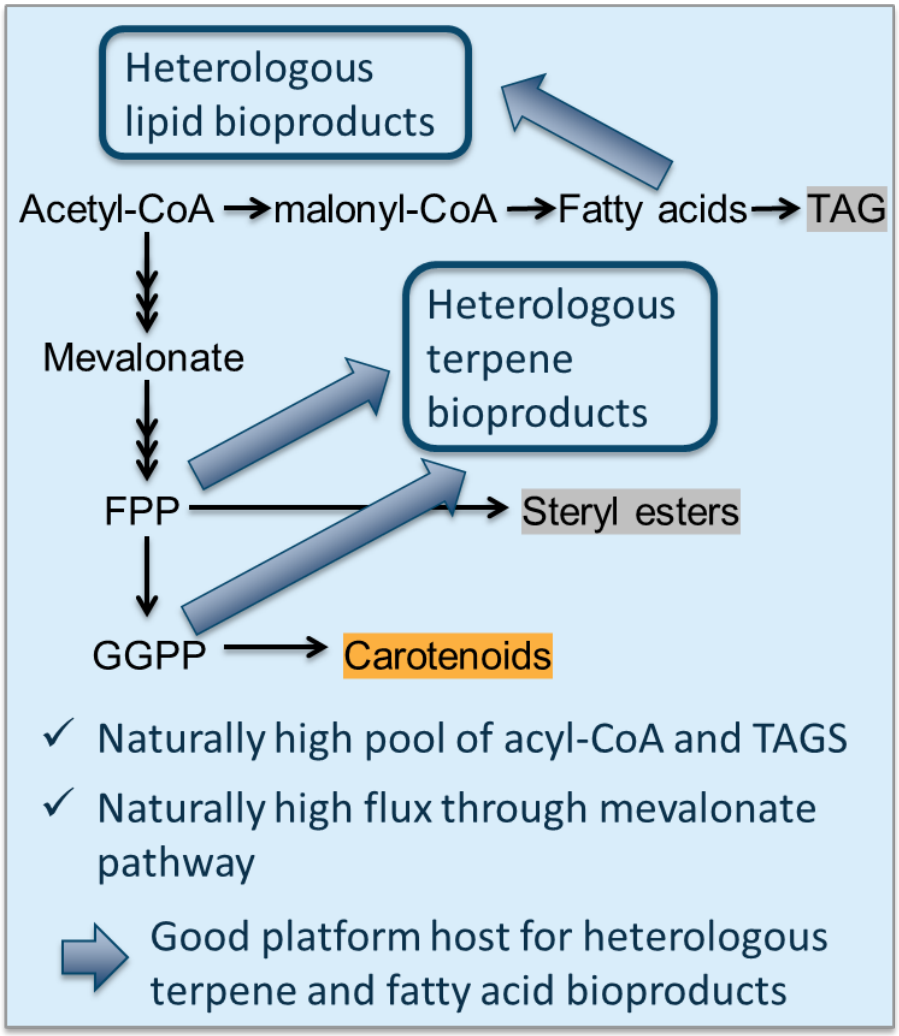
Project Overview: Why *R. toruloides*?





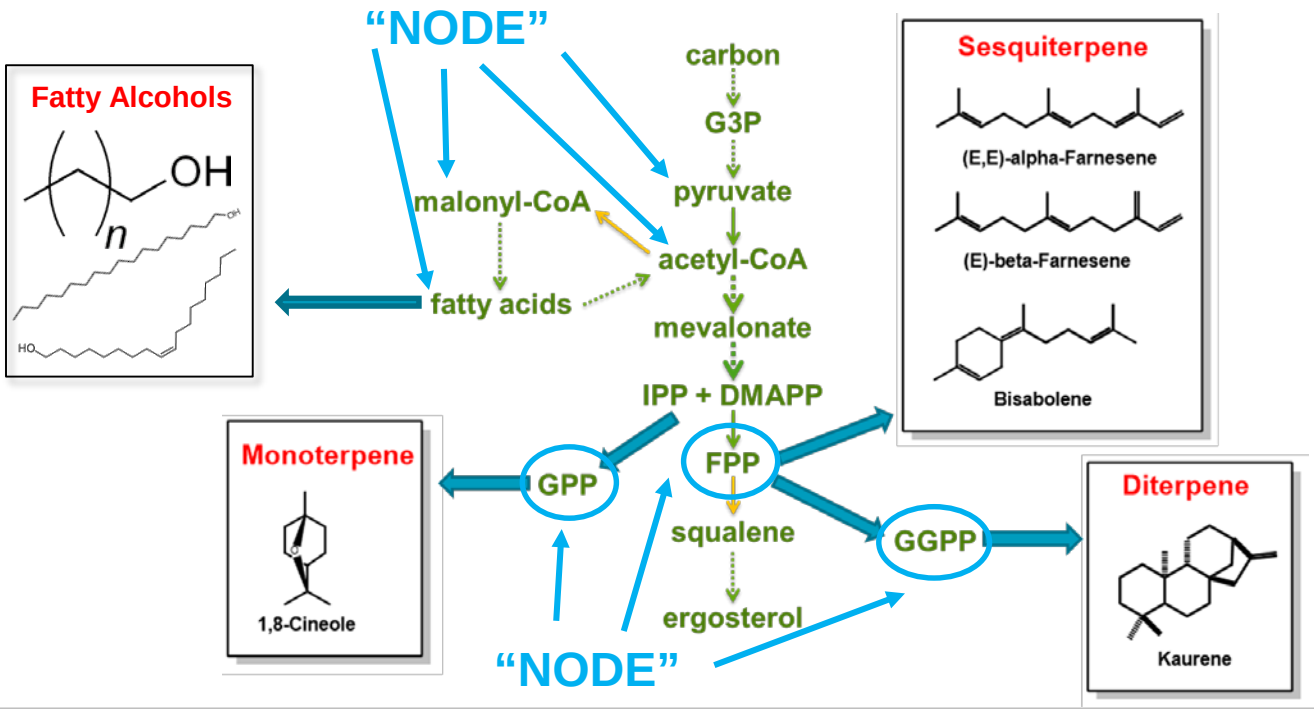
Rhodosporidium toruloides

- Utilizes lignocellulose
- Fast growing
- Oleaginous, carotenogenic
- Metabolically versatile
- Genetically tractable



Project Overview: Why these Targets?

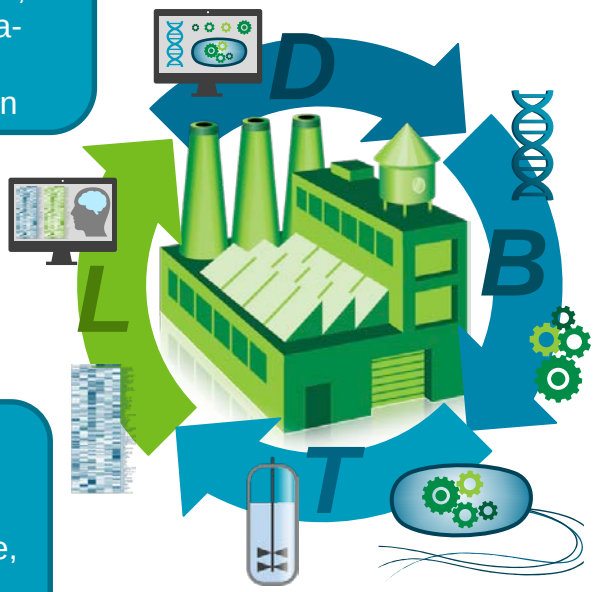
- **Target 1: Terpenes**- biofuels and bioproducts (adhesives, insect repellents, polymers, fragrances, food additives)
- **Target 2: Fatty Alcohols**- Detergents, lubricants, plastics and cosmetics. $5.2 billion in 2011 globally. Grow at 4% CAGR in next decade.
- **Nodes:** These targets pull from many versatile nodes. Provide opportunities to produce literally thousands of bioproducts.



2- Approach

Management Approach

- **Virtual meetings:** biweekly calls with *R. toruloides* team, monthly with Test/Learn teams
- **F2F meetings**: ABF annual all-hand, during year as needed
- **Updates**: regular team updates on task lead call, monthly DBTL tracking
- **Milestones:** DBTL cycle times, product performance metrics
- **Project interfacing:** *ad hoc* meetings with Integrated Analysis, Integration and Scaling, other BETO consortia



Lead, DBTL tools, applications

John Gladden

Design, Build, EDD tools

Nathan Hillson, Hector Garcia-Martin
John Gladden

Scale and Integration

Todd Pray, Gregg

Beckham

Learn tools

Hector Garcia-Martin, Phil Laible, Joonhoon Kim

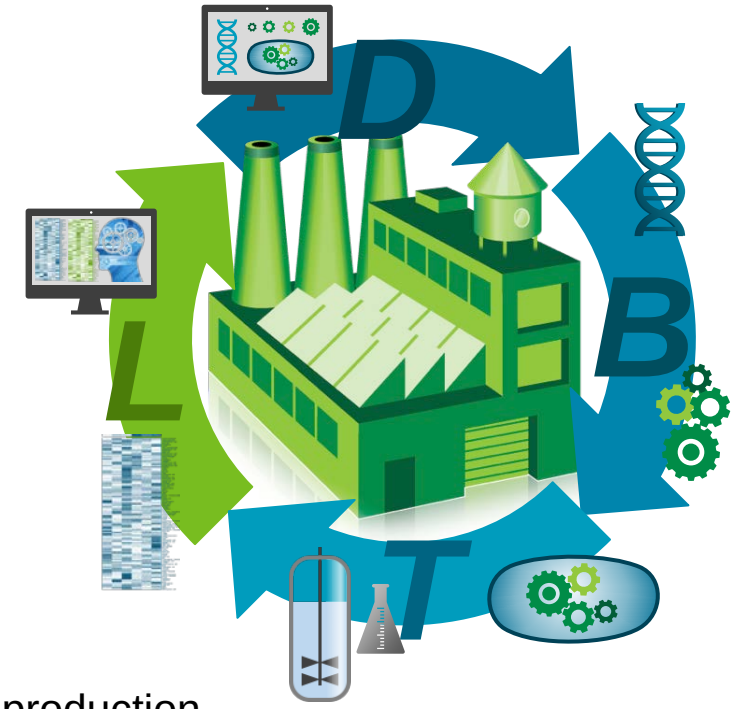
Test multi-omics

Jon Magnuson, Kristin Burnum-Johnson, Joonhoon Kim

Technical Approach

Critical success factors

- Demonstrate DBTL works through improvements to targets 1 and 2
- Meaningful DBTL cycles with output from Learn leading to strain improvements
- Identification and mitigation of key DTBL bottlenecks



Challenges

- Developing a versatile host for producing both terpene and lipid bioproducts
- Limited knowledgebase, needs improvement to enable more efficient DBTL
- Limited set of engineering tools and strategies can limit Design/Build space, e.g. no plasmids

Technical approach

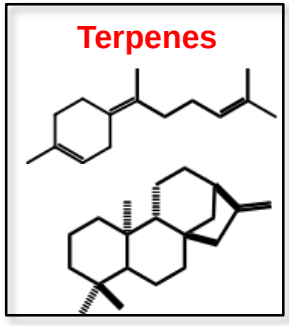
- Engineer target biosynthetic genes into *R. toruloides*
- Use DBTL understand metabolism and optimize target production
- Expand knowledgebase and tools by acquiring systems level multi-omic data, developing a metabolic model, testing new parts and engineering strategies
- Optimize cultivation conditions and examine scalability in DMR-EH hydrolysate

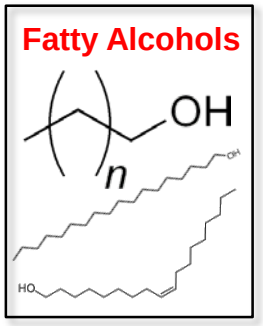
3- Technical Accomplishments/ Progress/Results

Outline of Technical Accomplishments

DBTL for Target 1: Terpenes

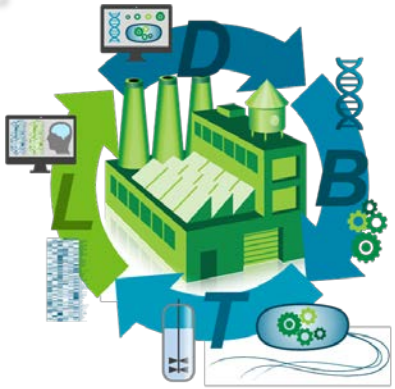
- Baselining production of 4 terpenes
- Improving titers through MEV pathway optimization
- Successful Learn cycles for strain improvements

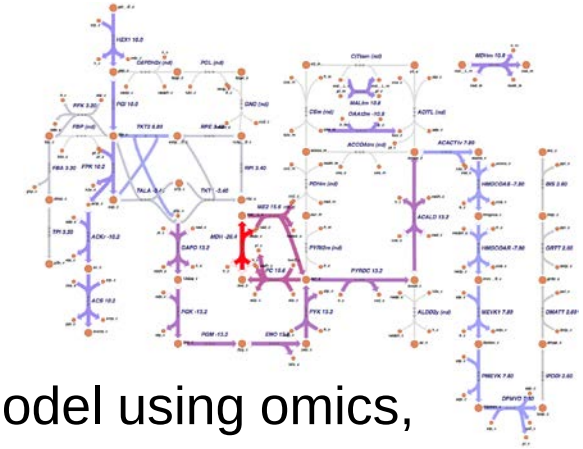




DBTL for Target 2: Fatty alcohols

- Baselining production of FOH
- Improving titers through optimization of metabolite pools



