Berkeley Lab
Community Advisory Group
January 13, 2014

Synthetic Biology @ Berkeley Lab

Jay Keasling
Associate Laboratory Director, Biosciences
Lawrence Berkeley National Laboratory
The world’s most productive genome sequencing center dedicated to sequencing plants, fungi, and microbes for energy and environmental applications.
2007
One of three DOE Bioenergy Research Facilities launched

- Reducing the nation’s dependence on foreign oil
- Safeguarding public health and the environment by curbing the effects of climate change
- Reducing organic waste by transforming non-edible biomass into biofuels
Sequencing = Reading DNA

Just as computer software is rendered in long strings of 0s and 1s, the GENOME or “software of life” is represented by long strings of the four nucleotides: A, T, C, and G, which encode function in genes/proteins.
Insulin production: early versus modern

- 1920s: from pancreases taken from slaughtered cows and pigs
- 1978: Genentech produced the first synthetically manufactured insulin creating miniature "factories" by inserting the human insulin gene into bacterial DNA.
Artemisinin production: early versus modern

- **2003-2013:** Artemisinin harvested from plants, subject to large swings in price and availability

- **2013 and beyond:** UC Berkeley and Amyris team build a yeast strains that produces artemisinin in a process like brewing beer

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**Chemistry Part - from Pilot to Industrial Scale**

- **Artemisinic Acid**
  - **Artemisinic Acid**
  - **Amorpha-4,11-diene**
  - **H**
  - **H**
  - **H**
  - **H**
  - **O**
  - **HO**

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**Non-Enzymatic**

- **AMO/CPR**
  - **AMO/CPR**
  - **AMO/CPR**
  - **Artemisinic acid**
  - **ADS**
  - **Amorpha-4,11-diene**
  - **H**
  - **H**
  - **H**
  - **O**
  - **HO**

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**Process development and industrial scale-up completed.**

- Facility and equipment are in place.
- Tech transfer to... Started
Genes responsible for artemisinin biosynthesis transferred to yeast
Artemisinin ready for tableting
Other Opportunities

Carbon-neutral fuels from non-edible plant biomass
Other Opportunities

Specialty and commodity chemicals

- $multi-billion global industry
- Polymers (polyethylene, polypropylene, polyvinyl chloride, polyethylene terephthalate, polystyrene and polycarbonate) make up 80% of output
- Nearly all polymers are derived from petrochemicals
Other Opportunities

Nitrogen-fixing crops

- $3B spent in 2006 for 12M tons of ammonia-based fertilizer for corn and wheat in US
- 1 ton of anhydrous ammonia fertilizer requires 33,500 ft$^3$ of methane
- 1/3 of all energy used in US agriculture sector is for nitrogen-based fertilizers
- 1% of the world’s total energy consumption (15 terawatts annually) is used for ammonia fertilizers
Synthetic Biology as a tool of Domestication

Sarah Richardson
Distinguished Postdoctoral Fellow, DOE Joint Genome Institute
Lawrence Berkeley National Laboratory
The Traits of Domesticity

- **CONTAINMENT**: do not live without humans
- **UTILITY**: make products that benefit humankind
- **DOCILITY**: be amenable, “trainable”
- **SAFETY**: do not harm people, livestock, or plants
The Traits of Domesticity

- **CONTAINMENT**: do not live without humans
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Domestication is a breeding process that encourages desired features and represses undesirable features to customize an organism.
Domesticated Animals

- Canis lupus (33,000 years)
- Sus scrofa (15,000 years)
- Meleagris gallopavo (2000 years)
- Cyprinus carpio (200 years)
Domesticated Plants

Fragaria vesca 300 years
Fragaria X ananassa

Daucus carota 1,000 years

Zea mays 12,000 years

Prunus amygdalus 5,000 years
Domesticated Microorganisms

Saccharomyces cerevisiae 6,000 years

Leuconostoc mesenteroides 4,000 years

Lactobacillus plantarum 4,000 years

Lactobacillus bulgaricus 7,000 years

Streptococcus thermophilus 7,000 years

Escherichia coli 70 years
Domesticating more with Synthetic Biology

- **CONTAINMENT**: do **not** live outside the lab
- **UTILITY**: make products that benefit humankind
- **DOCILITY**: be genetically “trainable”
- **SAFETY**: do **not** harm people, livestock, or plants
Domesticating more with Synthetic Biology

