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Industry Engagement & Outreach

Philip Laible, Christopher Johnson, Amanda Barry, and Emily Scott

IEO Team, DOE Agile BioFoundry

BETO Peer Review 2021 Conversion Technologies March 2021 Virtual Platform





1 - Management

1 – Project Overview

History: Task initiated at the inception of the Agile BioFoundry

- Efforts delocalized in early years of the Foundry
- Activities refocused and expanded with increased budget in rescoping exercise

Context: To fulfill Agile BioFoundry's mission, painpoints of industry need to be known and ABF efforts need to be visible

- Tremendous opportunity to learn how to increase success rate of relatively infant biomanufacturing industry
- Foundry succeeds only as industry is engaged and adopts resulting technologies

Project goals: Contribute significantly to the synthetic biology revolution

- Generate reports on industry needs (via interviews and surveys)
- Provide feedback from industry stakeholders to inform ABF R&D
- Organize yearly ABF Industry Days
- Facilitate transfer of ABF tools and technology to industry
- Advertise and educate potential partners about ABF







2 - Approach

2 – IEO Approach (management)

Outreach Leads: Amada Barry and Emily Scott Manage the ABF public profile and dissemination of engagement information to stakeholders.

Interactions

Lead: Philip Laible Coordinate communitybuilding activities and facilitate involvement of the IAB.

Assessment

Lead: Christopher Johnson Understand the needs of the biomanufacturing industry by interviewing and surveying its members.

> Report to ABF management and BETO

Team coordination and ABF integration

- Collaborative approach with leads focusing on strategic areas
- Biweekly internal calls
- Monthly calls with ABF management and BETO
- Coordination of outreach materials with Foundry members
- Involvement of Task leads in Industry Days & Industry Advisory Board (IAB) interactions
- Submission of annual interview reports to ABF and BETO



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2 – IEO Approach (technical)

Outreach

- Fact Sheet: Active distribution
- Website: Main source of visibility to industry
- IP FAQ sheet: Facilitates industrial interactions
- Social media: Presence expanding

Interactions

- IAB Meetings: Quarterly
- Conferences: As many as relevant and possible
- Industry Day: Annually





SIMB Annual Meeting

Assessment

- Energy I-Corps Approach
- Interviews: ~25 yearly
- Surveys: Effort expanding

Guiding IEO metrics:

- Numbers of public interactions
 - Twitter
 - Website
 - LinkedIn
- · Numbers of industry interactions
 - Interviews / Surveys
 - IAB meetings
- Timely responses to
 - ABF management
 - BETO
 - IAB feedback



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3 - Impact

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 to productionize synthetic biology.

Outcomes: Development and deployment of technologies enabling commercially relevant biomanufacturing of a wide range of bioproducts by both new and established industrial hosts.

Relevance: \$20M/year public infrastructure investment that increases U.S. industrial competitiveness and enables opportunities for private sector growth and jobs.

Risks: Past learnings do not always transfer well across target molecules and microbial hosts. Experiment data sets are sometimes of insufficient quality/quantity/consistency to learn from.









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Industry Engagement and Outreach (IEO) Goal Statement

Goals

- Identify and help remove barriers to industry adoption of biomanufacturing technologies
- Communicate how the ABF can address industry needs
- Maintain metrics for determining impact of ABF technologies
- Increase the visibility of the ABF

Outcomes

- Interactions between industry and the ABF will be established, organized, and facilitated
- Feedback from the industry stakeholder community to the ABF and BETO will support decision-making and project-planning activities

Relevance

 IEO will enable the ABF to serve the needs of, and be responsive to, the industrial biotech industry

Risks

- Feedback may not be representative of true / broadly held opinions
- Methods of disseminating information can quickly become obsolete

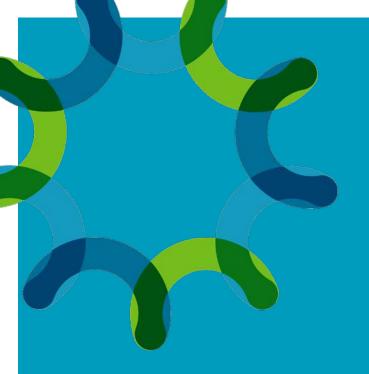












4 - Progress and Outcomes

4 – Progress and Outcomes

Potential Challenges

- Dependent upon interactions with biotech industry
 - Mitigation: Over-request input or interactions

(e.g., for 20 useful interviews, request 100; interview the 25 that respond).

