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Lawrence Berkeley National Laboratory

BioSciences

Berkeley Lab Community Advisory Group

January 13, 2014

Synthetic Biology @ Berkeley Lab

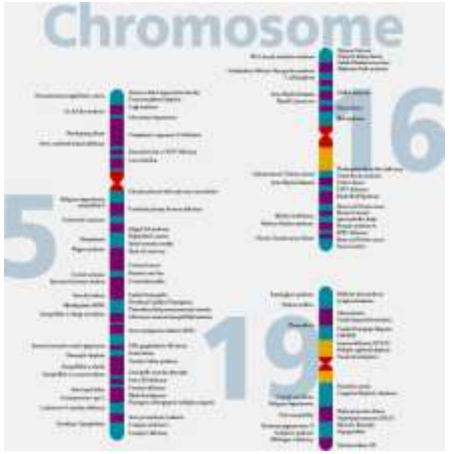
Jay Keasling

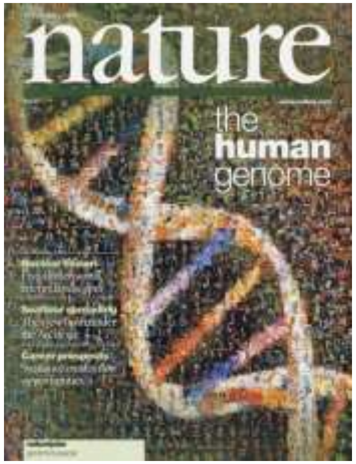
Associate Laboratory Director, Biosciences

Lawrence Berkeley National Laboratory

Joint Genome Institute (JGI)

1997-2003
Human Genome Project





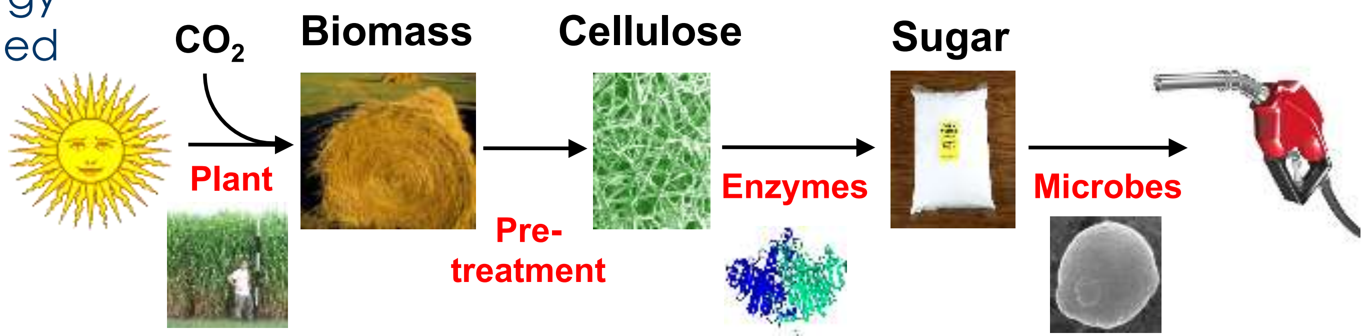
2004-2014
National User Facility

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

Joint BioEnergy Institute (JBEI)

