



BioSciences

**Berkeley Lab
Community Advisory
Group
January 13, 2014**

**Synthetic Biology @
Berkeley Lab**

Jay Keasling

**Associate Laboratory Director,
Biosciences**

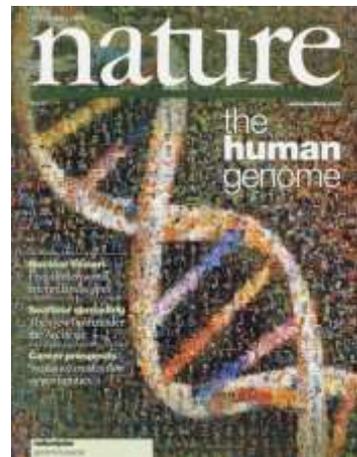
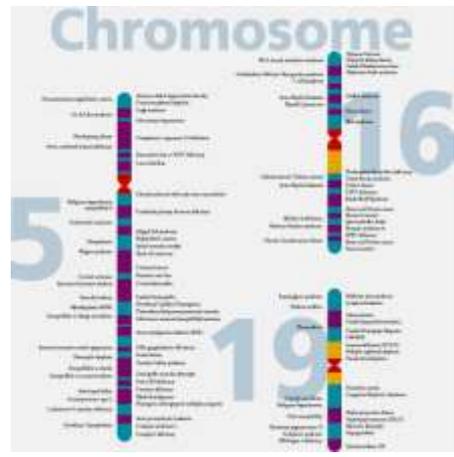
Lawrence Berkeley National Laboratory



Joint Genome Institute (JGI)



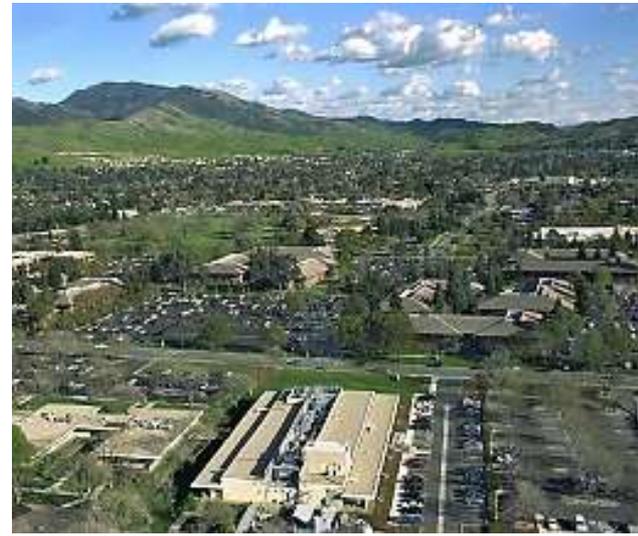
1997-2003 Human Genome Project



2004-2014 National User Facility



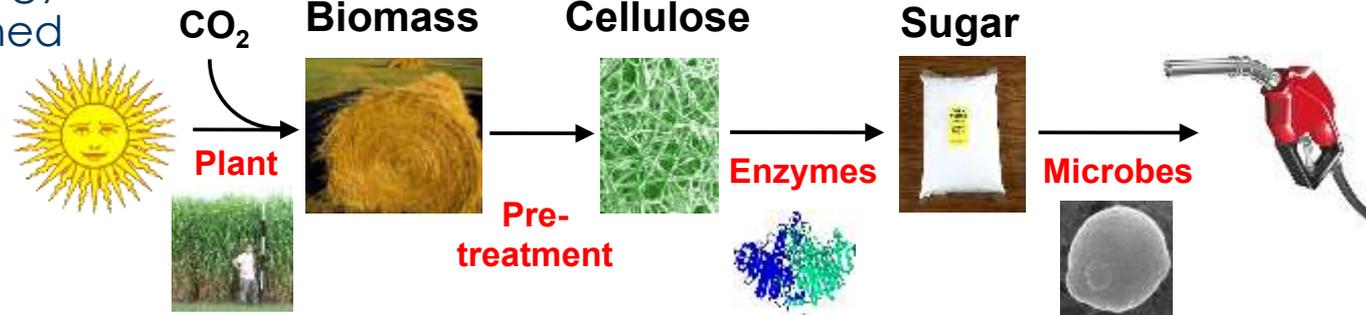
The world's most productive genome sequencing center dedicated to sequencing plants, fungi, and microbes for energy and environmental applications.