- Need clear, effective messaging of ABF value proposition
- Difficult to convey pre-competitive R&D message
 - Engage in efforts that the industry could not pursue on its own
 - Not working in competitive space

Critical Success Factors

• Rapid identification of relevant industry communities and members

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- Balance needs of start-ups with those of large, established companies
- Quorums at IAB meetings
- Attendance at Industry Days and virtual events
- Ability to attract visitors to website









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4 – Progress and Outcomes

Assessment: One-on-One Interviews

- Interviews are conducted each year
 - Numbers of interviews each year vary by need and approach
 - Diverse industrial biotechnology stakeholders scientists, executives, investors, etc. sampled
 - Diversity with respect to size, geography, product(s), and business model is targeted
- Energy-I-Corps approach utilized
 - Guided by a set of questions developed with the ABF management team and BETO
 - 30-60 minutes long; short ABF briefing used to introduce the interview
 - Part of continuous effort to refine the unique ABF value proposition
- Identities and responses are not shared outside ABF
 - Ensures privacy
 - Encourages candidacy and promotes honest feedback

84 interviews completed since FY17







4 – Progress and Outcomes Assessment: Key Learnings from one-on-one interviews



- The mission and goals of the ABF were viewed favorably
- Interest in learning how companies can work with the Agile BioFoundry is growing
- Providing cost share, even in-kind support, is a frequent concern, especially for smaller, less established companies
- A longer-term option to license an invention developed under a CRADA with the ABF would help to incentivize choosing non-exclusive, rather than an exclusive, license.
- Could benefit from making it easier to engage and work with industry
 - Distinguish from other ABF consortia, research centers, and user groups
 - Clearly communicate capabilities
 - Facilitate streamlined partnership agreements





4 – Progress and Outcomes Interactions: Industrial Advisory Board

Assembled diverse IAB

- Area of specialization
- Age/size of company
- Location of operation
- Gender

Established charter

- Expresses expectations and governs operations
- Operate without NDAs with IAB members or firms

Collected/reported feedback

- Approach
- Operations
- Dashboard metrics
- Milestone achievements
- Target/host selection process
- Outreach activities
- Overall impact

Companies represented in FY21 roster

amyris



CALYSTA

















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4 – Progress and Outcomes Interactions: Industry Day or Webcast Series

Themes

Introduction to the ABF

Beachheads / Exemplar Targets with Integrated Analysis Approach for their Selection

Host Onboarding and Development

Test and Learn Capabilities

Scaling Capabilities (Round Robin Experiments)

How to work with the ABF



Introduction to the Agile BioFoundry

In this short introductory video, Nathan Hillson, Principal Investigator of the ABF, provides a high-level overview of the consortium's vision, task structure, management, and long-term goals. In addition to highlighting many of the foundry's capabilities and successful collaborations with industry and academia, Dr. Hillson provides an overview of currently funded research areas through fiscal year 2021.



How to work with the Agile BioFoundry

If you are interested in working with the ABF, then this webcast by Project Manager James Gardner is recommended. In this detailed tutorial video, Dr. Gardner describes the various mechanisms that exist for collaborating with the ABF in propelling biomanufacturing forward in the private and public sectors. He discusses the pros and cons of various collaborative research agreements and highlights those that leverage public funds to enable technology advancement while preserving private investment. Several success stories are highlighted in the process, and we encourage you to consider submitting a proposal to <u>our current</u> <u>Directed Funding Opportunity</u> if your team is considering taking advantage of ABF expertise in fiscal year 2021 or beyond.