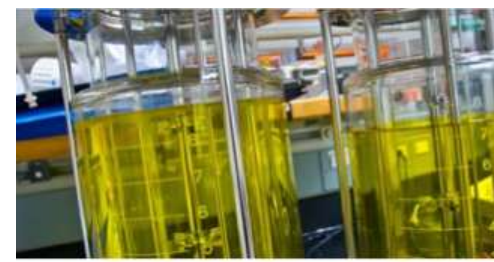
2007

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



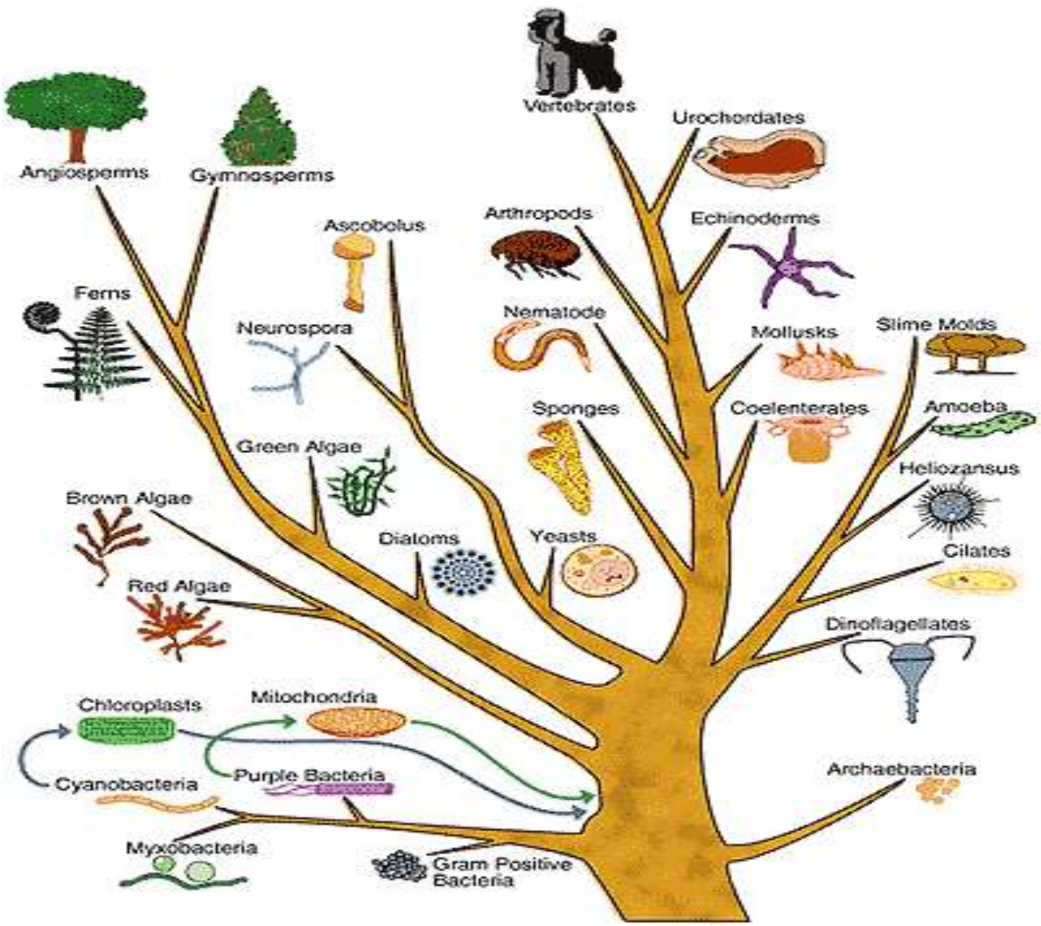
Fuels Synthesis

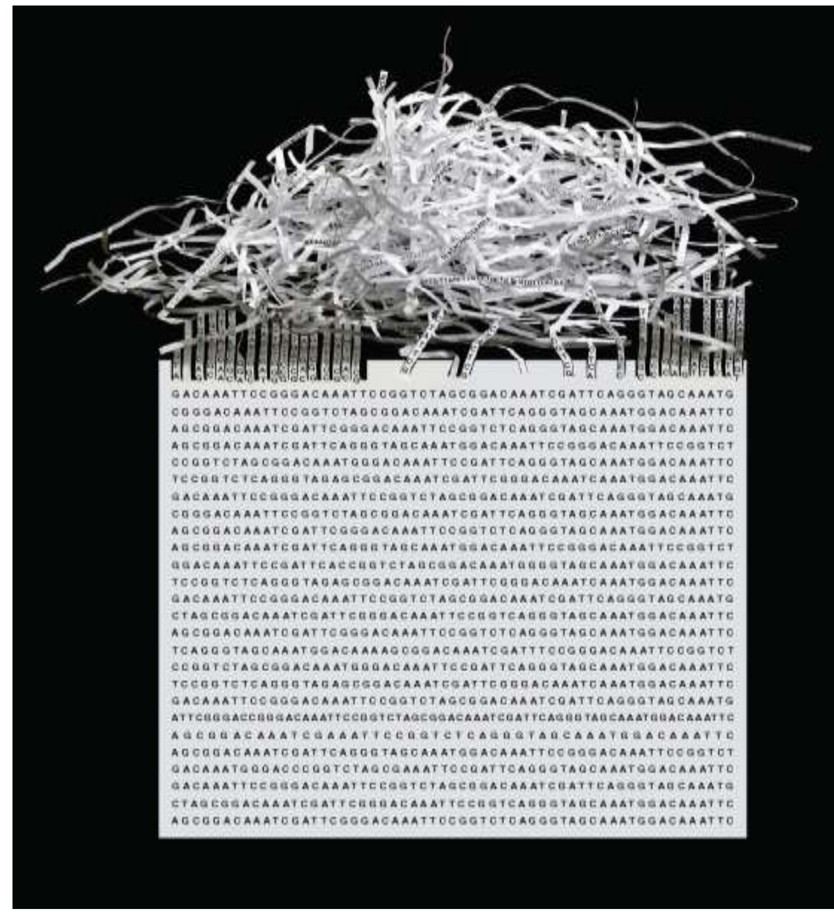
Deconstruction

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

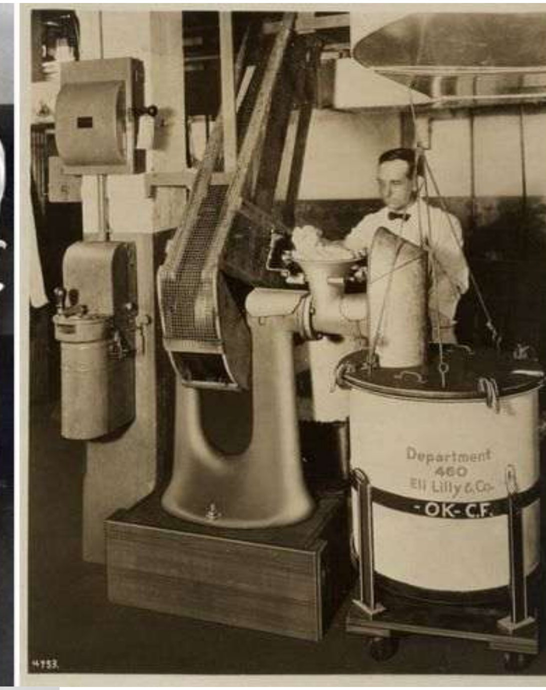




Insulin production: early versus modern

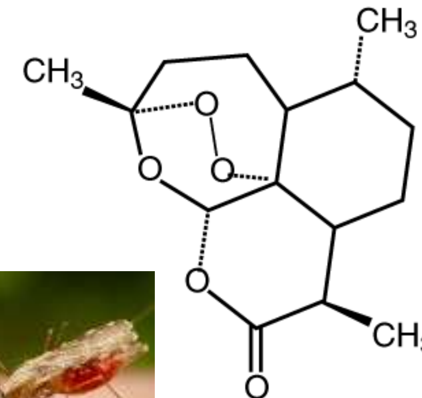
- 1920s: from pancreases taken from slaughtered cows and pigs

- 1978: Genentech produced the first synthetically manufactured insulin creating miniature "factories" by inserting the human insulin gene into bacterial DNA.