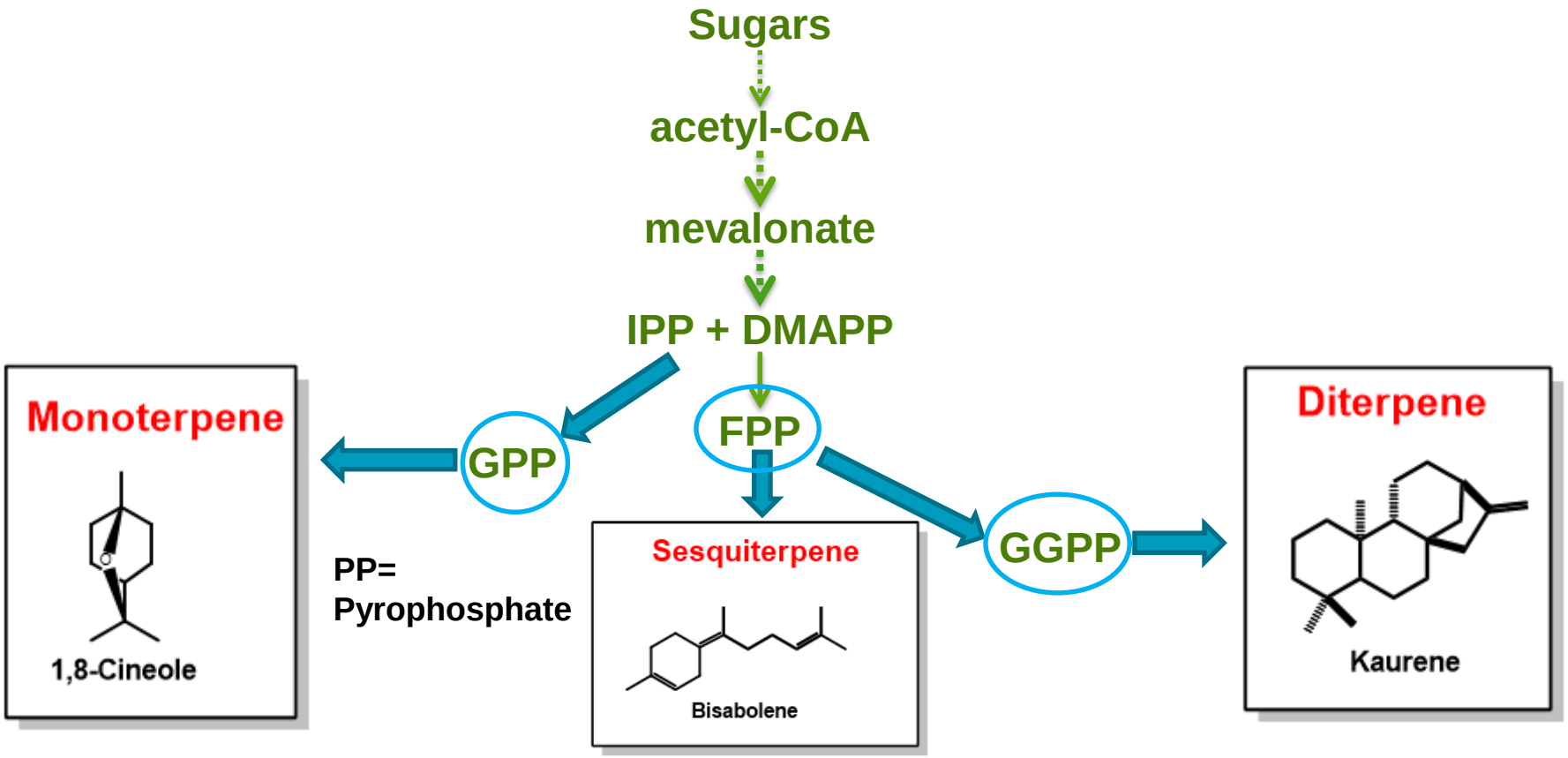


Metabolic model

- Built a tailored model using omics, TnSeq, and Biolog data
- Used model to contextualize Learn data

Design Target 1: Terpenes

- Demonstrate Terpene Synthase (TPS) Expression
- Optimize TPS Expression
- Balance PP precursor pools by modulating prenyltransferase expression



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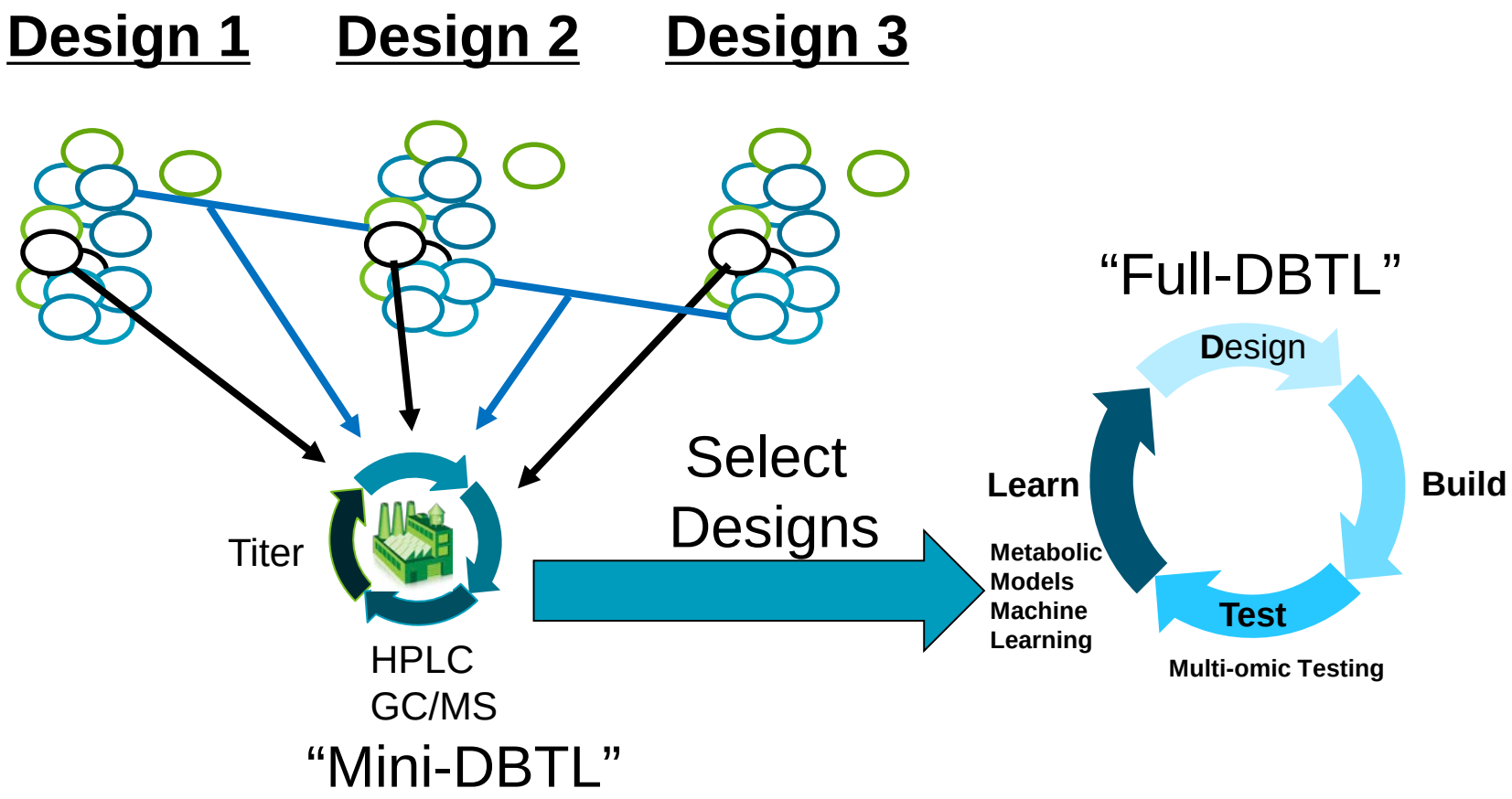
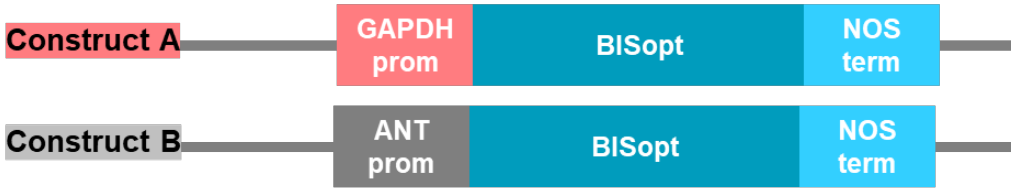
Basic Build Strategy

- Each Primary Design usually has a library of variants
- Rather than screen all of them, we use mini-DBTLs to hep prioritize most promising Design Strategies

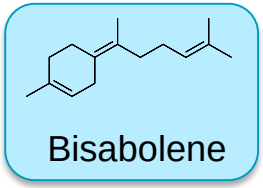


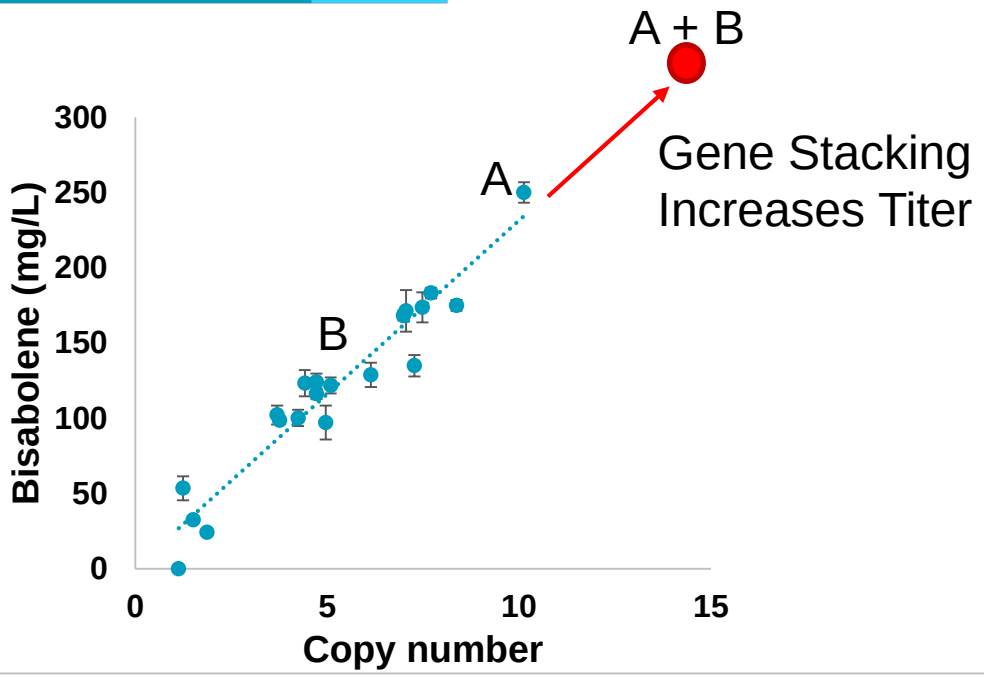
Mini-DBTL: TPS Expression Optimization

- Design strategies: promoters for TPS expression, stacking, solubility tags and PP fusions. Do mini-DBTL using Bisabolene
- Stacking works: this strategy was implemented with other TPS