4 – Progress and Outcomes

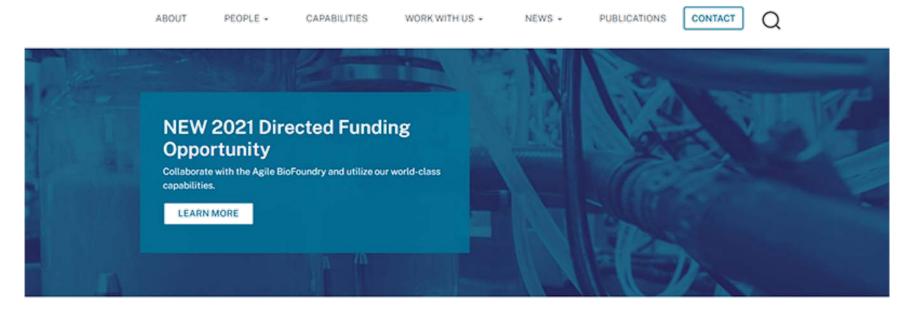
Outreach: Communication and Social Media Activities

- Report timely news and events related to ABF successes
- Amplify relevant announcements (funding opportunities, press releases, etc.) from BETO, DOE, or ABF member labs
- "Advertise" and "market" the ABF to potential collaborators/partners in industry and academia
- Encourage collaborative academic/industrial internships through communication tools
- Participate in an active online community focused on advancement of synthetic biology technology and applications, through original postings and re-tweets



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The Agile BioFoundry is a consortium of national laboratories dedicated to accelerating biomanufacturing and building the bioeconomy.

https://agilebiofoundry.org/

ABOUT US



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Website Metrics (since Jan 2020) - 10K users

- 33K pageviews



4 – Progress and Outcomes Outreach: Simplified ABF Vision

On average, it takes 10 years to fully scale up a bioprocess. Our goal is to cut that time in half.

Our objective is to develop and deploy technologies that enable commercially relevant biomanufacturing of a wide range of bioproducts by both new and established industrial hosts.

We collaborate with industry and academia to accelerate innovation and adopt new biomanufacturing methods. Our work is focused on developing industrially relevant host microbes – bacteria and fungi – for production of commodity chemicals and biofuels.

The Agite BioFoundry is a public infrastructure investment that increases U.S. industrial competitiveness and creates new opportunities for private sector growth and jobs.



https://agilebiofoundry.org/about/





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4 – Progress and Outcomes **Outreach: Non-negotiable CRADA**

Work With Us

The Agile BioFoundry actively collaborates with industry and academic groups to accelerate bioproduct research & development and promote the growth of the U.S. bioeconomy.

Summary: In interviews, this is received favorably and discussions helped to shape terms, like exclusivity clauses. How to work with us

We can collaborate with industry and academia through two mechanisms: Collaborative Research and Development Agreements (CRADAs) and Strategic Partnership Projects (SPPs).

SPPs tend to be more narrowly focused projects and often involve the Agile BioFoundry (ABF) performing a smaller number of unit operations (e.g., targeted proteomics analysis) for the industrial partner. SPPs may be very attractive to industry, as the industrial partner retains all intellectual property (IP) rights derived from the work performed.

CRADAs are typically larger engagements in which the ABF performs multiple unit operations in collaboration with the industrial partner (which may embed its staff at ABF facilities while pursuing the scope of the project's work).

Because CRADA-based projects are often larger in scope and more open-ended than SPPs, there is a greater chance that new IP will arise over the course of project execution. IP ownership follows inventorship, with the industrial partner generally having an option to negotiate an exclusive license to ABF (co-)invented IP, in a specific field(s) of use.

There may be other restrictions placed on CRADAs and SPPs. For example, the scope of the project's work must only include domain expertise and capabilities that are exclusively or uniquely available from the ABF national labs and not otherwise commercially available. Developed processes or products that are derivative of the work performed may need to be first substantially implemented or manufactured in the United States.

Tle Agile BioFoundry CRADA template ill be used for all of ABF's CRADA-based projects, and if the tment of Energy (DOE) funding, this CRADA is non-negotiable. If a CRADA project is funded entirely with non-DOE funds, changes will be considered. The CRADA is applicable only to ABF projects where there is one non-DOE lab party, although there may be any number of DOE labs.

ABF researchers are free to collaborate with other researchers from within academic, non-profit, or government institutions, with the work either needing to be directly aligned with the ABF's mission, or the collaborating parties required to secure additional sources of funding to pursue the collaborative work.