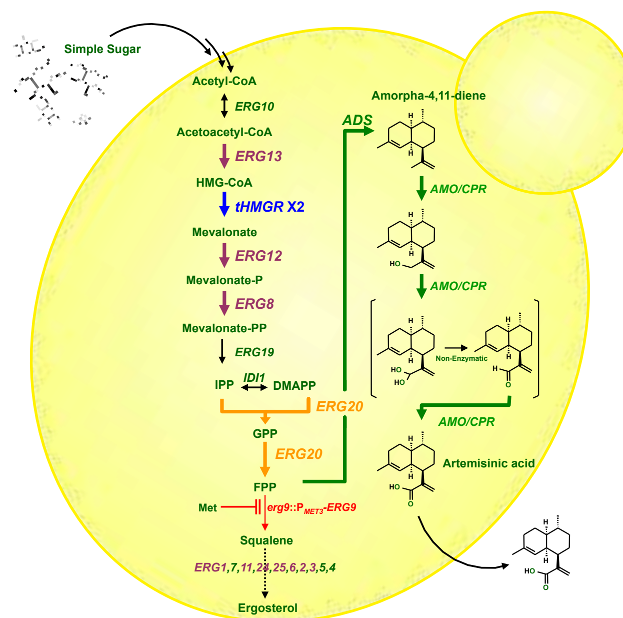


Artemisinin production: early versus modern

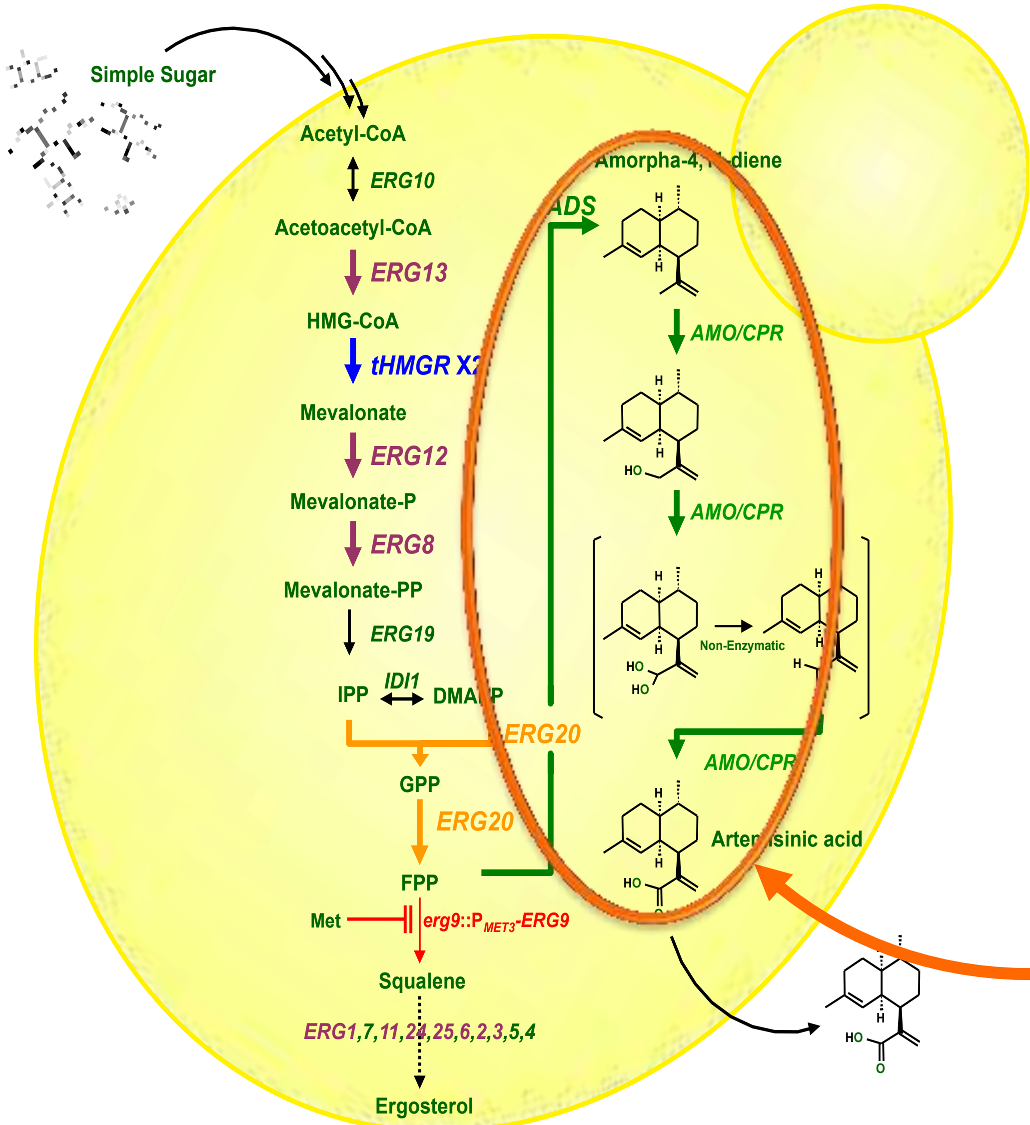
- 2003-2013: Artemisinin harvested from plants, subject to large swings in price and availability