Biofuel





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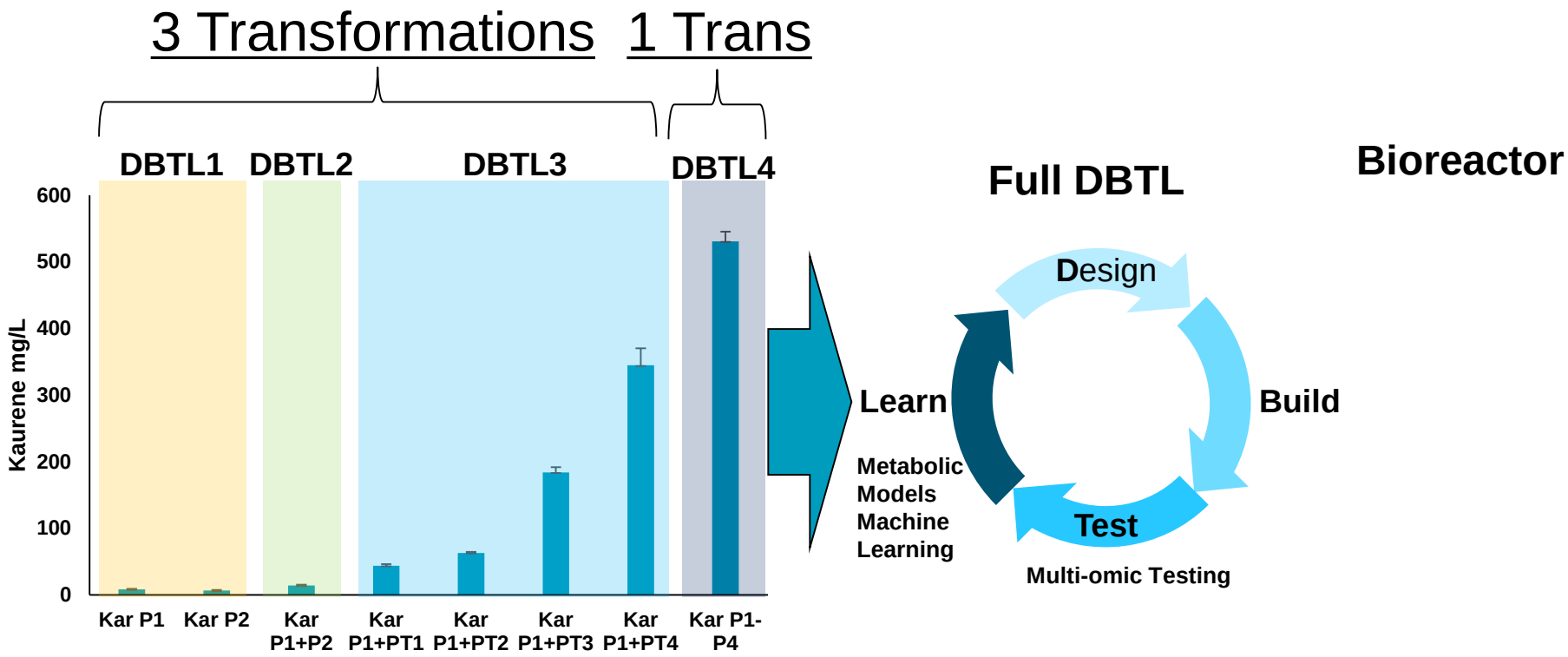
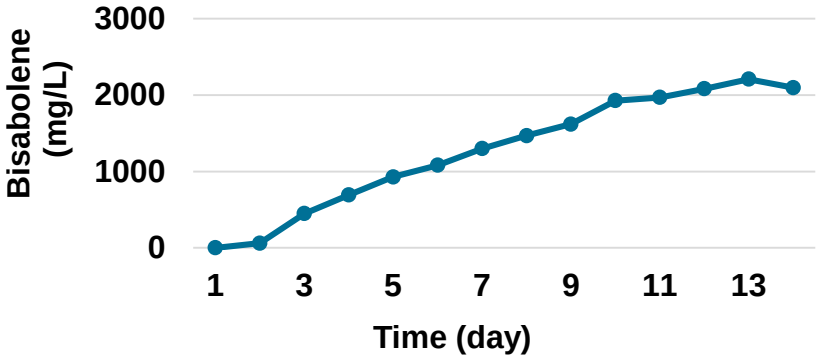
Build /Test: Kaurene mini-DBTLs

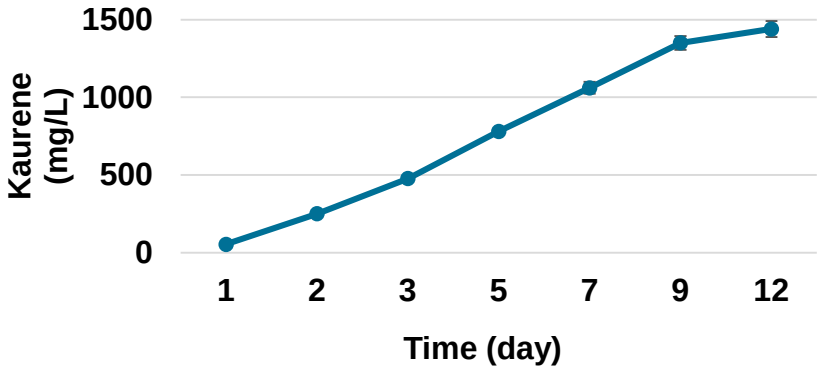
- Focus on stacking and GGPP synthase, four mini-DBTLs improved titers 100x
- Combined best Designs and redid 4th mini-DBTL in 1/3rd the time!!
- Build strategy will accelerate future terpene engineering efforts

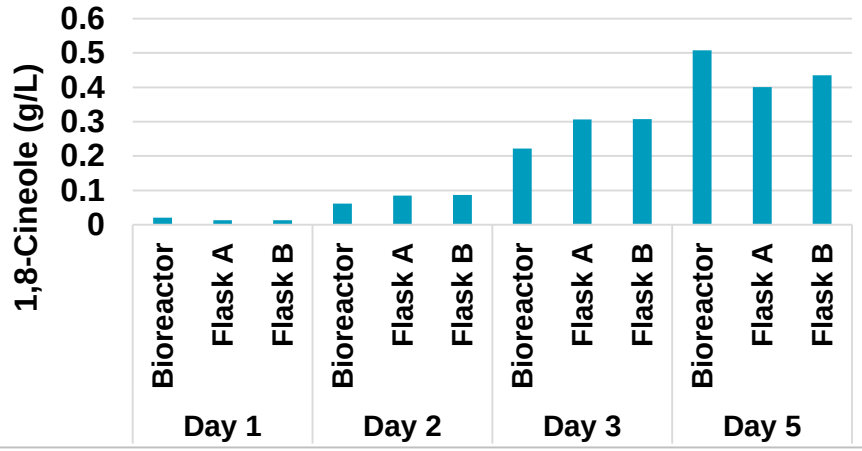


Scale-up: Bioreactor Cultivations

- Hit the Go/No-Go Decision, Q2 FY18 with >1g/L
- Bisabolene 2 g/L, Kaurene 1.4 g/L, cineole 0.5 g/L
- Lessons learned will speed up future bioreactor runs







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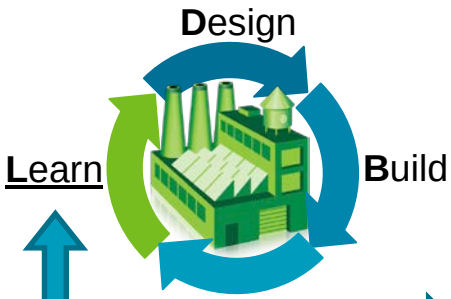
Test & Learn Workflow

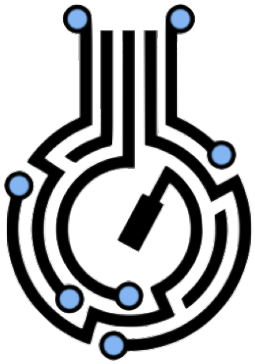


➢ **Bringing the DBTL together with the Experimental Data Depot**

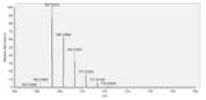
Multi-omic Experiments

EDD study

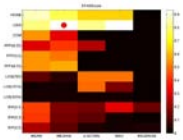
Test Samples



Test Data Generated

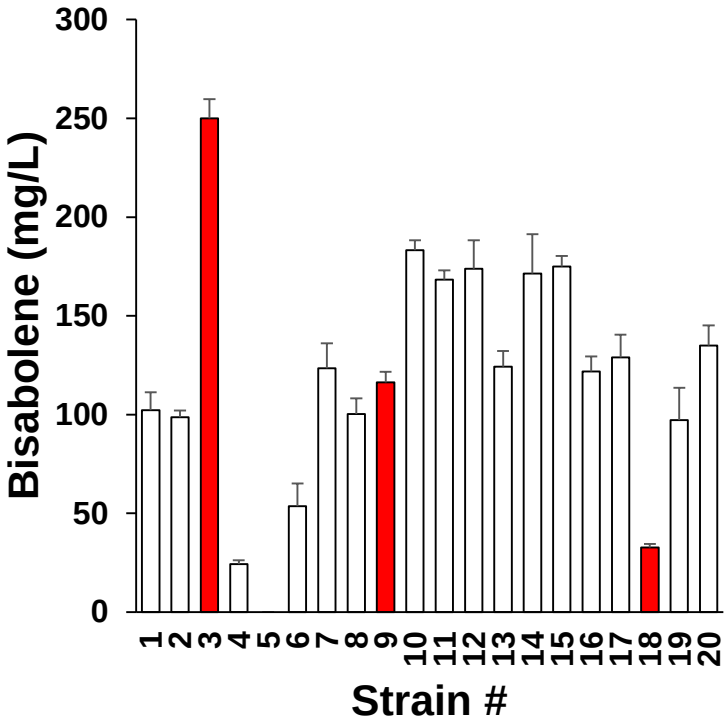


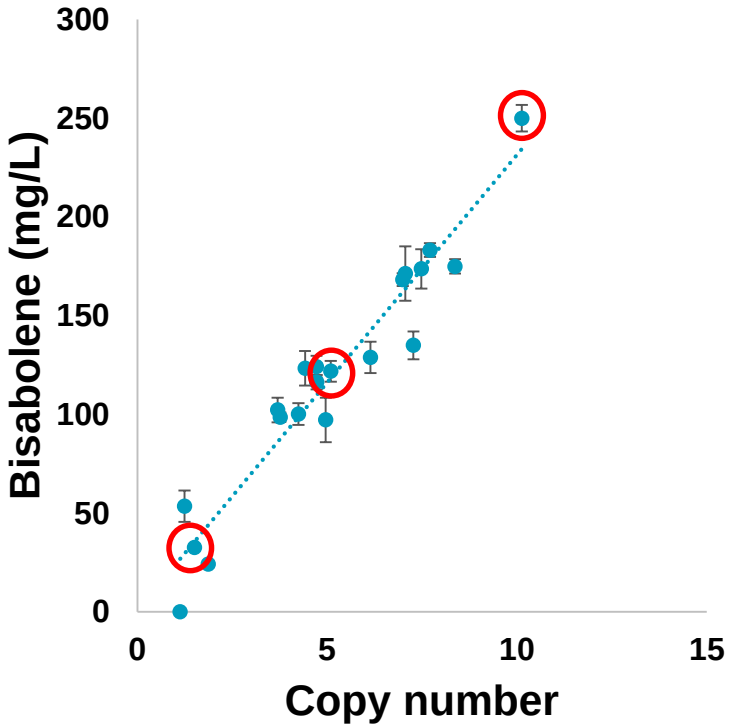
Test Data Processed



Full DBTL: Multi-omics Test

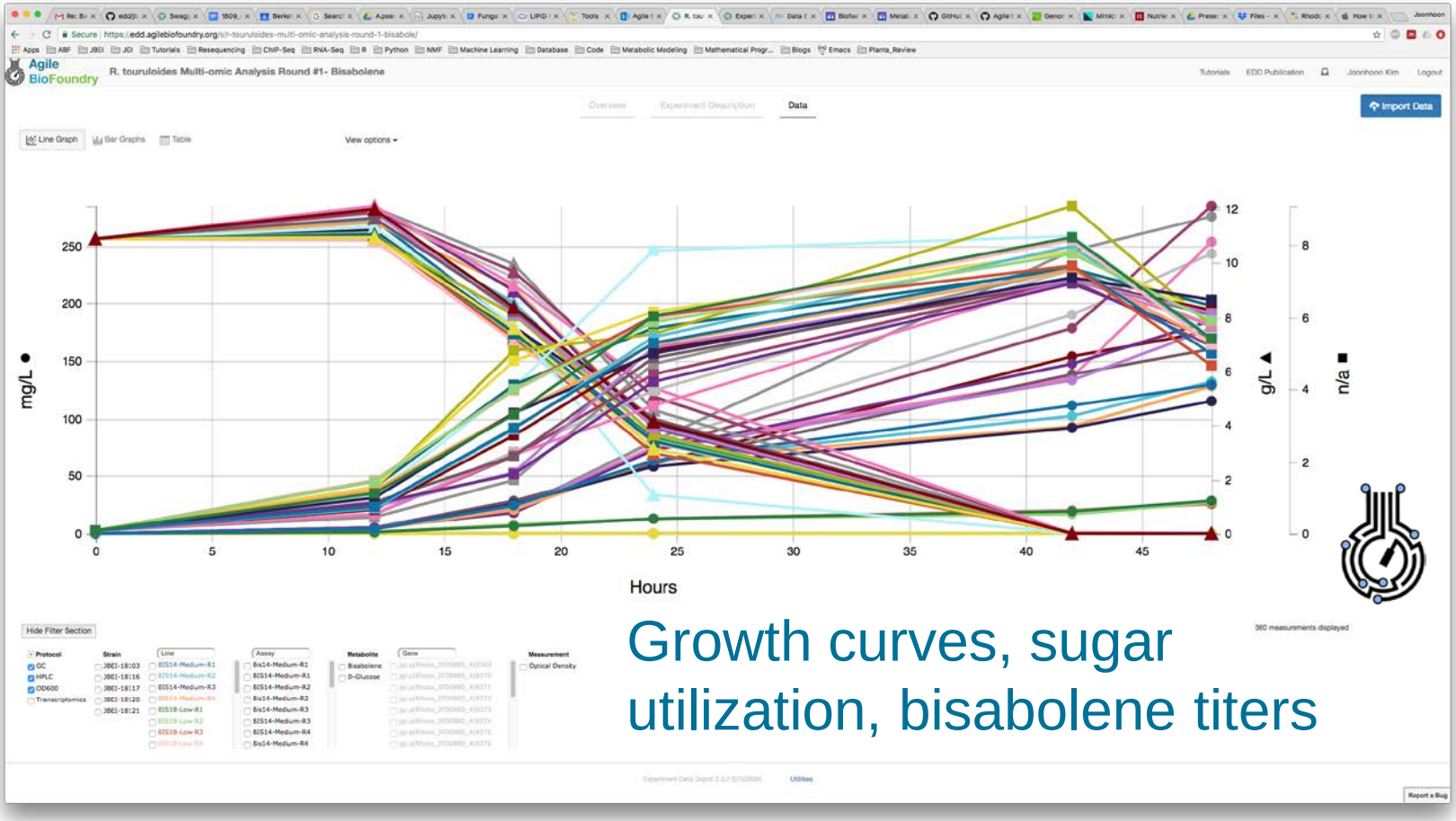
- What is the response to heterologous terpene production?
- Conduct 'omic comparison of bisabolene production strains
- Evaluate data in Learn, make predications for next DBTL cycle