Joint BioEnergy Institute (JBEI)

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



Feedstocks



Fuels Synthesis



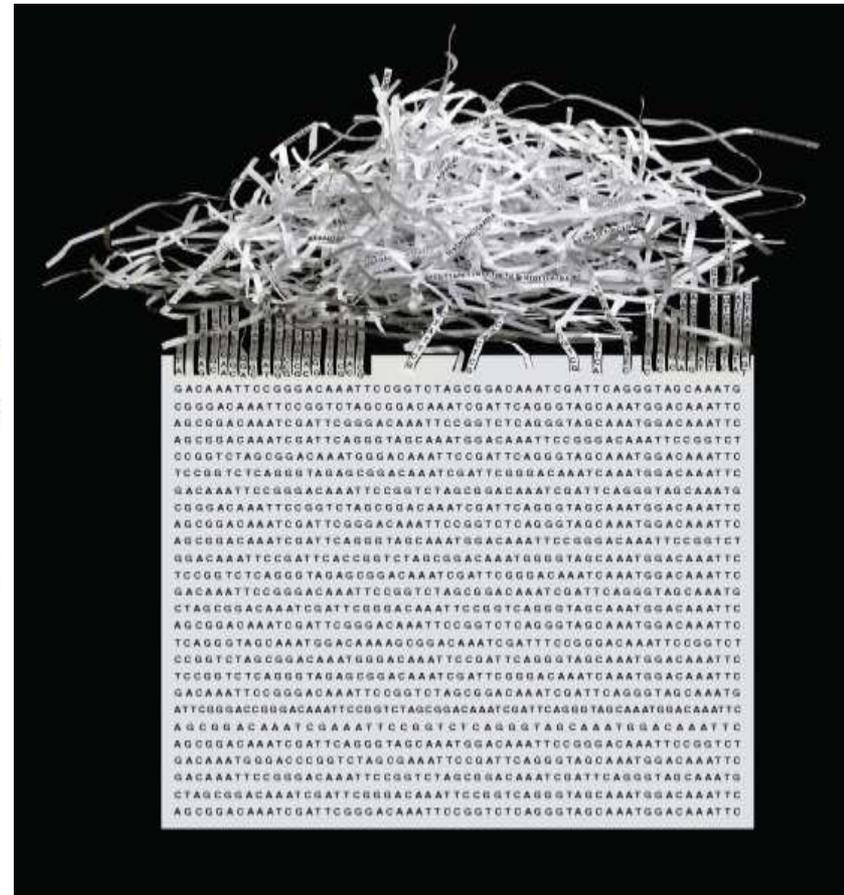
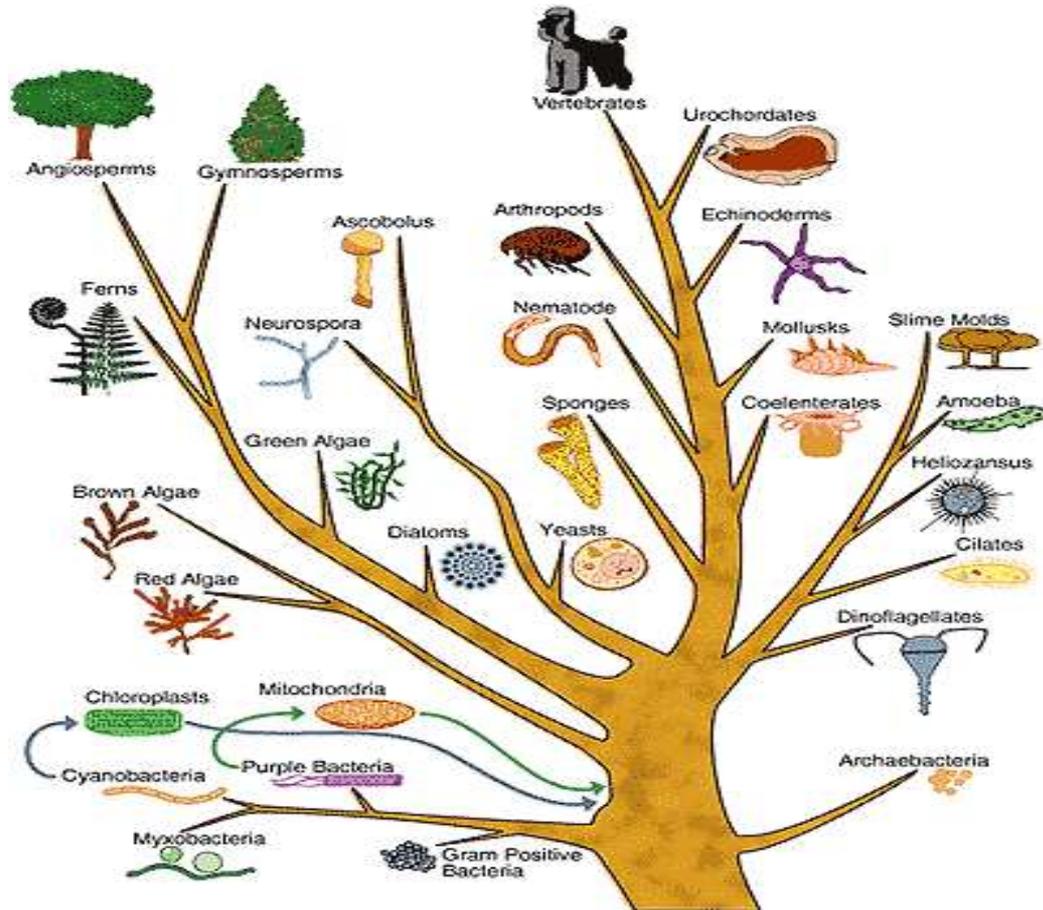
Deconstruction



