

Introduction of Synthetic Biology – DNA Syn. Sci. Program

Yasuo Yoshikuni
JGI User Meeting
Genomic Technologies Workshop
Mar 24, 2015

A 10-Year Strategic Vision (2012)



DNA Sequencing

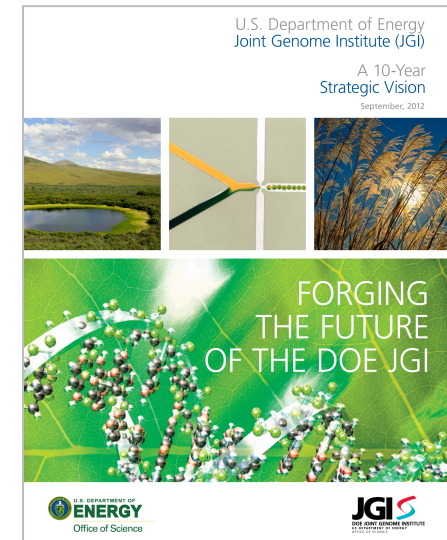
DOE JGI Strategic
Planning Workshop
Asilomar, CA,
September 2011
Synthetic Biology
DNA Synthesis Science

Next-gen. Genome Science
Biological Function

VISION:

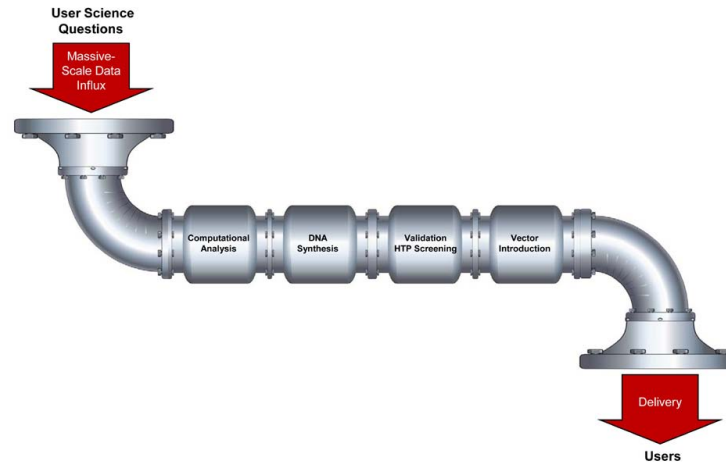
Evolve from a production sequencing center to a **Next-Generation Genome Science User Facility**

Specific emphasis on the development of capabilities for the high through-put addition of functional information to sequence data



DNA Synthesis Science Program

Mission: To enable our users to perform state-of-the-art science that can only be realized by Large-Scale DNA Synthesis



DOE JGI integrated DNA synthesis pipeline for the conversion of digital sequence information into biological parts.

STRATEGIES AND VALUE PROPOSITIONS:

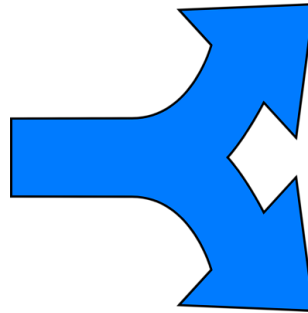
- Access to large-scale DNA synthesis and assembly
- Access to integrated DNA synthesis pipelines
- Access to project management capability

Synthesis capacity is adjusted based on price / base
for our users to stay ahead of the rests