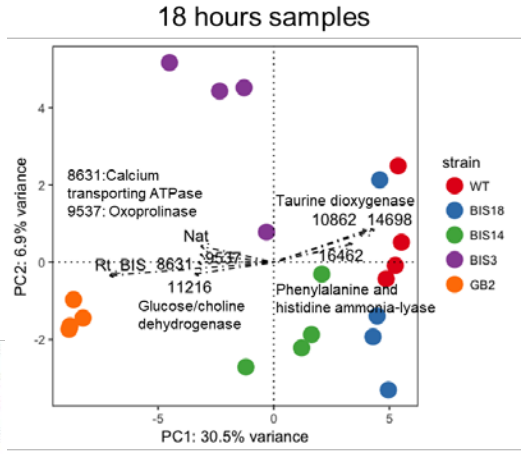
Test/Learn: Create an EDD study

- Create and EDD study
- Import experimental data for multi-omics analysis



Test: Multi-omics

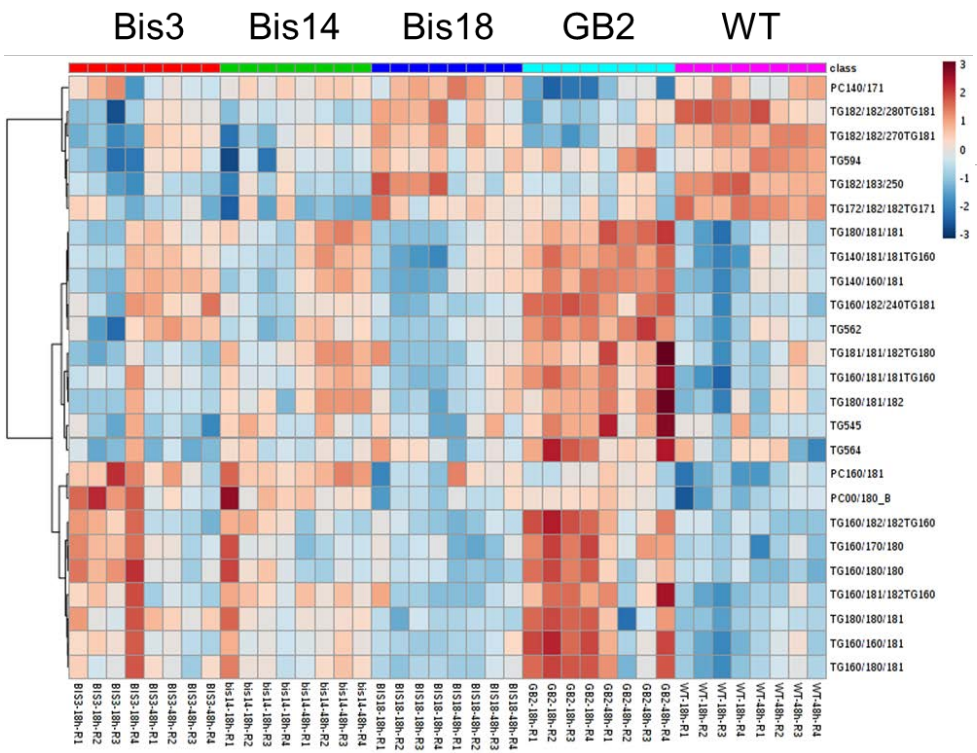
Proteomics



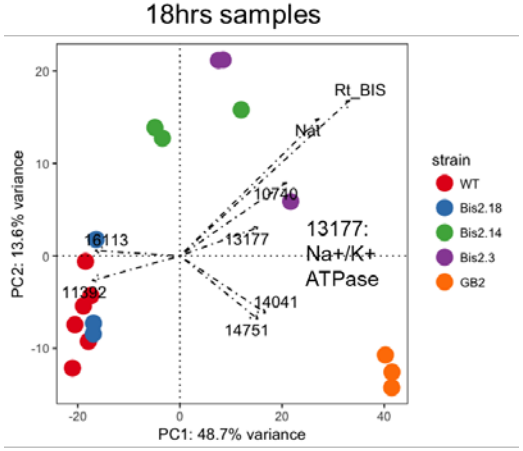
Bisabolene production

Metabolomics

Top 25 significant lipids



Transcriptomics



Bisabolene production

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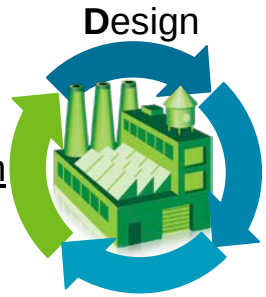
Test & Learn Workflow



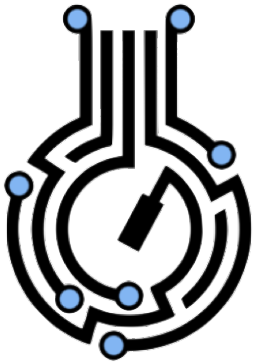
- **Bringing the DBTL together with the Experimental Data Depot**

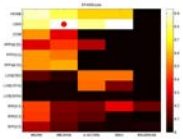
Multi-omic Experiments

EDD study

Test Samples

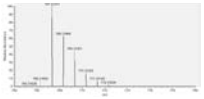
- **Export EDD study to Learn**





Test Data Processed

Test Data Generated



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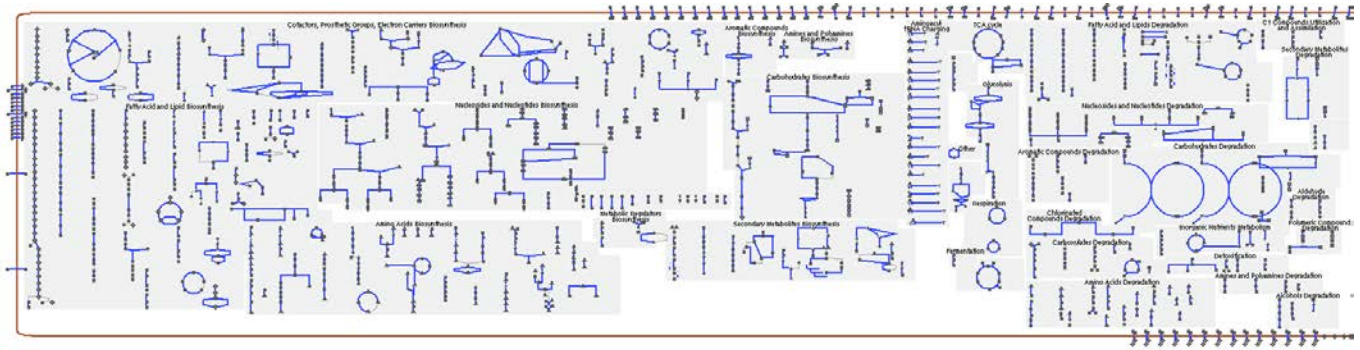
Learn: Building a Metabolic Model

➢ Expand knowledgebase: built a metabolic model of *R. toruloides*



BioCyc Database Collection

Pathway Tools

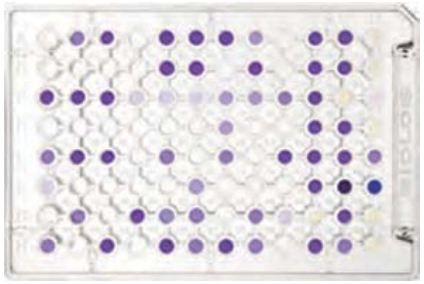
Assemble metabolic network pathways in pathway tools

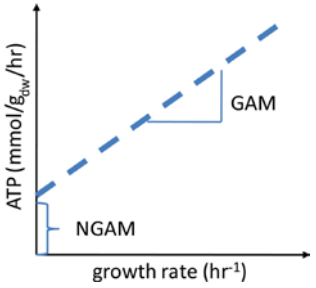
Metabolic model building using BiGG Models and openCOBRA

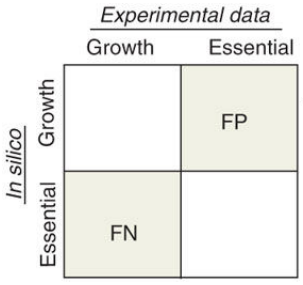
- High quality metabolic models with gene association
- Orthologous gene mapping from OrthoMCL

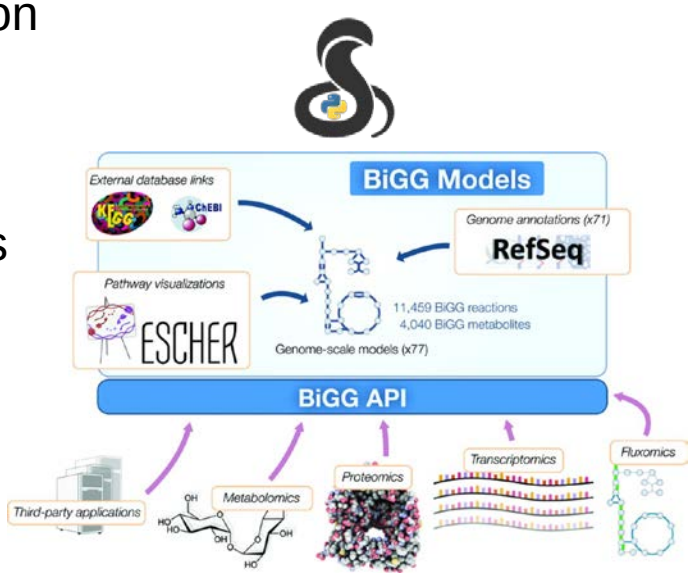
Experimental validation and refinement

- Biomass composition and ATP-maintenance
- Growth phenotyping and gene essentiality analysis









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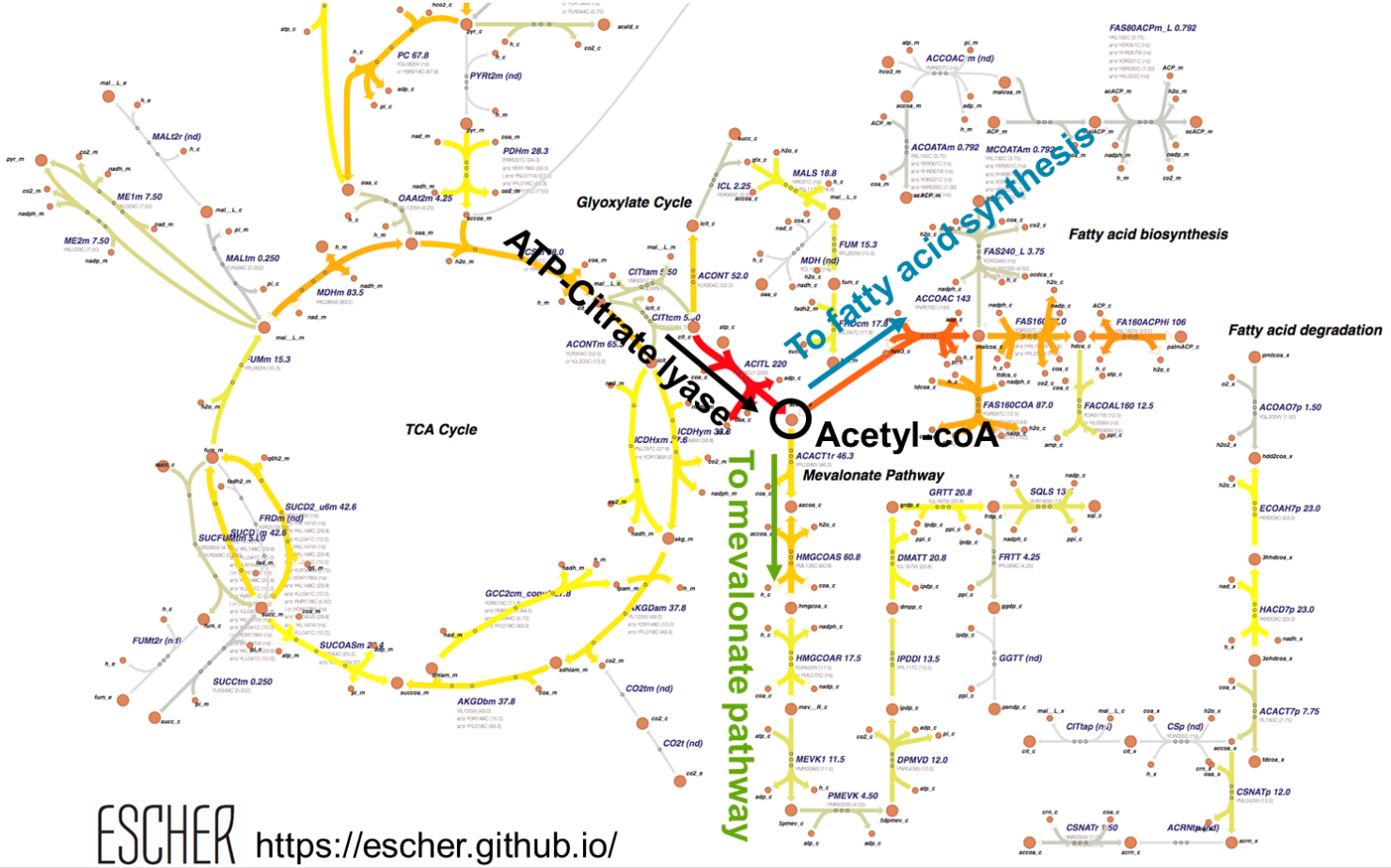
Learn: Test Data Overlay on Metabolic Model

- Overlay multi-omic data on metabolic model: wt vs bisabolene
- Assess global trends: both FA and MEV pathway upregulated



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Learn: How are Lipids Upregulated?