Technology

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



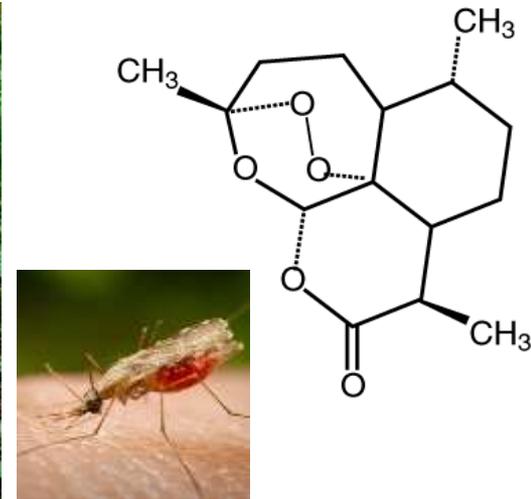
Insulin production: early versus modern

- 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.

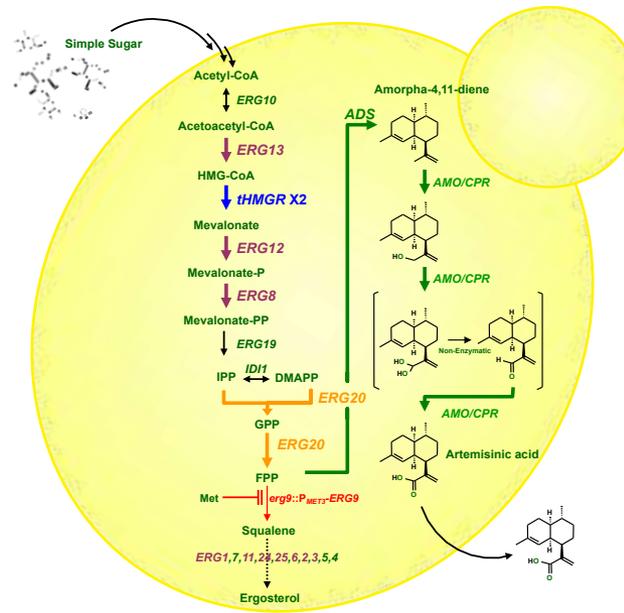