GET IN TOUCH







Summary Overview

- Facilitate transfer of ABF tools and technology to industry

Approach

- Focus on assessment, interactions, and outreach
- Continually conduct interviews and surveys, provide feedback from industry stakeholders to inform ABF R&D, and participate in active online community

Technical accomplishments

- Submitted yearly reports on findings from interviews and surveys
- Conducted regular meetings with IAB
- Organized Industry Days and advertised the ABF on website and fact sheets

Relevance

 Provide feedback supporting project-planning and decision-making activities to ensure industry responsiveness

Future work

- Coordinate strategic planning exercise
- Continue interviews and surveys
- Plan panels and sessions at national meetings





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Acknowledgements

Alastair Robinson James Gardner Katy Christiansen Nathan Hillson Christopher Johnson Philip Laible Amanda Barry Emily Scott Alastair Robinson Blake Simmons Leah Freeman Sloan





Quad Chart Overview

Timeline

- Start: October 1, 2019
- End: September 30, 2022

	FY20	FY21	FY22	Total Active
DOE Funding	\$0.36M	\$0.36M	\$0.36M	\$1.08M

Project Partners

 LBNL (11%), SNL (8%), NREL (39%), ANL (39%), LANL (3%),

Barriers addressed

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

Project 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

End of Project Milestone

- 5X efficiency improvement in DBTL engineering cycle
- 20 microbial hosts (20 species) brough to at least Tier 1
- 10-15 beachheads of strategic interest to BETO in at least 3 onboarded hosts
- At least one representative target of a beachhead at a TRY of 80 g/L, 1 g/L/hr, and 70% of theoretical yield

Funding Mechanism



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Additional Slides

• General Comment: The goal of this subproject is to identify and remove obstacles for technology transfer. In addition, they proposed to expand the number of industrial partners. This task is necessary to broaden the impact and relevance of the Agile Biofoundry. Overall, the team is making solid progress. The project would benefit by including explicit milestones in order to evaluate progress and to define success: Regarding milestones, we could have explicitly shown that we have a detailed project plan that includes quarterly IEO task milestones: Each IEO subtask has 2 or 3 SMART milestones throughout the year. Joint monthly IEO/management discussions help to keep the subtask on track and accountable. Since these internal milestones might have been confused with formal ABF milestones, we erred on the side of not showing them. They can be made available to the review team upon request.





• Approach Weakness: It is not clear how extensive the engagement list needs to be to fill the pipe with a consistent flow of high quality project, and whether the team is represented in a sufficiently wide array of industry conferences/symposium. IAB may need to be more diverse in company type and geography: We examine the diversity of interviews, conferences attended and the composition of the the IAB yearly. As one such outcome, we are actively are working to expand or restructure the IAB for better geographic and company representation. Somewhat outside of our jurisdiction are the multifaceted factors that contribute to the flow of high-quality projects into and out of the ABF. The efforts of the IEO are only part of that equation. Our plan to help contribute to that flow is to continue with and possibly expand engagement efforts every year, targeting new industry and academic groups whenever possible.





- Approach Weakness: Goals are based on gathering information, but no goals on technology transfer, collaborations with industry, or implementation of industry suggestions: We actively coordinate with ABF management and CRADA oversight. Many of these weaknesses that are listed are outside of the scope/control of the IEO task.
- Accomplishments/Progress Weakness: At this stage it is not entirely clear how much of the significant success in ABF projects has been accomplished through this specific effort, vs. by other means (e.g. more grass roots discussions between scientists, although this may already be considered in scope). This should be assessed, and if appropriate, apply learnings to synergise efforts and apply resources most effectively: Quantititation of the effectiveness of the IEO is difficult. If there were multiple ABFs we could compare effectiveness with and without an IEO task. In future years we will work to get a better feeling for the return on investment for the IEO work.





 Accomplishments/Progress Weakness: The IAB would be strengthened by expanding its perspective by adding companies outside of bio-energy/bio-conversion and with some representation outside of the US: As we examine the the composition of the the IAB yearly, we will take these considerations into account. We worry that BETO would not support international input to the IAB, but we can certainly start such a dialog with them.





• Future Work Weakness: Data, reports and recommendations will only be of value if they carry appropriate gravitas by stakeholders. Ultimately it will be important to close the loop on this effort by tracking how decisions and direction of the ABF are influenced. Having specific examples to illustrate this will be helpful, e.g. new technology/tools initiated or prioritized (and leveraged!) due to feedback, and types of relationships developed: We agree that we could do a better job in identifying IEO recommendations that have been considered and/or implemented by the ABF. There are several known examples now with increases to Host Onboarding efforts and the drafting, adoption, and implementation of a non-negotiable CRADA. We will highlight these successes in the future.