2015 H2 ~

~ 2015 H1

All-type
250 K bases / proposal



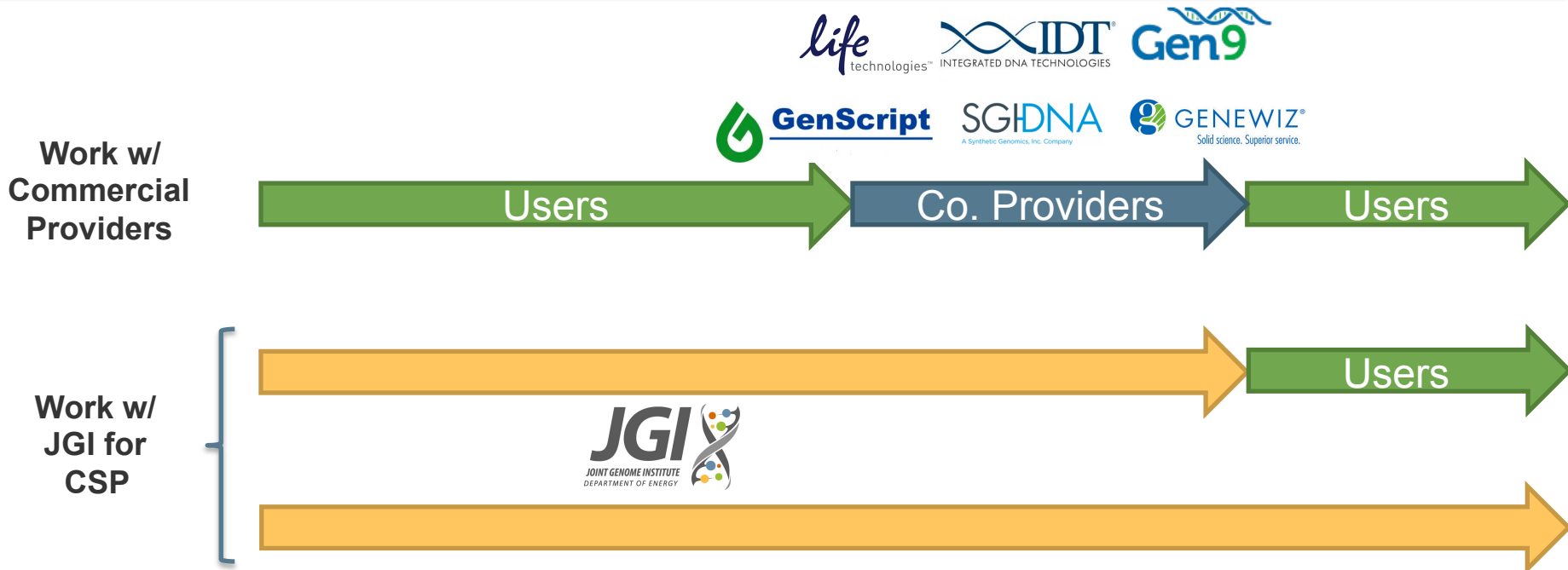
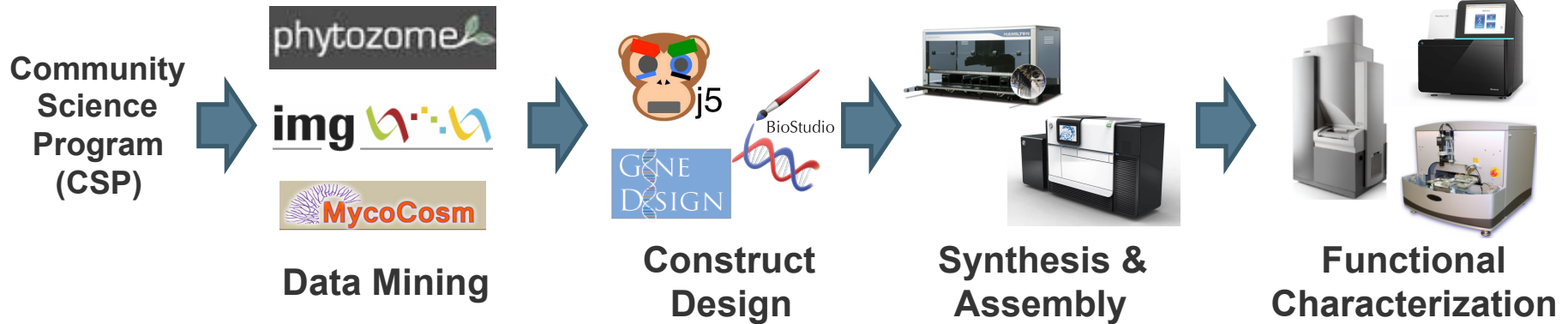
Independent-type