Artemisinin production: early versus modern

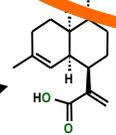
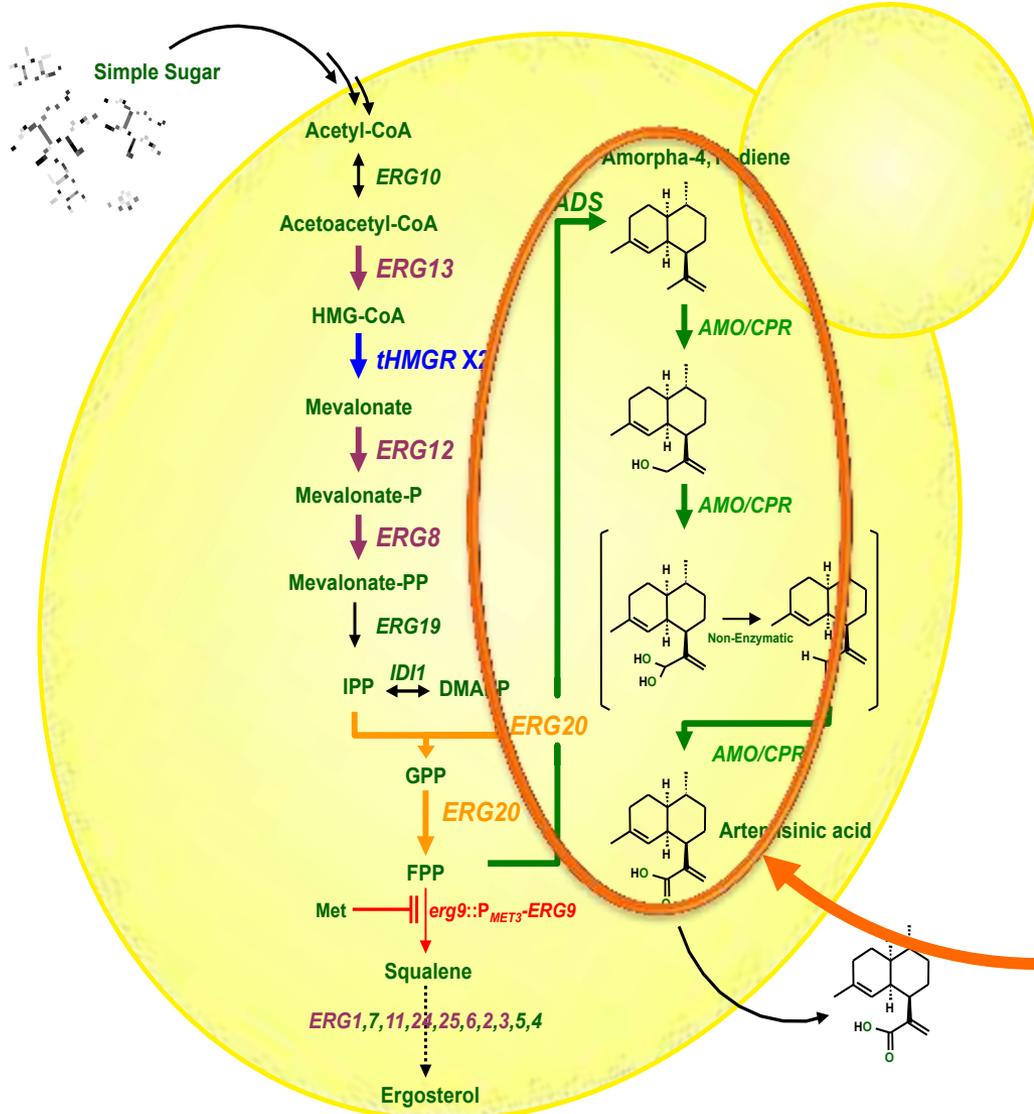
- 2003-2013: Artemisinin harvested from plants, subject to large swings in price and availability