- Future Work Weakness: Metrics for success not established: Quantititation of the effectiveness of the IEO is difficult. See details above on response to a Criteria 2 weakness. We will work to make the establishment of metrics for success a milestone for the IEO going forward. As one such example, we have established a dashboard that is delivered to the IAB every quarter to help track IEO and ABF effectiveness (categories include number of publications, publication impact, tools developed, intellectual property, CRADAs, CRADA approval efficiency, SPPs or WFOs initiated and/or established and alumni in biomanufacturing).
- Future Work Weakness: To further enhance engagement, team should devise way to publicly disseminate/publish some of its findings, possibly through heavy retraction or by limiting to very highlevel findings (e.g. host organisms, process bottlenecks, etc..): We agree and have internal documents that may be used as starting points. We will work with ABF and BETO management to determine what level of publication is possible and/or if these findings could appear more prominently on the ABF website.





- 50 publications, 126 presentations to date
 - 16 publications and 20 presentations since FY20
 - The following slides provide explicit lists thereof
- 2020 R&D 100 Award
 - Awarded to Smart Microbial Cell Technology for rapid optimization of biocatalysts
 - Special Recognition (Silver Medal) for Market Disruptor in the Services category

36 patents, records of invention, software disclosures, & licenses

The following slides list these intellectual property assets





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 "Production of ent-kaurene from lignocellulosic hydrolysate in Rhodosporidium toruloides." Microb Cell Fact. 19(1):24. (2020).
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- (Publication) Radivojević, T., Costello, Z., Workman, K., & Martin, H. G. "A machine learning Automated Recommendation Tool for synthetic biology." Nature Communications, 11(1), 1-14.(2020).
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- (Presentation) Nathan J. Hillson "U.S. DOE Agile BioFoundry: Organization and Capabilities", Invited Talk, ABF Industry Day 2019, Emeryville, CA October 4, 2019
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- (Presentation) Benavides PT, Davis R, Klein, B. "Economic and environmental assessment of biological conversions of Agile BioFoundry (ABF) bio-derived chemicals". 2nd Bioenergy Sustainability Conference 2020, Virtual meeting, October 15th, 2020
- (Poster) Tijana Radivojevic, Zak Costello, Kenneth Workman, Soren Petersen, Jie Zhang, Andres Ramirez, Andres Perez, Eduardo Abeliuk, Benjamin Sanchez, Yu Chen, Mike Fero, Jens Nielsen, Jay Keasling, Michael K. Jensen, Hector Garcia Martin, "ART: A machine learning Automated Recommendation Tool for synthetic biology", BRC Workshop on Al and ML for Biosystems Design, Washington, DC, February 27, 2020





- (Presentation) Garcia Martin, H. "ART: a machine learning Automated Recommendation Tool for guiding synthetic biology". Al4Synbio Symposium, Arlington VA, November 8th, 2019.
- (Presentation) Garcia Martin, H. "Opportunities in the intersection of:Artificial Intelligence & Synthetic Biology & Automation". Army Science Planning and Strategy Meeting, Burlington MA, November 13th, 2019.
- (Presentation) "ART: A machine learning Automatic Recommendation Tool for guiding synthetic biology", Invited Talk, Computational Bio-Science Meeting, Berkeley, CA, April 23, 2020
- (Presentation) Garcia Martin, H. "Opportunities in the intersection of machine learning, synthetic biology, and automation". ABLC 2020, Virtual meeting, July 10th, 2020.
- (Presentation) Garcia Martin, H. "Leveraging machine learning and automation to make synthetic biology predictable". SPIE Optics + Photonics 2020, Virtual meeting, August 24th, 2020.
- (Panel) Garcia Martin, H. "Sustainable Living Systems". LA Life Summit, Virtual meeting, October 15th, 2020.