- ~400 K bases / proposal
- 50 K bases minimum
- Comparable to USD 100-150 K

Consortium-type

- ~1.2 M bases / proposal
- 50 K bases minimum
- Comparable to USD 300-450 K
- 3 PIs from different institutions
- Org. & Mgt. help

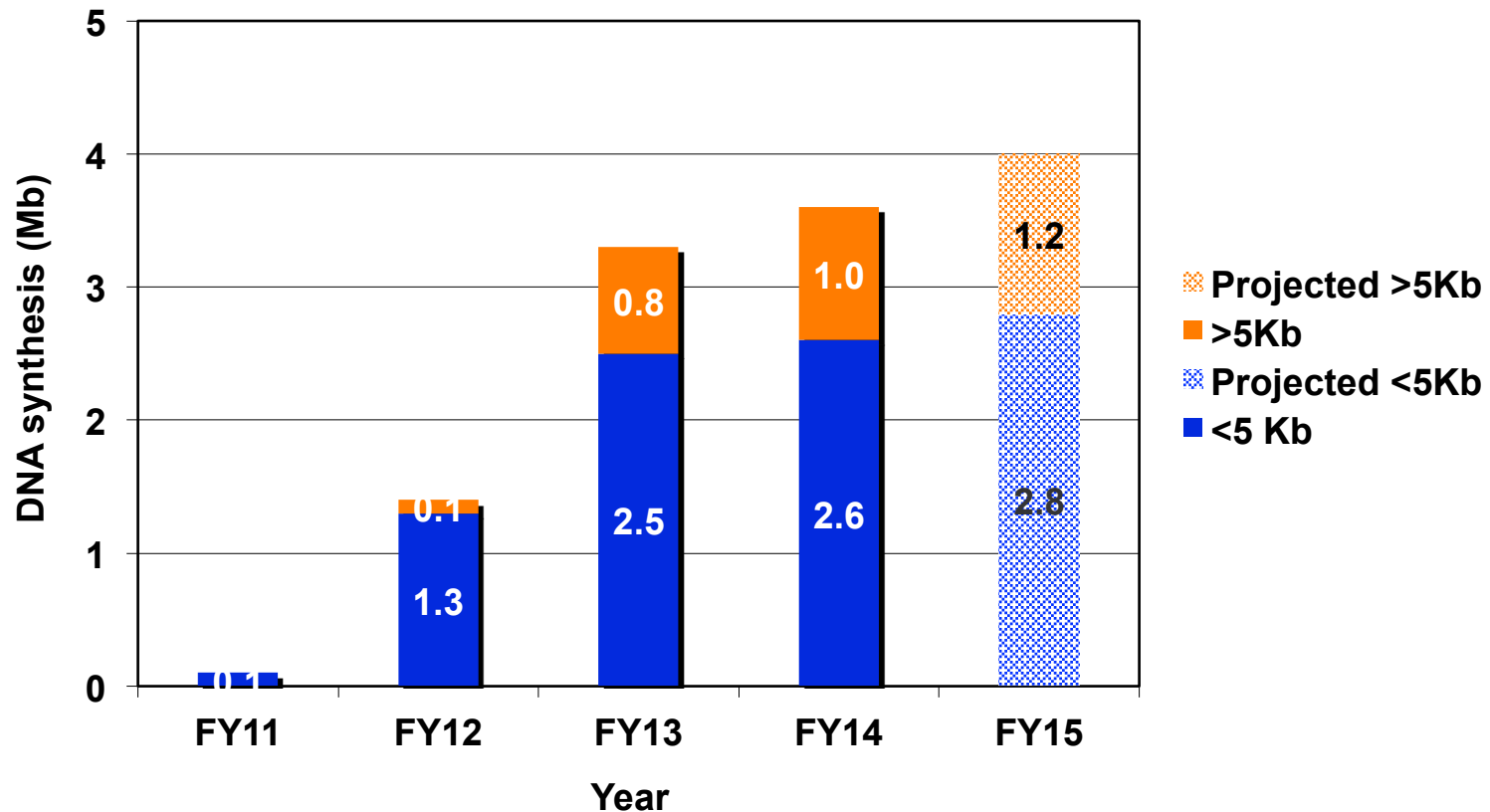
Integrated DNA Synthesis Pipeline



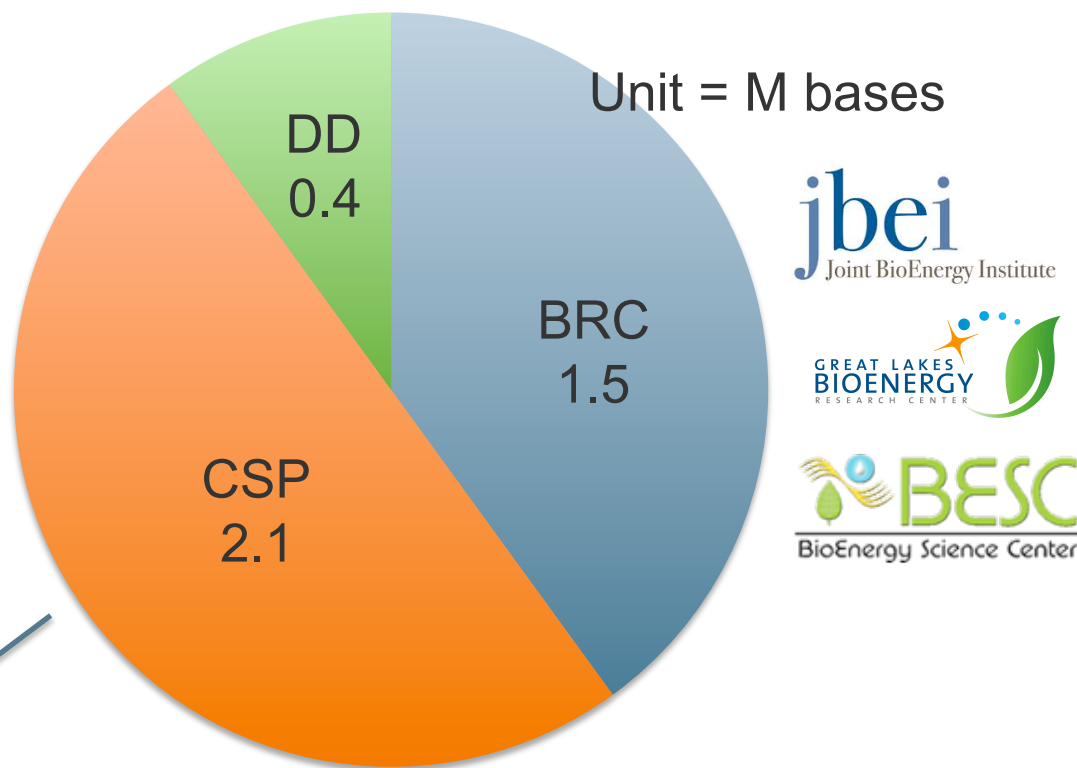