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Take naturally diffident bacteria

Use synthetic biology to encourage domesticity

Put the bacteria to work
Synthetic Biology-Enabled Science

Sam Deutsch
Synthetic Biology Group Lead
DOE Joint Genome Institute
Lawrence Berkeley National Laboratory
JGI was a major contributor to the human genome sequence. Focus on environmental and energy issues sequencing large numbers of bacteria, fungi, plants and environmental samples.

Many genes potentially useful, for example Enzymes (Clean-up of contaminated sites, industrial processes) or genes necessary for small molecule biosynthesis.
Top 200 Brand Name Drugs by US Retail Sales in 2010

Compiled and Produced by the Njardarson Group (The University of Arizona): Daniel J. Mack, Melissa L. Weinrich, Edun Vitaku, Jón T. Njardarson
Harnessing nature’s potential

1. Breakdown of plant material
2. Oil Degrading Enzymes
3. Regulate health and fight disease
What exactly are we doing?

Sequence of value

Synthesize

Model organisms

Test for function
Cow rumen: Plants to sugar

PLANTS

SUGARS

Fuels

Industrial process

Synthetic Biology

Identification many enzymes that work under industrial conditions
Conclusion

Synthetic Biology allows to harness the natural biological potential of enzymes and pathways for useful applications in Biomedicine and Green technologies.
Synthetic Biology @ Berkeley Lab: Background, Significance, & Promise

Nathan J. Hillson
Staff Scientist, Physical Biosciences Division
Lawrence Berkeley National Laboratory
Regulatory compliance

- Berkeley Lab is already subject to and complying with:
  - The California Medical Waste Management Act
  - Federal regulatory agencies including:
    - Centers for Disease Control and Prevention
    - Occupational Health and Safety Administration
    - U.S. Department of Agriculture
  - Stricter policies placed upon research supported by:
    - U.S. Department of Energy
    - National Institutes of Health
    - Other funding agencies
We are looking forward

- Synthetic Biology will have significant global implications
  - Decrease cost and increase access to medicines and fuels
  - Stabilize boom/bust supply cycles
  - Significantly change modes of production (who and how)

- We are considering the broader implications of our research

- Our approach:
  - Apply existing industry-standard best-practices
  - Learn from human and animal research internal review boards
  - Lead the development of new Synthetic Biology best-practices
Biosecurity best-practices

- International Gene Synthesis Consortium
  - Harmonized screening protocol

- User screening
  - “Black lists” from U.S. Commerce, State, and Treasury Depts.
  - Visual Compliance (VC) software for restricted party screening

- Sequence screening
  - “Sequences of concern”
  - Select Agents and Toxins; Commerce and EU control lists
  - GenoGuard software (Virginia Tech) for sequence screening
SynBio Internal Review Committee

- **Purpose**
  - Review all procedures related to Synthetic Biology
  - Ensure best practices
  - Consider environmental, ethical, legal, and societal issues

- **Composition**
  - Berkeley Lab staff
  - External experts
  - Member of the public

- To our knowledge, this committee is the first of its kind
  - Berkeley Lab is providing leadership
  - Other institutions will adopt our successful process
  - Review process software will facilitate replication
Review Process

Research Proposal Submitted

Biosafety and Biosecurity Review Processes

SynBio Internal Review Committee

Each Reviewer Votes

“Approve”

“Discuss”

Monthly Meeting

“Approved”

“Rejected”

“Modifications Required”

Research Begins

Modifications Made
Web-based Review System

Synthetic Biology Internal Review System

Proposal SBIRC#: 14
Submitted by Jane Submitter on 2013.09.27
Final Determination: Approved on 2013.09.27

Title:
hsdkfl [jpdlj] [jiskjlas asdjkljk ljsdlj] sdjflkjd

Abstract:

Reviewer Comments:

General:

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