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



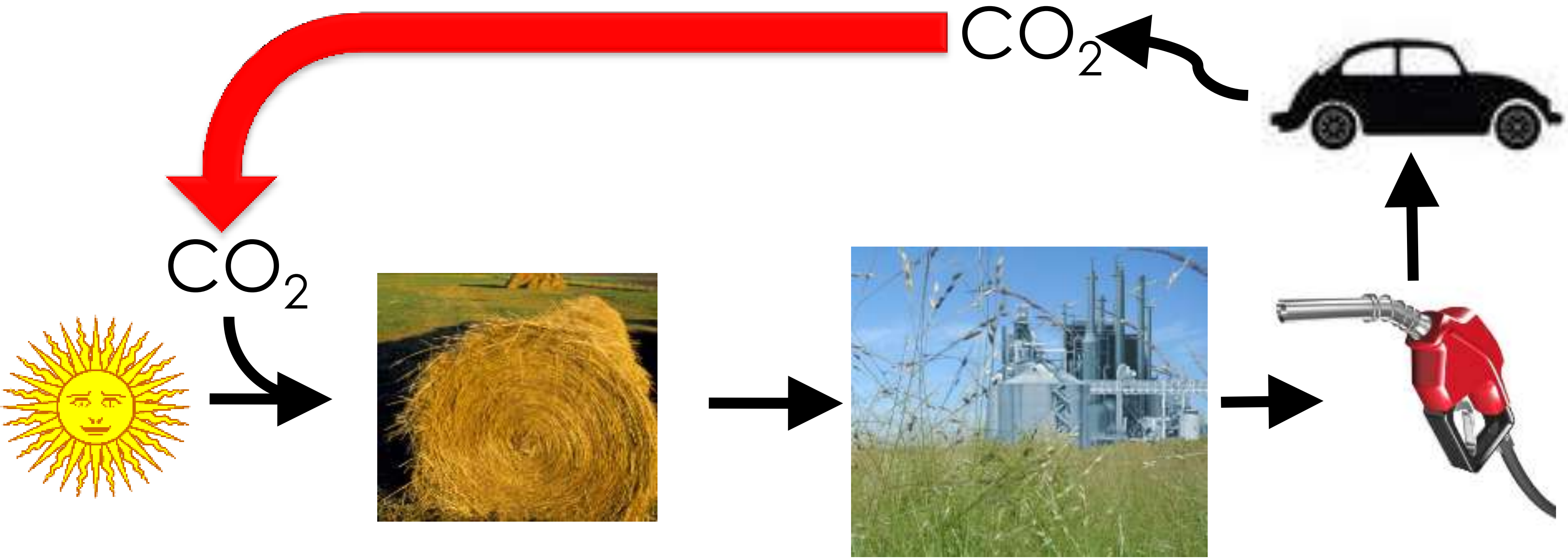
Genes responsible for artemisinin biosynthesis transferred to yeast



Artemisinin ready for tableting

Other Opportunities

Carbon-neutral fuels from non-edible plant biomass

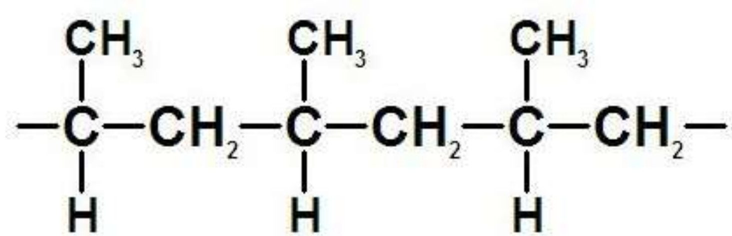


Joint BioEnergy Institute

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

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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

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Domestication is a breeding process that encourages desired features and represses undesirable features to customize an organism.