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



Genes responsible for artemisinin biosynthesis transferred to yeast

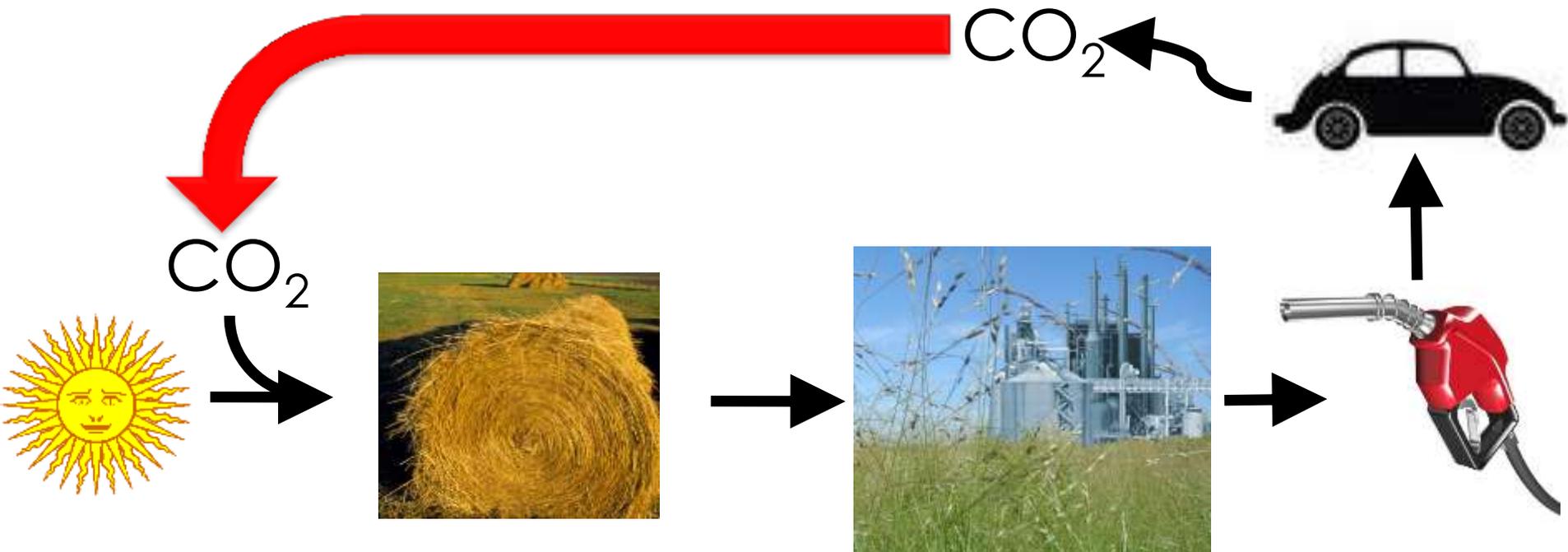


Artemisinin ready for tableting



Other Opportunities

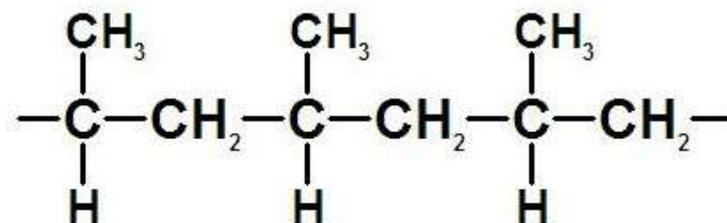
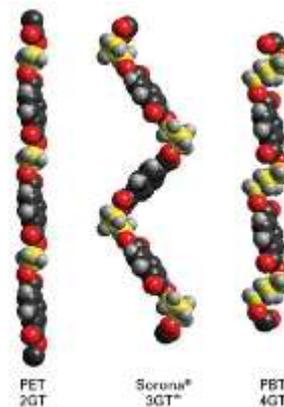
Carbon-neutral fuels from non-edible plant biomass



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 ft³ 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





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January 13, 2014**

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

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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