- (Presentation) T. Radivojevic, "Automatic Recommendation Tool", Invited Talk, Agile BioFoundry Learn Summit 2020, Argonne/Lemont, IL, March 4, 2020
- (Presentation) T. Radivojevic, "Using ART to improve tryptophan production", Invited Talk, Agile BioFoundry Learn Summit 2020, Argonne/Lemont, IL, March 4, 2020
- (Presentation) T. Radivojevic, "Guiding synthetic biology via machine learning", Invited Talk, Biofuels & Bioproducts Division Meeting, JBEI, Emeryville, CA, March 11, 2020
- (Presentation) T. Radivojevic, "ART: A machine learning Automatic Recommendation Tool for guiding synthetic biology", Invited Talk, Computational Bio-Science Meeting, Berkeley, CA, April 23, 2020
- (Presentation) Nathan J. Hillson, "FY20 ABF CRADA Call: Process, Applications, and Selections", Conversion R&D Standing Lab Update Call, via WebEx, July 27, 2020





- (Presentation) Nathan J. Hillson, "Perspectives from the U.S. DOE Agile BioFoundry", OECD BNCT Virtual Workshop, Session 1: Biofoundries and COVID-19, via Zoom, July 29, 2020
- (Presentation) Garcia Martin, H. "Opportunities in the intersection of machine learning, synthetic biology, and automation". ABLC 2020, Virtual meeting, July 10th, 2020.
- (Presentation) Garcia Martin, H. "Leveraging machine learning and automation to make synthetic biology predictable". SPIE Optics + Photonics 2020, Virtual meeting, August 24th, 2020.
- (Presentation) Nathan J. Hillson, "FY20 ABF CRADA Call: Process, Applications, and Selections", Conversion R&D Standing Lab Update Call, via WebEx, July 27, 2020
- (Presentation) Nathan J. Hillson, "Perspectives from the U.S. DOE Agile BioFoundry", OECD BNCT Virtual Workshop, Session 1: Biofoundries and COVID-19, via Zoom, July 29, 2020





License partners

- University of Georgia
- Kiverdi, Inc.
- LanzaTech, Inc.
- Visolis, Inc.
- Danimer Scientific

Patent Applications

- Terephthalate biosensor and applications thereof
- Mutant transporters for bacterial uptake of terephthalic acid
- Alleviating the bottleneck in enzyme evolution and pathway optimization using novel biosensors (Disclosure Title) Modified Biosensors and Biocatalysts and Methods of Use (Application Title)
- Mutant transporters for bacterial uptake of terephthalic acid
- ART: A machine learning Automated Recommendation Tool for guiding synthetic biology





Patent Applications (cont.)

- A Generative Model for Protein Sequences for the Purpose of Protein Design or Phenotypic Inference
- Predicting Metabolic Pathway Dynamics from Time Series Multiomics
 Data Using Machine Learning Techniques
- Use of Statistical Learn Approaches to Predict Next Generation Sequencing Subsequence Depth of Coverage
- Mutant transporters for bacterial update of terepthalic acid
- Method and strain for sugar conversion
- Engineered Microorganisms for the Production of Intermediates and Final Products (1st)
- Engineered Microorganisms for the Production of Intermediates and Final Products (2nd)
- Production of organic acids from Aspergillus pseduoterreus cadA deletion strain (1st)
- Production of organic acids from Aspergillus pseduoterreus cadA deletion strain (2nd)





Patent Applications (cont.)

- Genetically engineering an industrial filamentous fungus Aspergillus niger for 3-hydroxypropionic acid production
- A specific exporter responsible for aconitic acid high production in Aspergillus pseduoterreus

Records of Invention

- Bioproduction of limonene from syngas
- Mutant transporters for bacterial update of terepthalic acid
- Method to produce branched chain polyhydroxyalkanoates and branched chain 3-hydroxyacids
- A genetic circuit to reduce cell-to-cell production heterogeneity
- High yield conversion of D-xylose to D-arabitol in *R. toruloides*
- Manipulation of tRNA thiolation gene ncs2 for enhanced production of fatty-acyl-CoA derived chemicals in *R. toruloides*





Software Disclosures

- Automated Recommendation Tool (ART) v2.0
- Kinetic Learning v0.1
- Automated Recommendation Tool (ART): v1.0
- PIACE: Parallel Integration and Chromosomal Expansion of Metabolic Pathways
- OMG, Omics Mock Generator Library: v0.1.1
- Fermentation Data Processing
- Fermentation Data Manipulation and Analysis Once imported