- Proteomics data detected a downregulated transcription factor of unknown function in *R. toruloides* in high bisabolene production strains
- Careful examination indicates a slight homology to ASG1, a negative regulator of lipid metabolism in *S. cerevisiae*
- Could this be driving the upregulation of lipid biosynthesis?
- Unintuitive prediction: overexpress this TF and shut down lipid production
- Will test in an upcoming DBTL cycle

Bisabolene Titer

Low → High

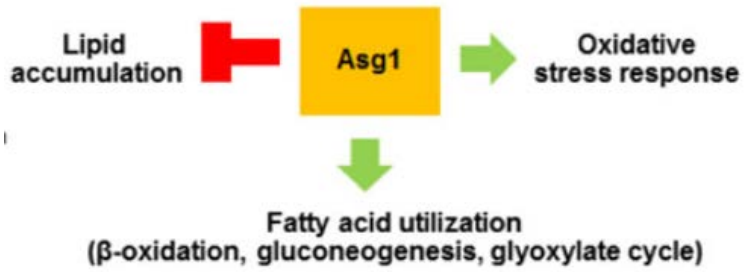
Proteomics Data

WT	Bis2.18	Bis2.14	Bis2.3	GB2
2.3	2.3	1.0	0.8	0.5

High → Low

Downregulated transcription factor

Does it function like ASG1?



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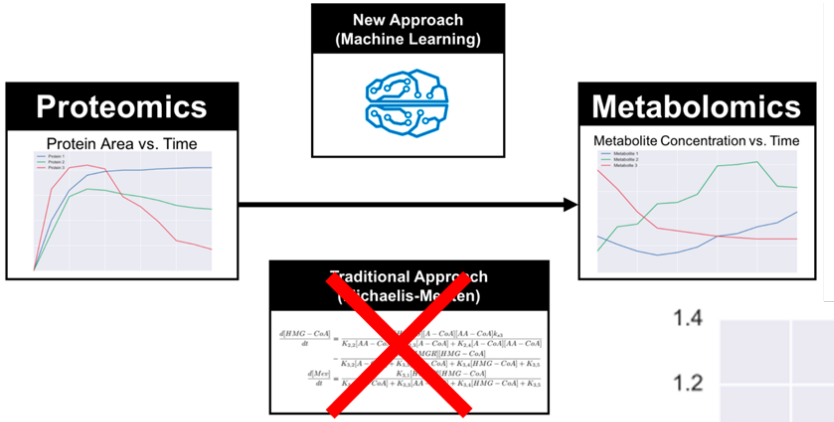
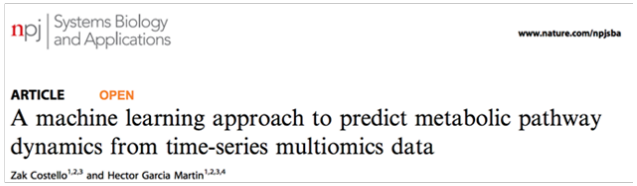
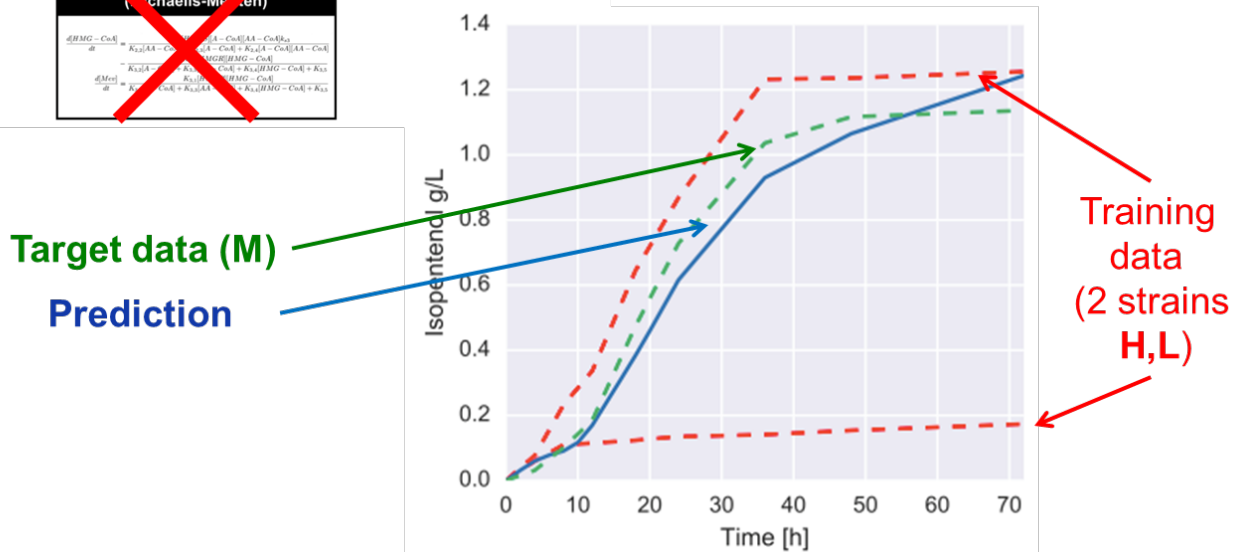
Learn: Machine Learning for Pathway Dynamics

- This kinetic learning method takes protein time series data and predicts metabolomic data
- It can be used to predict protein levels for optimal pathway flux







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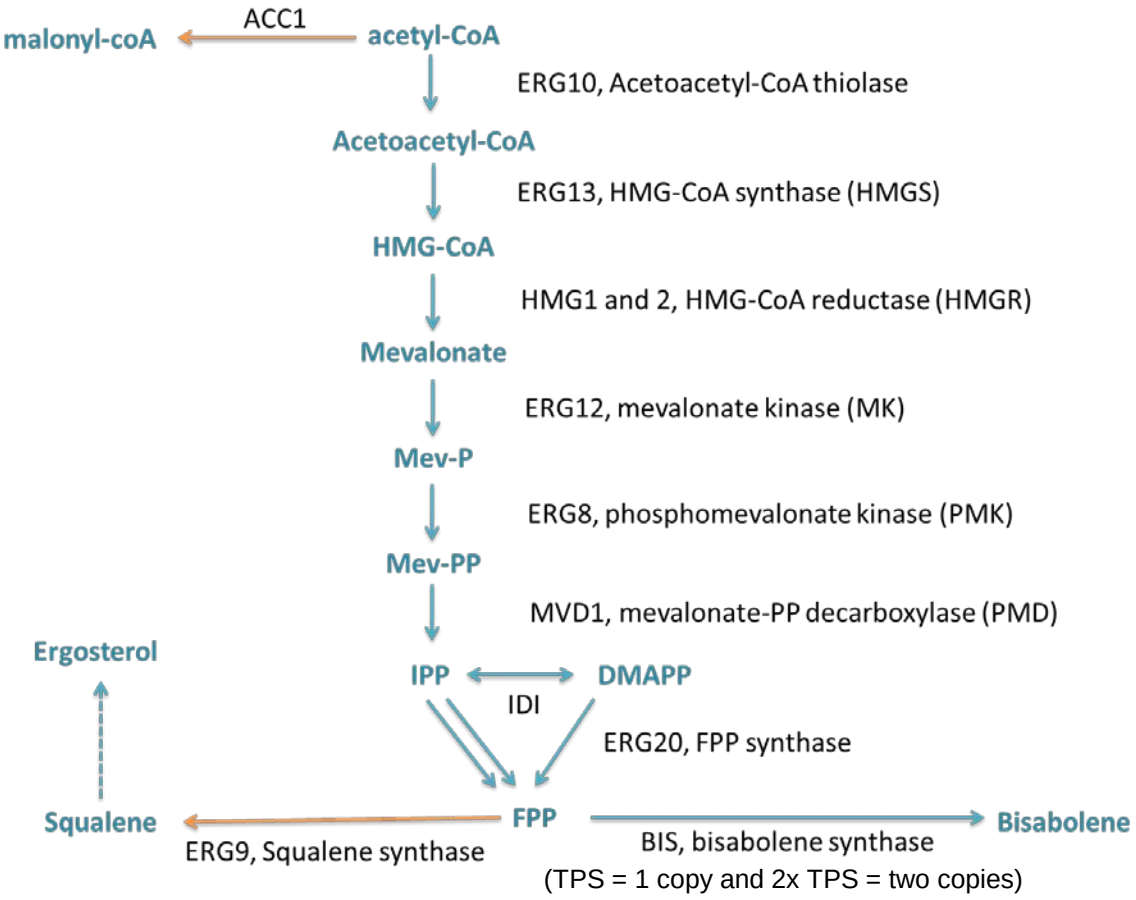
Kinetic Learn: MEV Pathway Variants

- **This kinetic learning method requires protein time series data from pathway variants**

Overexpressed MEV Pathway Enzymes:

Wild-type
TSP
2x TPS
2x TPS + HMGR
2x TPS + MK
2x TPS + PMK
2x TPS + PMD
2x TPS + ACC_{sup}
2x TPS + $ERG9_{sup}$



(TPS = 1 copy and 2x TPS = two copies)

Learn: Targets for Next DBTL Cycle

- Down regulate Fatty acid biosynthesis at earliest step: ACC1
- Downregulate sterol biosynthesis: ERG9
- Overexpress potential negative regulator of lipid biosynthesis
- Balance expression levels of MEV pathway genes
- Testing many of these in Cycle 2, which is in progress

Cycle 2: Designs for Testing Predictions

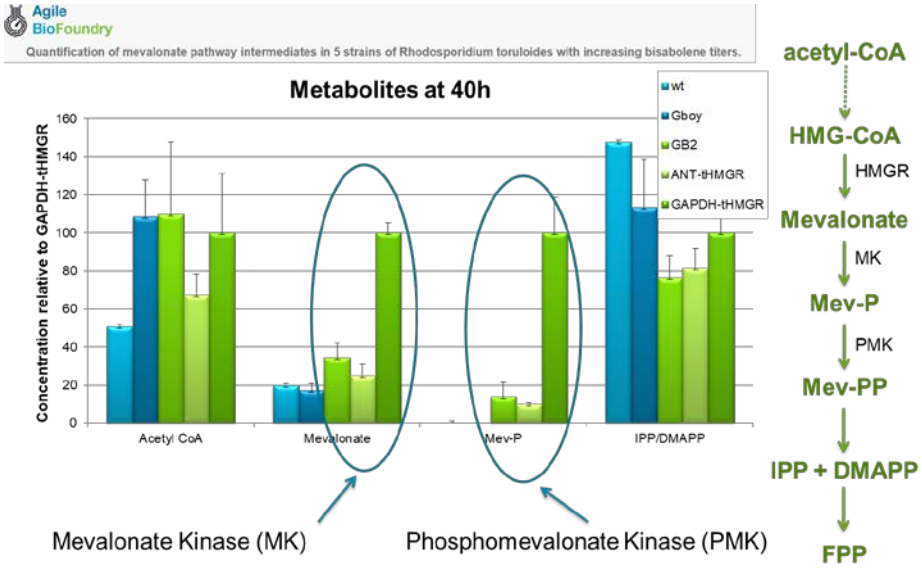
- Total of 98 designs entered through the ABF DIVA Design tool
- Have conducted six Mini-DBTL cycles
- Currently in progress, nearing completion
- Several Designs are showing higher TRY

Learnings on Design and DNA construction:

- *R. toruloides* DNA is challenging for synthesis
- Synthesis portion took longer than assembly
- Learning curve for new users was long
- Collaborated on a Beginners Guide to DIVA
- Worked with DIVA team to debug issues
- Expect future cycles to be considerably shorter

pGEN-292	MK_or_PMK
pGEN-292_BbvCI_KpnI	ANT-BpHMGR
pGEN-292_BbvCI_KpnI	ANT-SmHMGR
pGEN-292_BbvCI_KpnI	ANT-DaHMGR
pGEN-292_BbvCI_KpnI	ANT-MmMevK
pGEN-292_BbvCI_KpnI	ANT-McMevK
pGEN-292_BbvCI_KpnI	ANT-MpMevK
pGEN-292_BbvCI_KpnI	ANT-ScPMK
pGEN-292_BbvCI_KpnI	ANT-SpPMK
pGEN-292_BbvCI_KpnI	ANT-SsPMK
pGEN-292_BbvCI_KpnI	ANT-HsPMK
pGEN-292_PmeI_KpnI	SKP1-BpHMGR
pGEN-292_PmeI_KpnI	SKP1-SmHMGR
pGEN-292_PmeI_KpnI	SKP1-DaHMGR
pGEN-292_PmeI_KpnI	SKP1-MmMevK
pGEN-292_PmeI_KpnI	SKP1-McMevK
pGEN-292_PmeI_KpnI	SKP1-MpMevK
pGEN-292_PmeI_KpnI	SKP1-ScPMK
pGEN-292_PmeI_KpnI	SKP1-SpPMK
pGEN-292_PmeI_KpnI	SKP1-SsPMK
pGEN-292_PmeI_KpnI	SKP1-HsPMK
pGEN-292_PmeI_KpnI	DUF-BpHMGR
pGEN-292_PmeI_KpnI	DUF-SmHMGR
pGEN-292_PmeI_KpnI	DUF-DaHMGR
pGEN-292_PmeI_KpnI	DUF-MmMevK
pGEN-292_PmeI_KpnI	DUF-McMevK
pGEN-292_PmeI_KpnI	DUF-MpMevK
pGEN-292_PmeI_KpnI	DUF-ScPMK
pGEN-292_PmeI_KpnI	DUF_SpPMK
pGEN-292_PmeI_KpnI	DUF-SsPMK
pGEN-292_PmeI_KpnI	DUF-HsPMK

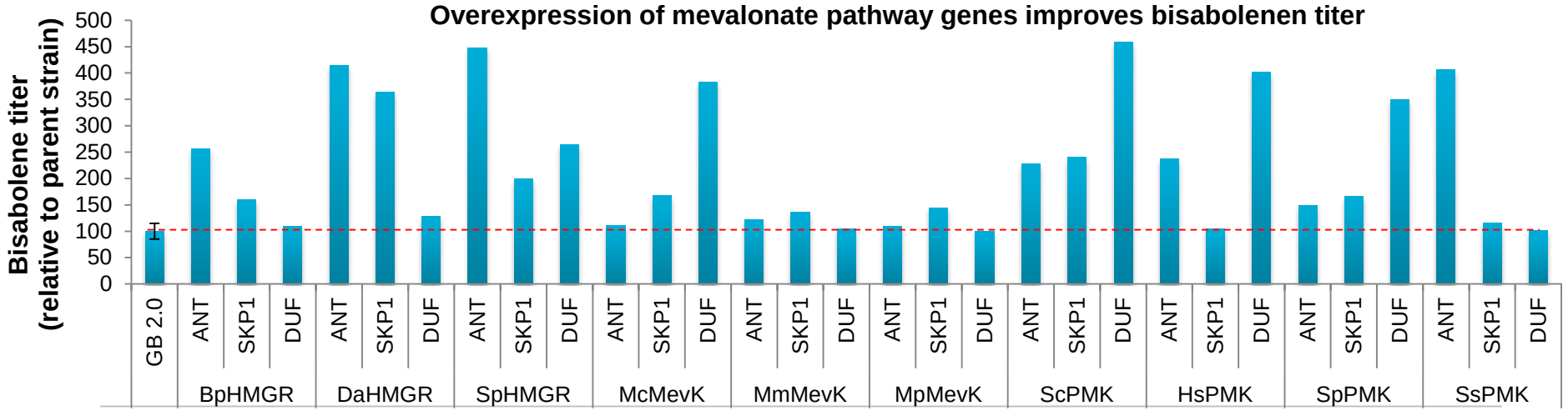
Mevalonate Pathway Engineering to Improve TRY



Candidate genes for overexpression selected based on multi-omic data

Paired with promoters of different strengths, informed by 'omics data from Cycle 1

	RTO4 proteinId	RTO4 transcriptId	RNA Log2 (FPKM+1) Mean	RNA Log2 (FPKM+1) Stdev	Protein spectral counts Mean	Protein spectral counts Stdev
ANT	12704	12832	11.1	0.9	64.4	7.4
SKP1	9048	9176	8.7	0.4	13.1	2.1
DUF	12844	12972	7.5	0.5	6.8	0.7



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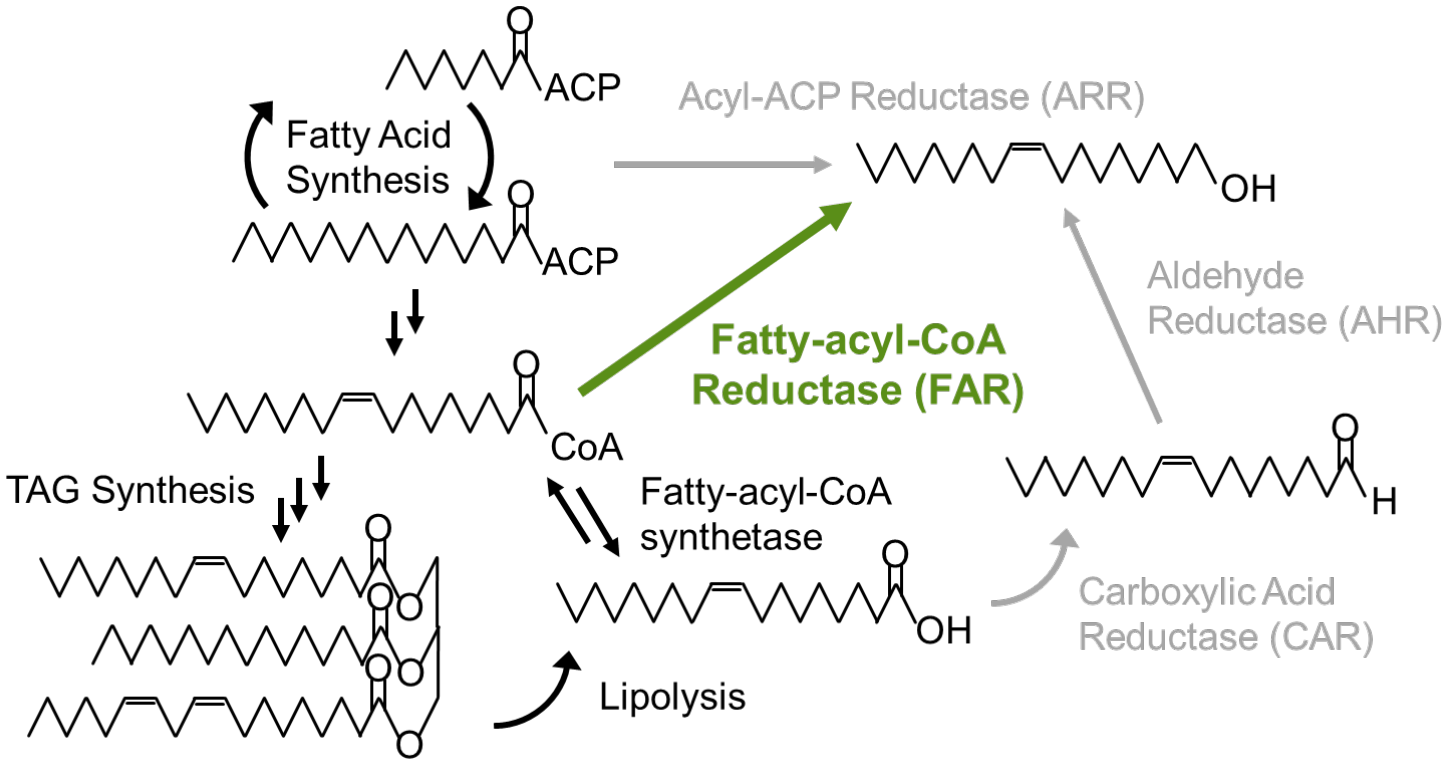
Target 2: Fatty Alcohols

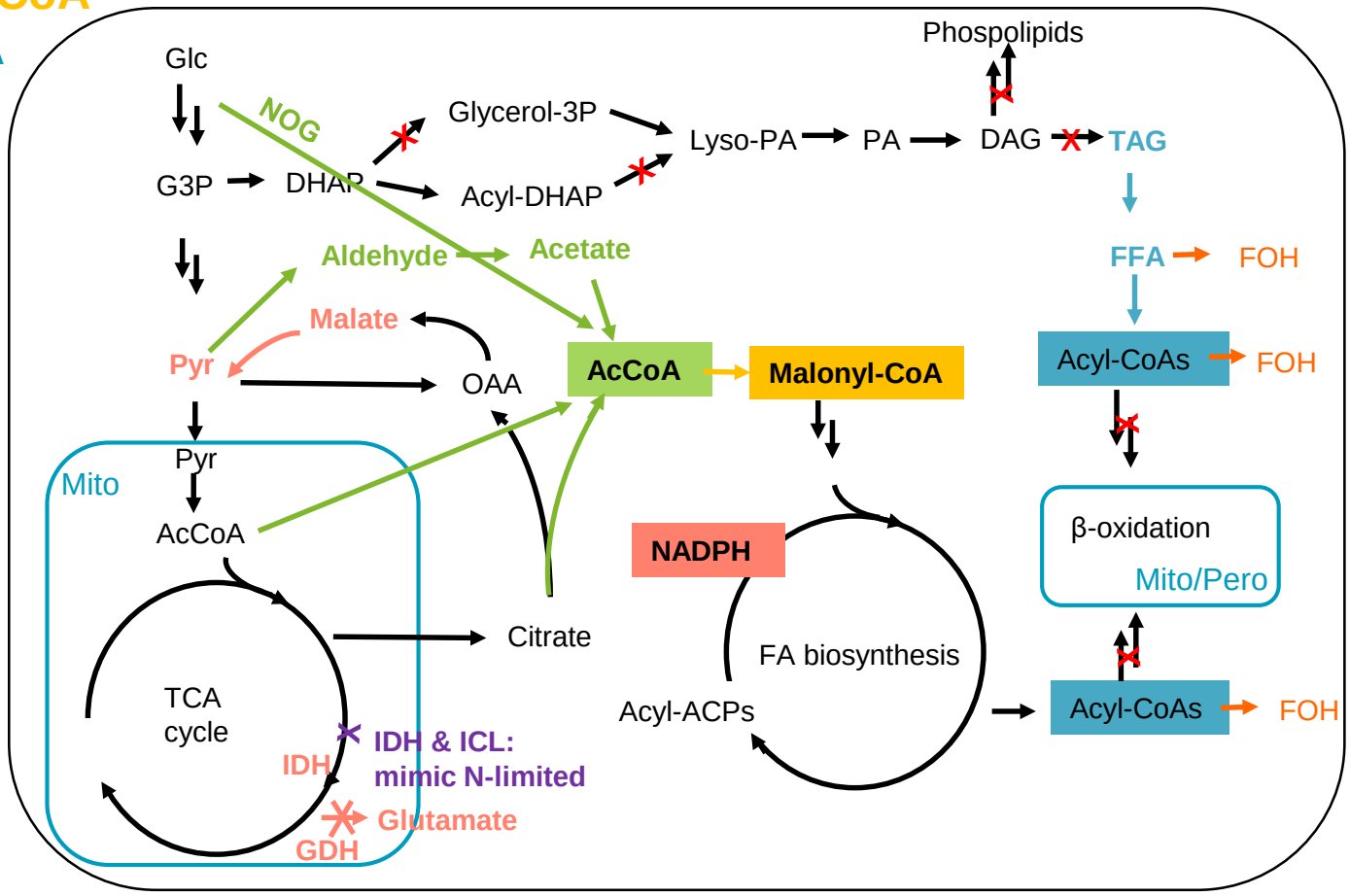
- **Cycle 1 Designs:**
  - **Demonstrate and optimize FOH production via FAR enzyme**
  - **Modify host targets to improve titers**



FOH Host Pathway Engineering

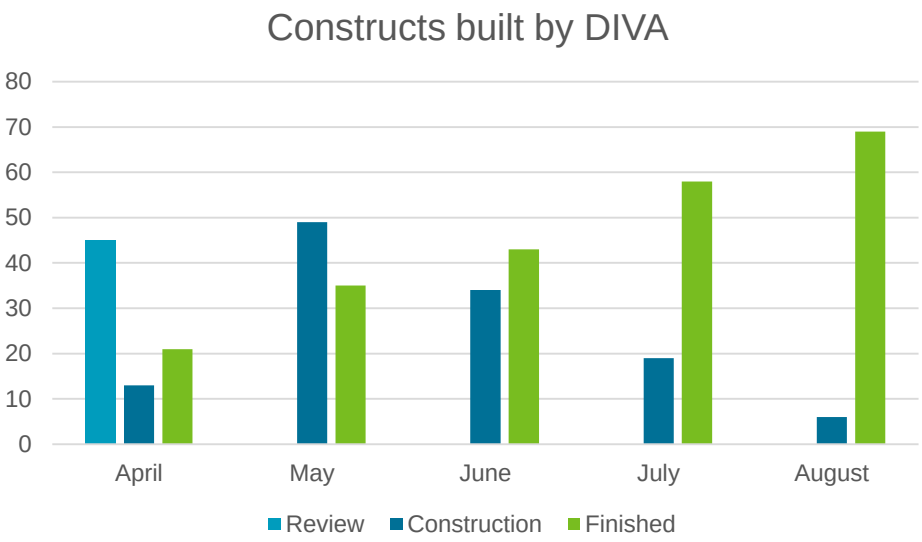
Host engineering to enhance the pool of:

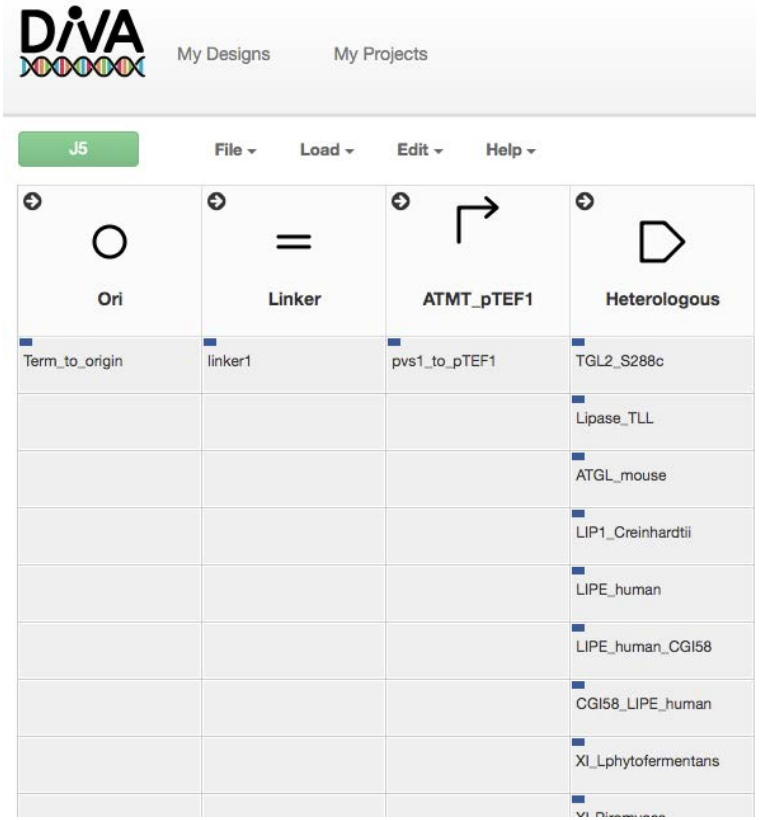
- acetyl-CoA
- malonyl-CoA
- acyl-CoA
- NADPH



ABF Design and Build Infrastructure

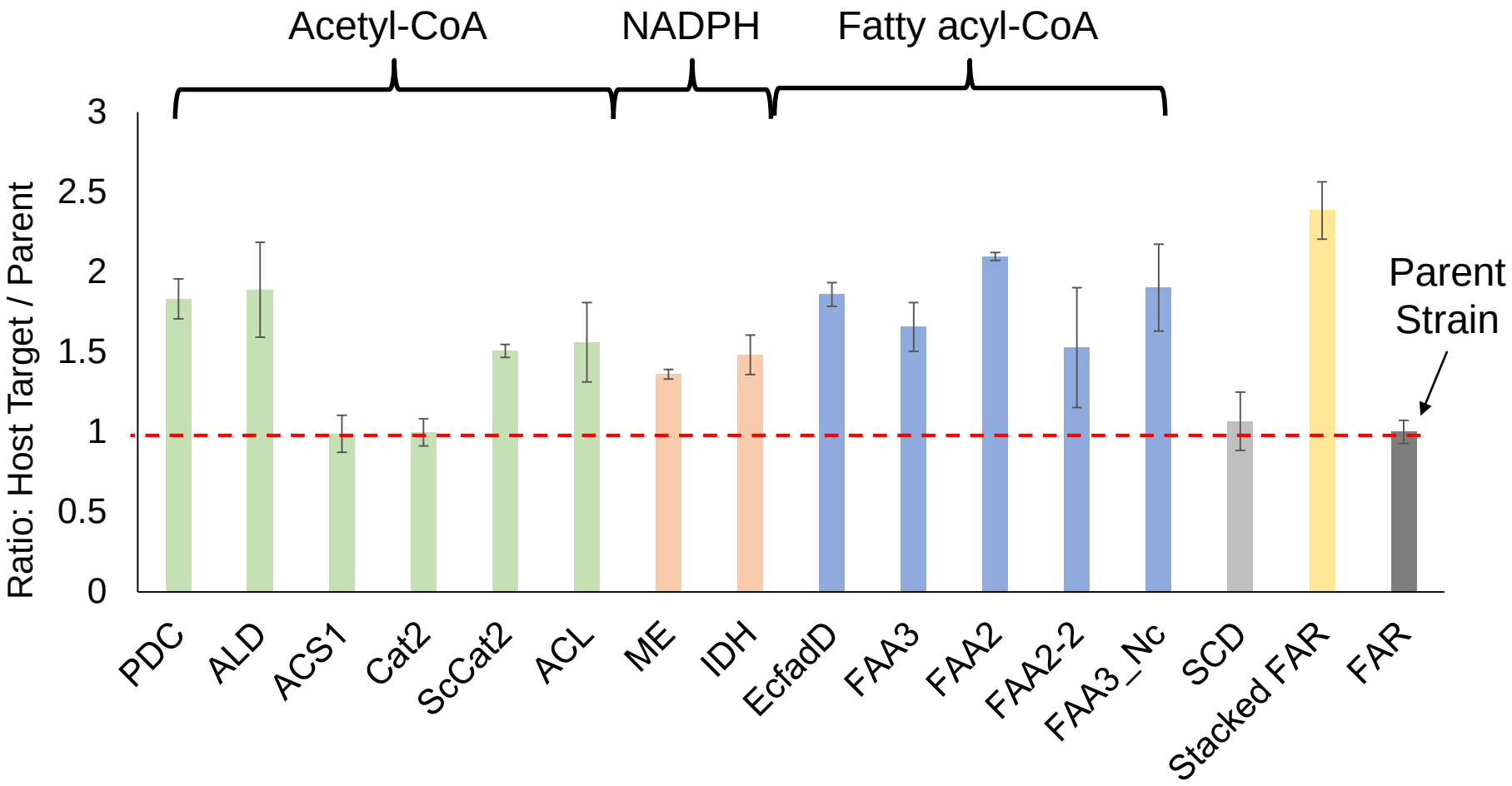
- **Use ABF DIVA for Design and Build the majority of FOH constructs**
  - **106 constructs built**
  - **Most screened**
  - **Some moved to Test/Learn**





FOH Host Pathway Engineering

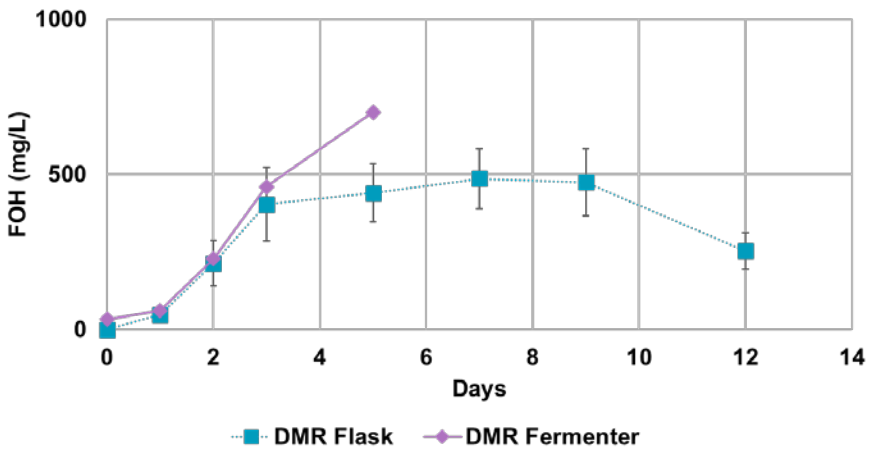
- **Overexpression of several host targets increases FOH titers**



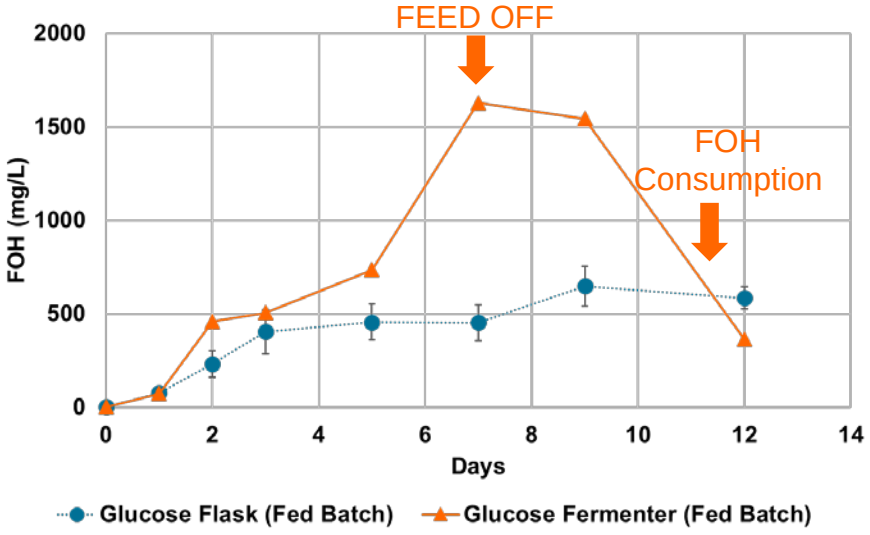
Scale-Up FOH Production in Bioreactors

- Bioreactor mirrored media response trend in flask, but higher titer (~700 mg/L in DMR-EH and 1.5 g/L in defined medium)
- Longer cultivations will likely increase titers
- Detected possible FOH catabolism, more targets for Cycle 2
- Met our FY18 Annual SMART milestone of >100mg/L in DMR

DMR-EH Media



Glucose Media



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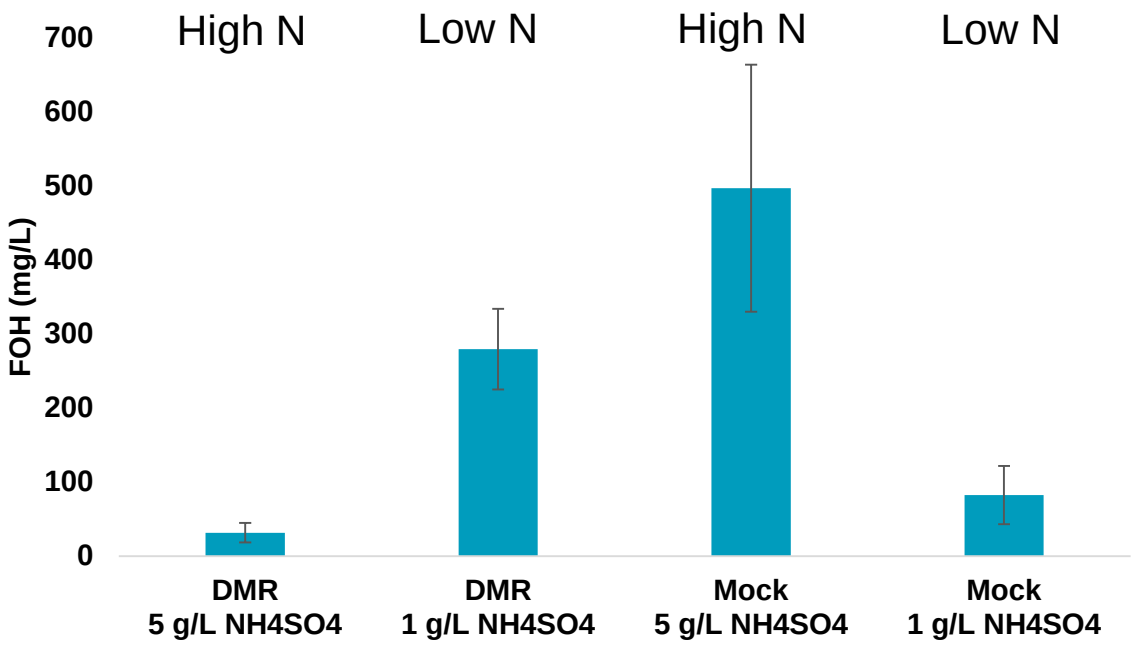
Test: Media Optimization for FOH Production

- Optimal FOH production had opposite N requirements
- Lower FOH production observed in DMR
- Using machine learning to optimize medium, maximize FOH TRY



DMR medium

- 75% DMR-EH (~110 g/L sugars)
- 0.5 – 5 g/L NH_4SO_4, 100 mM KPO_4, 100 µM $FeSO_4$
- 0.1% Tergitol

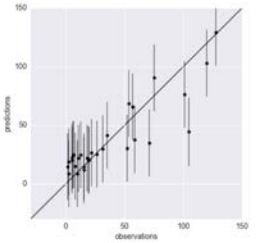
Mock DMR medium

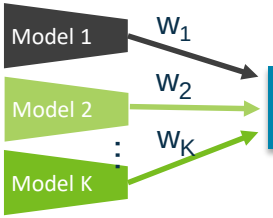
- 75:30:4 g/L Glucose/Xylose/Arabinose
- 0.5 – 5 g/L NH_4SO_4, 100 mM KPO_4, 100 µM $FeSO_4$
- 0.1% Tergitol
- Yeast Nitrogen Base
- Complete Supplement Mix

Learn: Automated Recommendation Tool (ART)

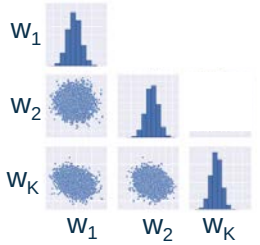
- ART uses machine learning to analyze variant data sets and make predictions for optimal configurations
- Flexible, can be used to make pathway recommendations, optimize media, etc.