PROGRAM PERFORMANCE

Program's Historical Outputs & FY15 Projected Capacity

Total Construct Size Synthesized



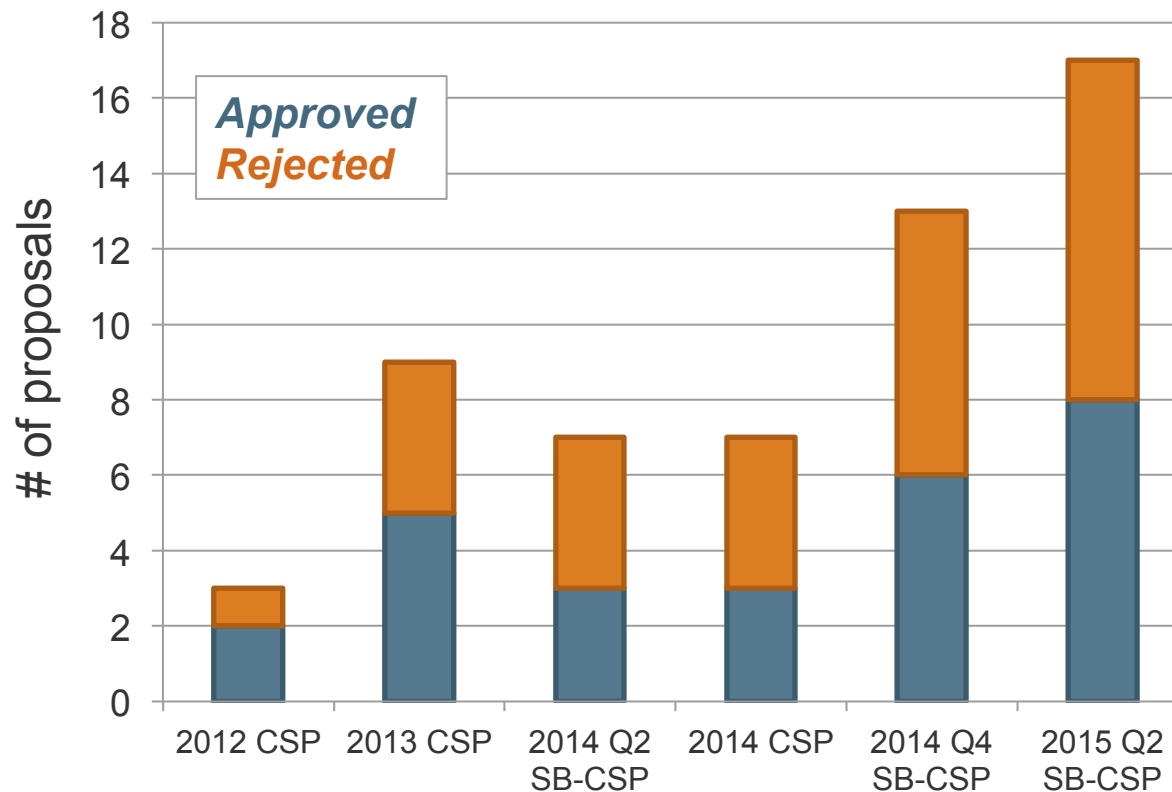
FY15 projections