Zea mays 12,000 years

Daucus carota 1,000 years



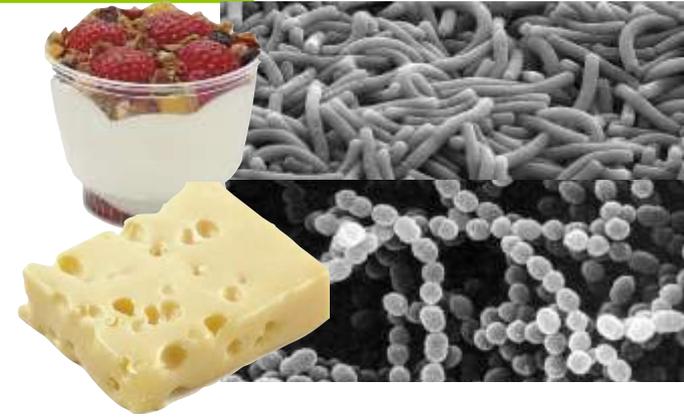
Prunus amygdalus 5,000 years



Domesticated Microorganisms

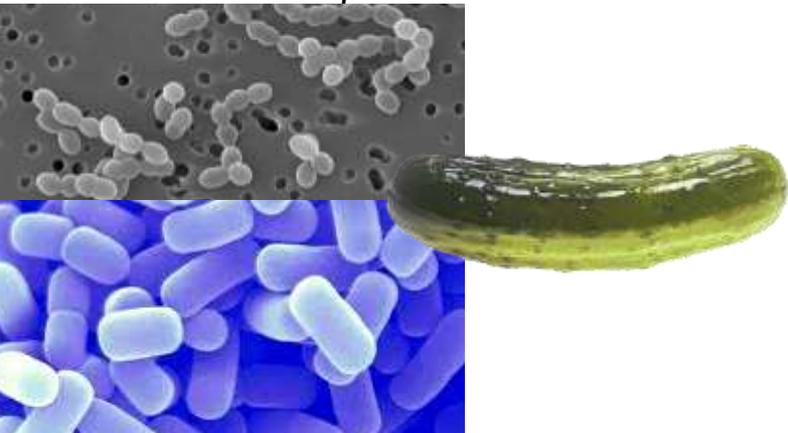


Saccharomyces cerevisiae 6,000 years



Lactobacillus bulgaricus 7,000 years
Streptococcus thermophilus

Leuconostoc mesenteroides
Lactobacillus plantarum 4,000 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

- **CONTAINMENT:** do not live outside the lab
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Take naturally diffident bacteria



Use synthetic biology to encourage domesticity



Put the bacteria to work





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**Synthetic Biology-
Enabled Science**