Machine learning

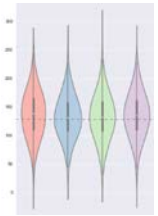




Bayesian ensemble modeling



Global optimization through Parallel Tempering



Probabilistic characterization of predictions

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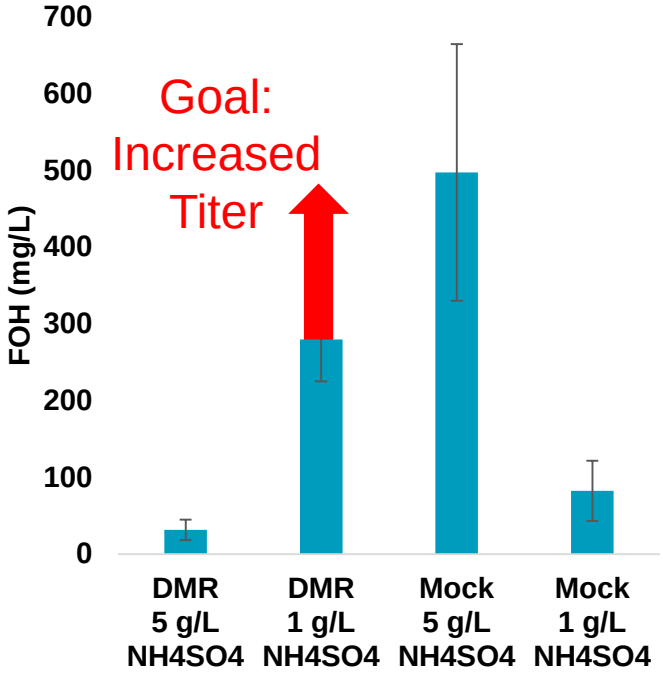
Learn: ART for FOH Media Optimization

- Use ART to help optimize FOH titers in DMR-EH
- Preliminary data looks promising
- Currently testing initial media predictions

Use biolector or Ambr 250 to test many media additions to DMR-EH

Use ART to predict optimal medium for FOH production in DMR-EH



Learn: Artificial Neural Network (ANN)

➢ **Use systems-level multi-component modeling of microbial response to DMR hydrolysate to optimize FOH TRY**

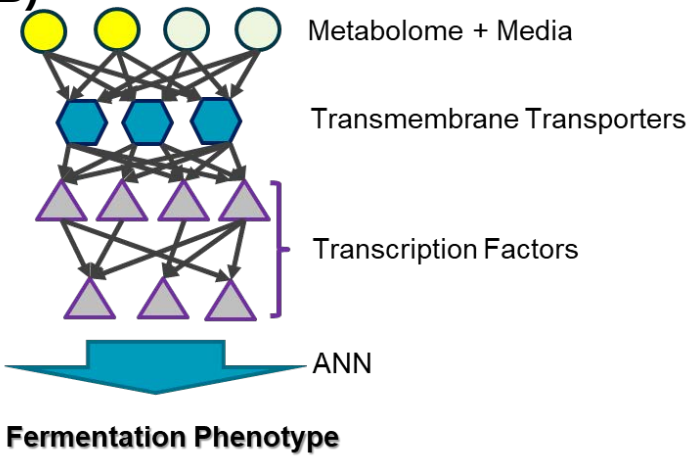
- **Observation:** multi-omic data reveals media composition causes big changes in *R. toruloides* gene expression and metabolism (A).
- **Learn Goal**: Identify transporter/sensors and gene regulators that lead to observed differences in fermentation phenotypes in DMR-EH vs defined medium
- **Learn Approach:** A multi-omics, multi-scale model is proposed (B).
  - Use media conditions and expressed array of sensors/transporters, predict patterns of TF expression
  - Given patterns of TF expression, predict fermentation phenotype using ANN approach
- **Outcome:** Use model to predict specific modifications of transporters and/or TFs to increase FOH TRY in DMR-EH

(A) Percent Features Significantly Differential by Experimental Condition

	Strain	Media	Interact
Metabolome	24	73	16
Proteome	22	52	11
Transcriptome	67	89	65

	DMR	Nitrogen	Interact
Metabolome	79	52	41
Proteome	72	40	25
Transcriptome	73	68	61

(B)



Outline of Target 1 and 2 DBTL

- **Tracking cycle time will help monitor progress and identify specific areas to focus on DBTL improvements**

Target 1: Terpenes

Cycle Time (days)	Design	Build	Test	Learn	Outcomes
Cycle 1	71	99	181	130	Demonstrated g/L production of several terpenes
Cycle 2	16	134	Ongoing		Enhance flux through MEV pathway

Target 2: FOH

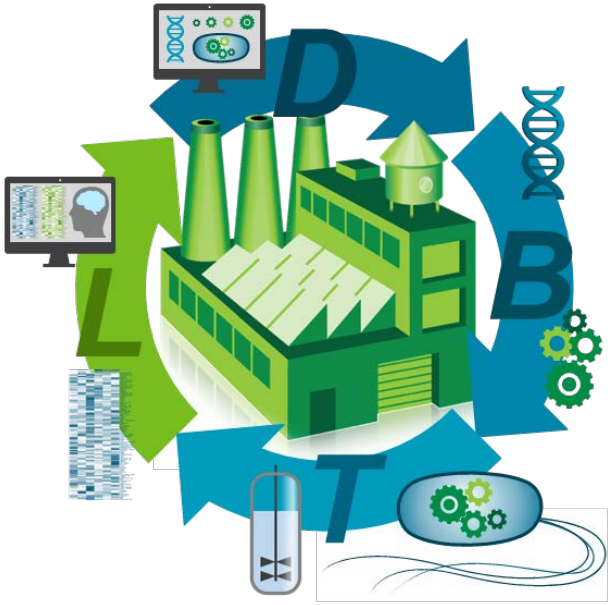
Cycle Time (days)	Design	Build	Test	Learn	Outcomes
Cycle 1	45	132	125	62	PLANNED
Cycle 2	31	73	Ongoing		ACTUAL: Demonstrated g/L production of FOHs

4- Relevance

Relevance

Goal: Demonstrate the ABF concept towards improved strain performance by employing targets in a robust oleaginous and carotenogenic host, *R. toruloides*

- Target 1: Terpenes- bisabolene, cineole, kaurene
- Target 2: C16-18 fatty alcohols
- Can be used as performance-advantaged bioproducts or direct replacements



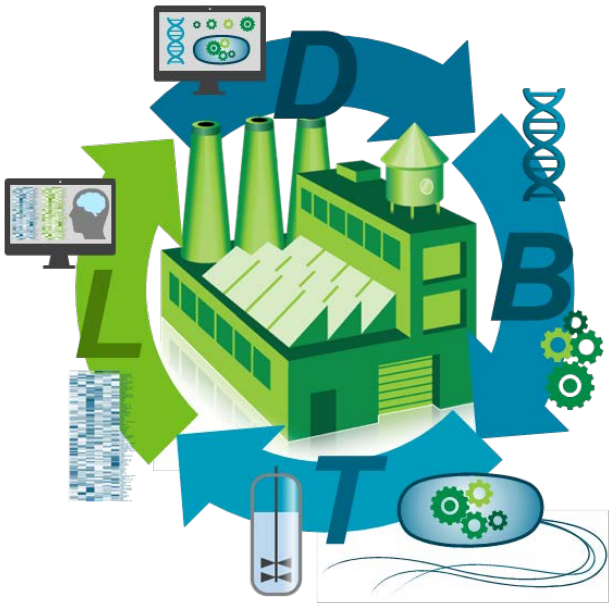
Why is this project important? What is the relevance to BETO/bioenergy goals?

- Improved strain performance enabled by DBTL to reduce time-to-scale up
- 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
- *R. toruloides* is a promising chassis for bioproduction, especially terpenes and lipid-based products



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

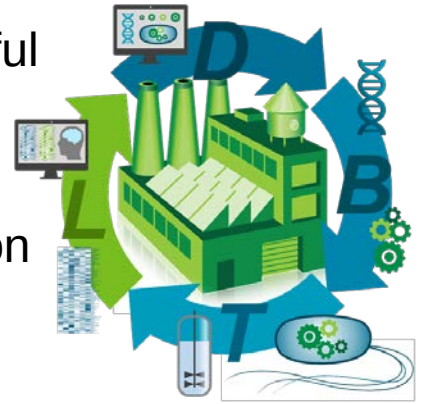
5- Future Work

Future Work

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

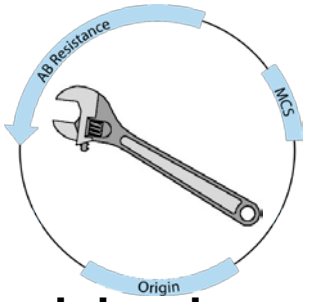
DBTL for Target 1: Terpenes

- Assessing ability of several non-intuitive Learn tools to make useful predictions for next DBTL
- Improve terpene titer through MEV pathway optimization
- Disrupt fatty acid metabolism to improve rate of terpene production

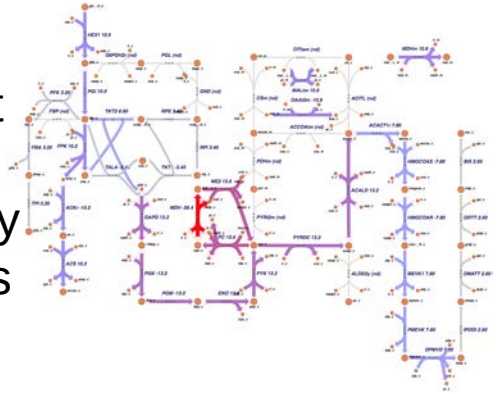


DBTL for Target 2: Fatty Alcohols

- Stack beneficial host modifications to improve FOH TRY
- Use machine learning tool ART to optimize medium and cultivation conditions to maximize TRY
- Scale up production to >100L with ART output



Use **metabolic model** to conduct flux balance analysis to identify host modifications to improve yield



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

- Expand parts list
- Optimize targeted engineering
- Recyclable markers

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Future Work Beyond FY19

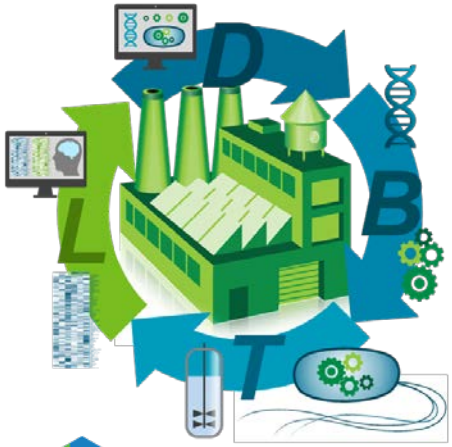
Standardization of DBTL workflow across T/H pairs

- 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



fcic
FEEDSTOCK-CONVERSION INTERFACE CONSORTIUM

Co-Optimization of Fuels & Engines

ChemCatBio

BIOPROCESSING SEPARATIONS CONSORTIUM

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Summary

Overview

– To demonstrate ABF concept via *R. tourloides* with two novel target molecules from versatile “nodes”: terpenes and fatty alcohols

Approach

– Employ DBTL cycle for increasing target titer

– Expand knowledgebase by building a metabolic model

Technical accomplishments

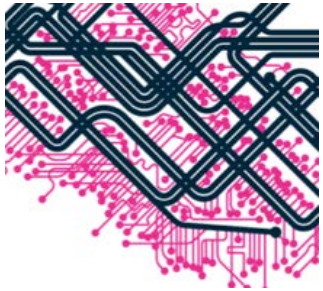
– Used DBTL to increase titers on DMR-EH, in some cased 100x

– Employed Learn to make non-intuitive predictions

Relevance

– DBTL demonstrations in non-model yeast

– Nodes form each target pathway can be used to make biofuels and performance-advantaged co-products to meet DOE cost targets



Future work

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

– Develop host tools, expand metabolic capacity, new targets, automation

Acknowledgements

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Mark Butcher

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Jan-Philip Prahl
Mona Mirsiaghi
Carolina Barcelos
Isaac Wolf
Ning Sun
Deepti Tanjore
Todd Pray
Jeffrey M. Skerker
Edward Baidoo
Veronica Benites
Nathan Hillson
Jennifer Chiniquy
Nurgul Kaplan
Garima Goyal
Hector Plahar

Gregg Beckham
Davinia Salvachua
Phil Liable
Peter Larson
Masakazu Ito
Adam P. Arkin
Blake A. Simmons

Additional Slides

Responses to Previous Reviewers' Comments

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

Responses to Previous Reviewers' Comments (cont.)

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

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

Responses to Previous Reviewers' Comments (cont.)

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

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

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

Publications, Patents, Presentations, Awards, and Commercialization

Publications

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

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

Publications (cont.)

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

Presentations

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

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

Presentations (cont.)

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

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

Presentations (cont.)

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

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

Presentations (cont.)

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

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

Presentations (cont.)

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

Posters

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

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

Posters (cont.)

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

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

Posters (cont.)

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

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

Posters (cont.)

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