Three project types:

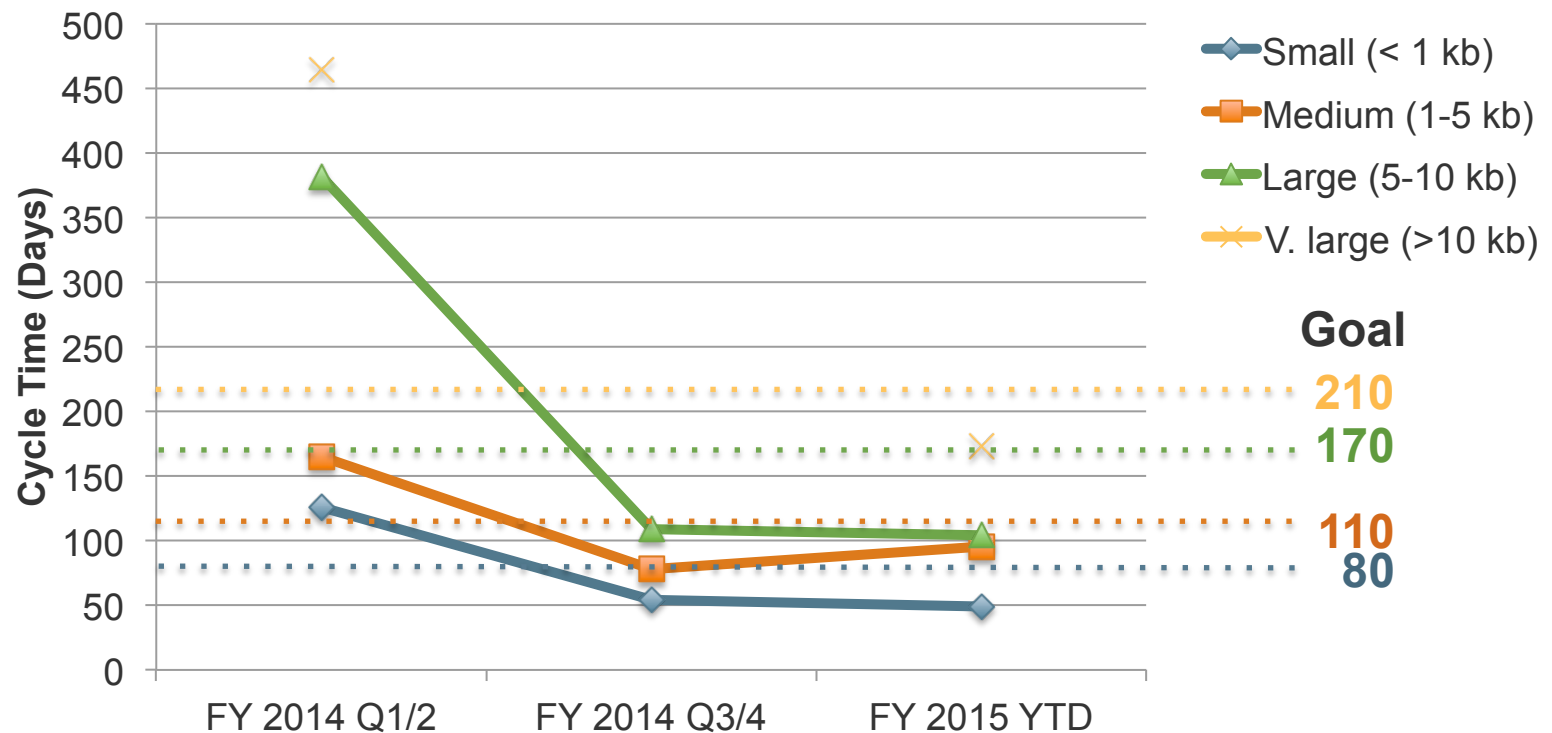
1. Community Science Program (CSP)
2. Bioenergy Research Centers (BRC)
3. Director's Discretionary (DD)