Sam Deutsch

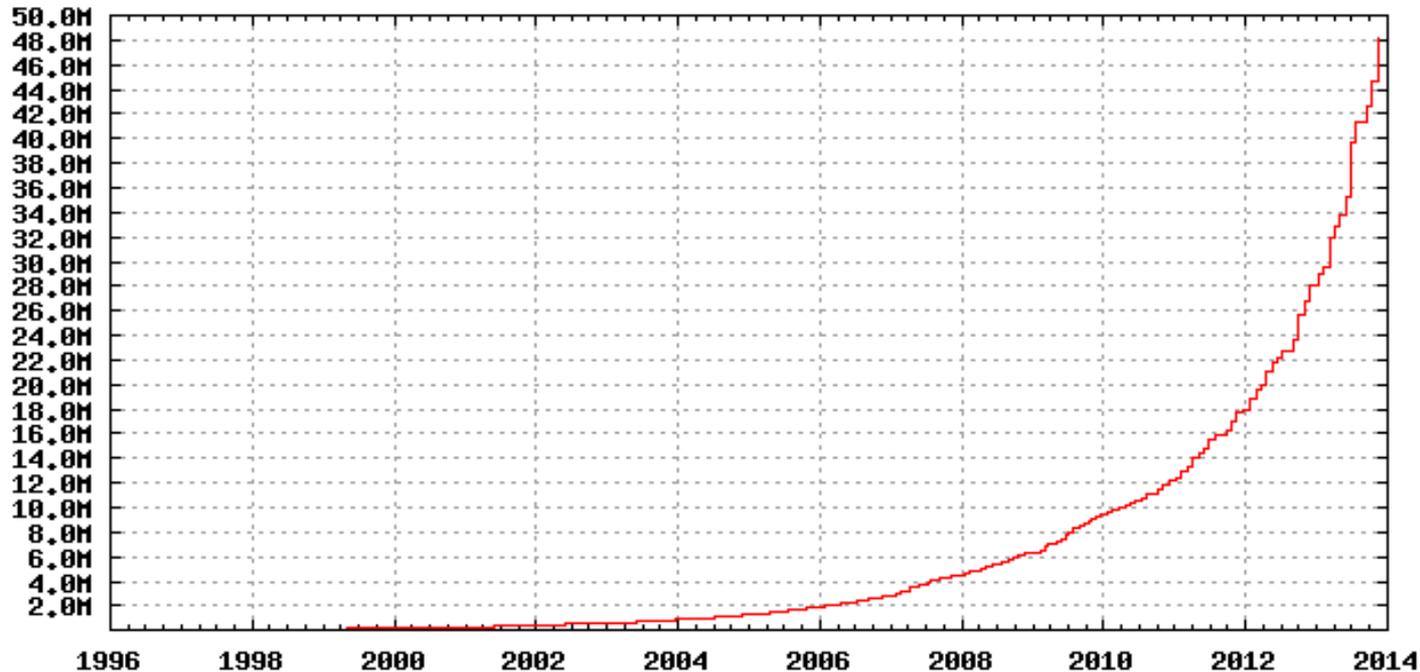
**Synthetic Biology Group Lead
DOE Joint Genome Institute
Lawrence Berkeley National Laboratory**



Millions of novel genes

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

Number of Novel genes



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, Edon Vitaku, Jón T. Njardarson



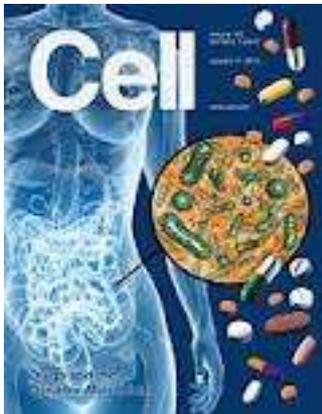
Harnessing nature's potential



Breakdown of plant material



Oil Degrading Enzymes



Regulate health and fight disease

What exactly are we doing ?

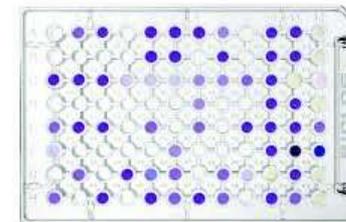
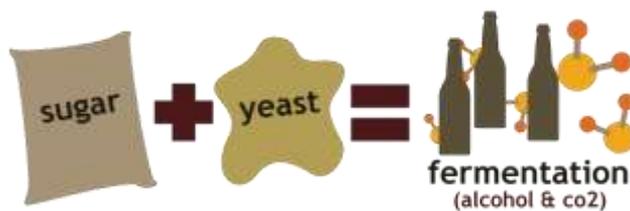
Sequence of value



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**



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**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