In average, 45% of the proposals are approved
The number will be closer to 35% as the program matures



Cycle Time

- In FY2014 Q2, we implemented two major modifications in our pipeline and improved the cycle time tremendously
 - Consensus dsDNA fragments as raw materials
 - Yeast TAR-assembly protocol
- In FY2015, we operate the same way and maintain good cycle time



Cycle Time Comparison with Commercial Vendors

Size	JGI Average FY2015 YTD (days)	Commercial Vendors (N = 8) (days)
Small (< 1 Kb)	49	28-42 ^{*1,2}
Medium (1-5 Kb)	95	35-56 ^{*1,2}
Large (5-10 Kb)	104	63-91 ^{*1,2} or inquiry
V. Large (> 10 Kb)	173	Inquiry

^{*1} Biz days are converted to calendar days

^{*2} Cloning in custom vectors, add 14 days

PROGRAM FOCUS AREAS & FUTURE VISION

1. Microbes to Biomes

A LBNL-wide initiative designed to reveal, decode, and harness microbes that are relevant to bioenergy supply and environment protection. Our program focuses on studies of biological systems modulated secondary metabolites.

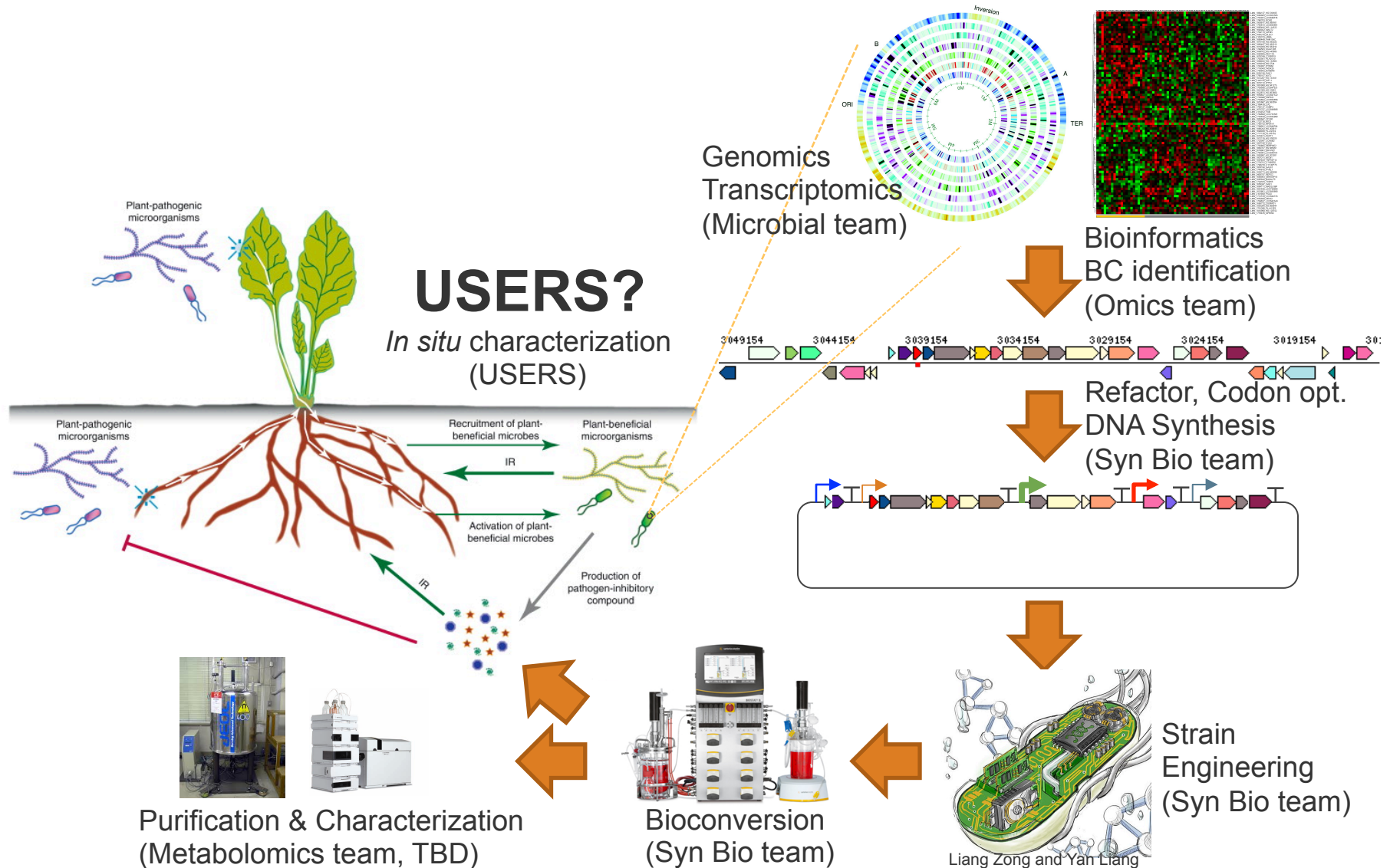
2. Genomes to Enzymes and Pathways

Large-scale characterization of enzymes and pathways leveraging data mining through the JGI genome portals.