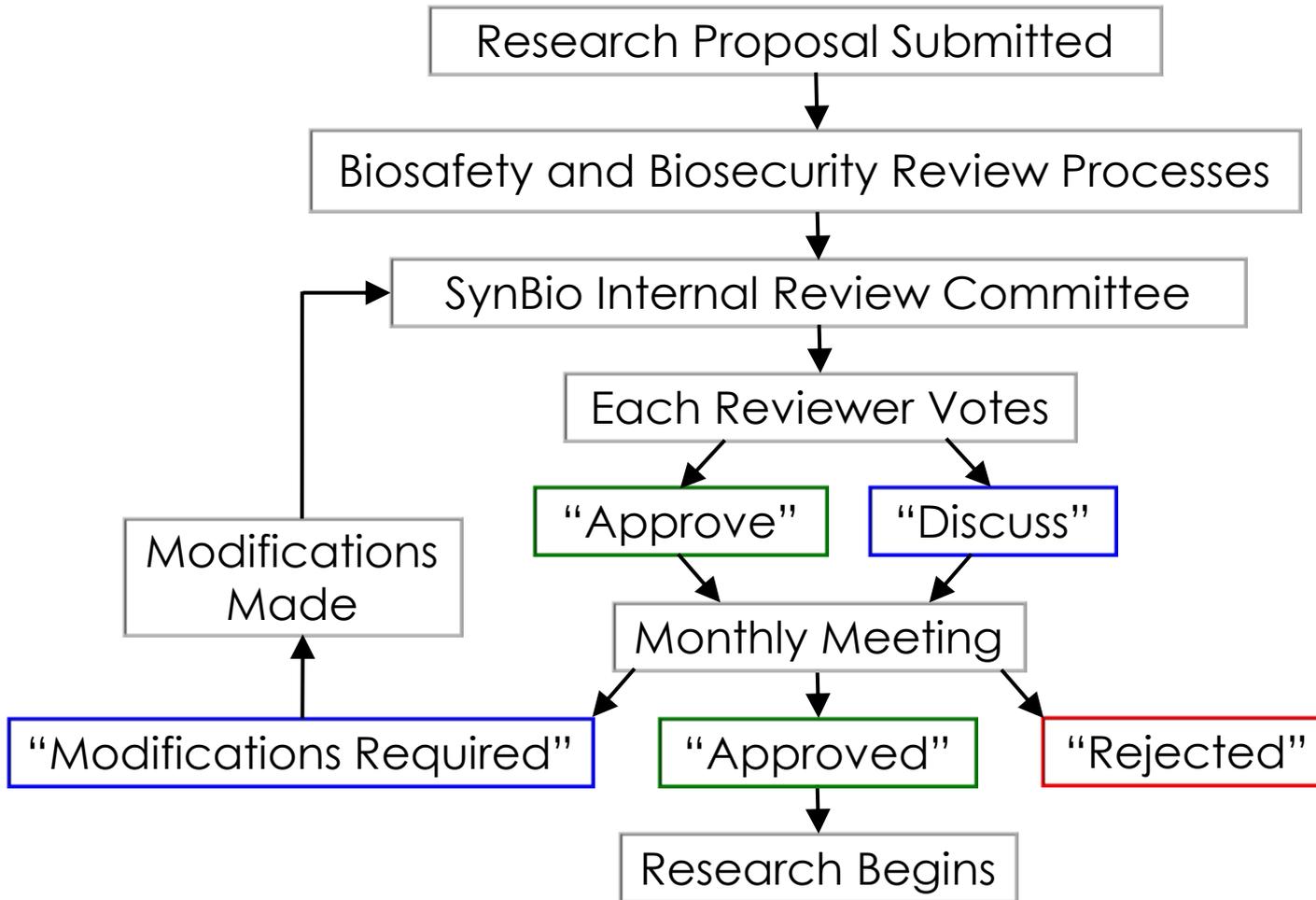
Biosecurity best-practices

- 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



Web-based Review System



Synthetic Biology Internal Review System

Welcome John Reviewer

SBIRC #:25
Mining Evolutionary Space for Im
 Submitted by Jonathan Walton on 2013.1

The cost of enzymes for converting economical development of second such as Trichoderma reesei, Asperg is cellobiohydrolase 1 (CBH1, also k units from the reducing end of crystal glucose. As such, it is the single mo

Little work has been done to improv CBH1 in heterologous systems such disulfide bonds. In this project, we p with filamentous fungi including tran

Glycosyl hydrolase (GH) family 7, to of many fungi and other "lower" eu these new DNA resources and our r with the goal of identifying a CBH1 profiles, and temperature optima of potential of this important of e The genes will need to thesis Many of the genes that we will m

[Download](#)

Comments:

General [0] BioSafety [0] BioS

Concern: General

Comment:



Synthetic Biology Internal Review

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

Title:
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Abstract:
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Full proposal attached at end of report

Reviewer Comments

General:
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