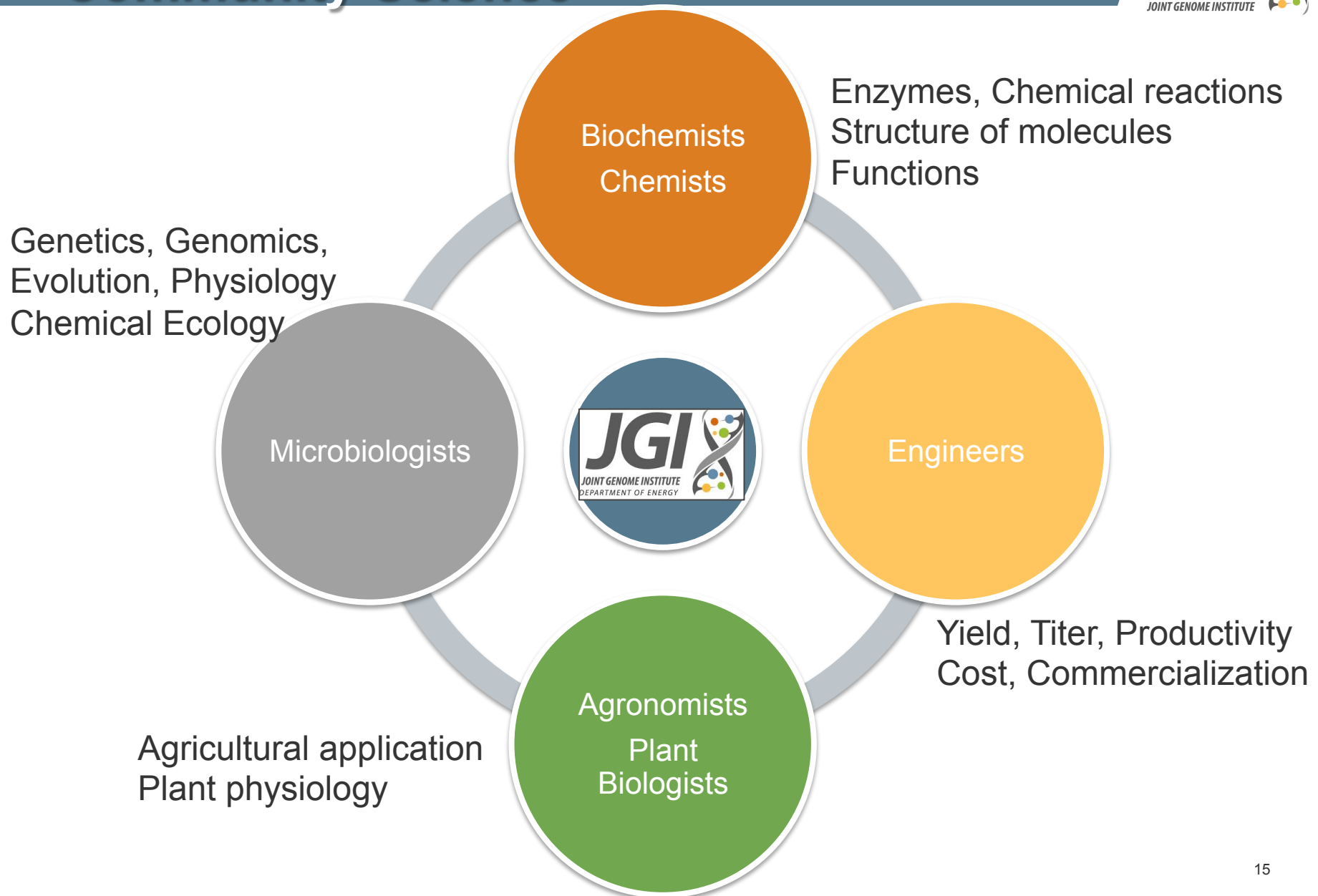
3. Fast-paced Metabolic Engineering

Simultaneous optimization for choice of enzymes, promoters, RBSs, terminators, etc.

Microbe- and Plant-Microbe Interactions Mediated by Secondary Metabolites



Future Vision; Open Innovation Hub for Community Science



Future Vision; How Does the Program Evolve (A 10-Yr Strategic Vision) ?

Toward Synthetic Biology Super Program (?)

Fermentation engineering

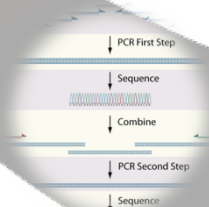
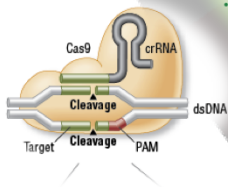
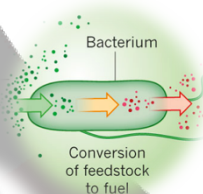
- HTP micro-scale fermentation & screening platforms
- Scaling up to 10L-scale bioreactors
- Cultivating previously uncultivated microbes

Strain engineering

- Engineering non-traditional lab strains
- CRISPR/CAS9-based editing
- Physiology and expression systems

DNA Synthesis Science

- 100 + M bases/yr
- Genome-scale design and synthesis
- Integrated bioprocessing



Thanks for Your Attentions !

Please Meet DNA Syn. Sci. Team