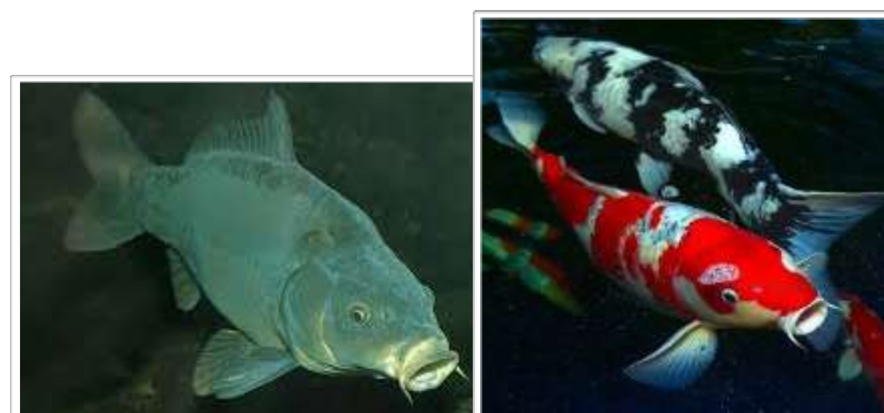
Domesticated Animals

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

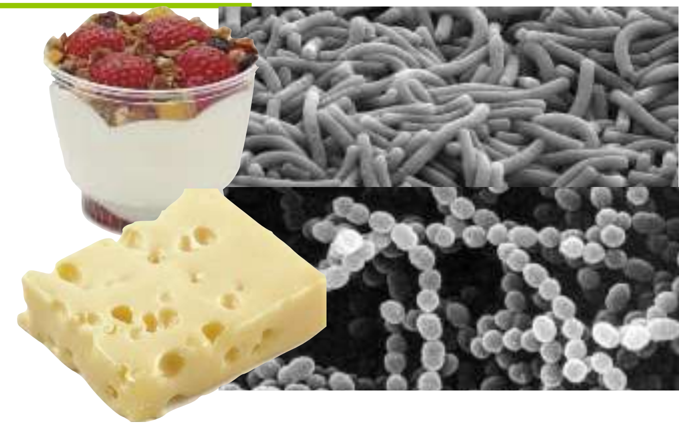
Zea mays 12,000 years

Daucus carota 1,000 years

Prunus amygdalus 5,000 years

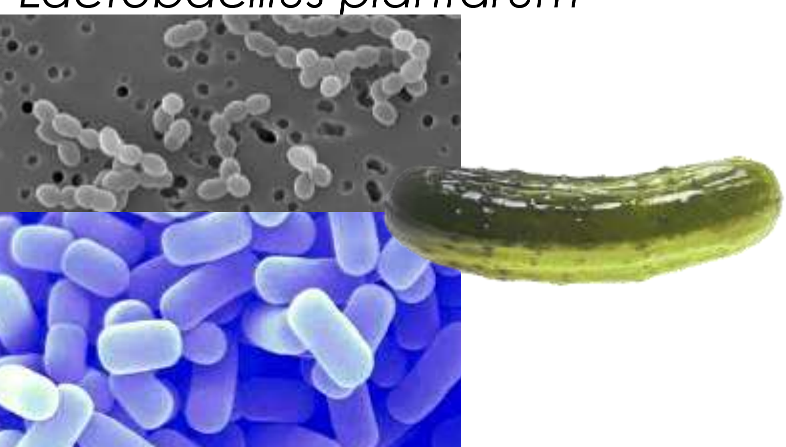
Domesticated Microorganisms

Saccharomyces cerevisiae 6,000 years

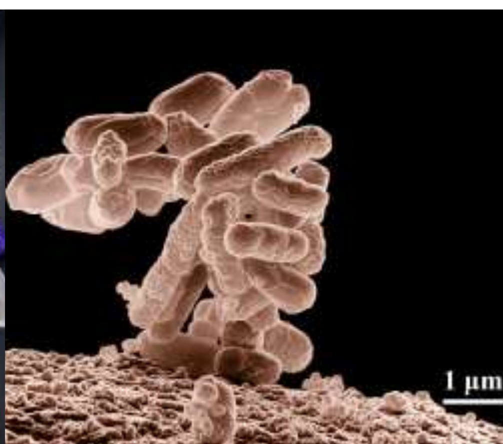


Lactobacillus bulgaricus
Streptococcus thermophilus 7,000 years

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 <u>not</u> 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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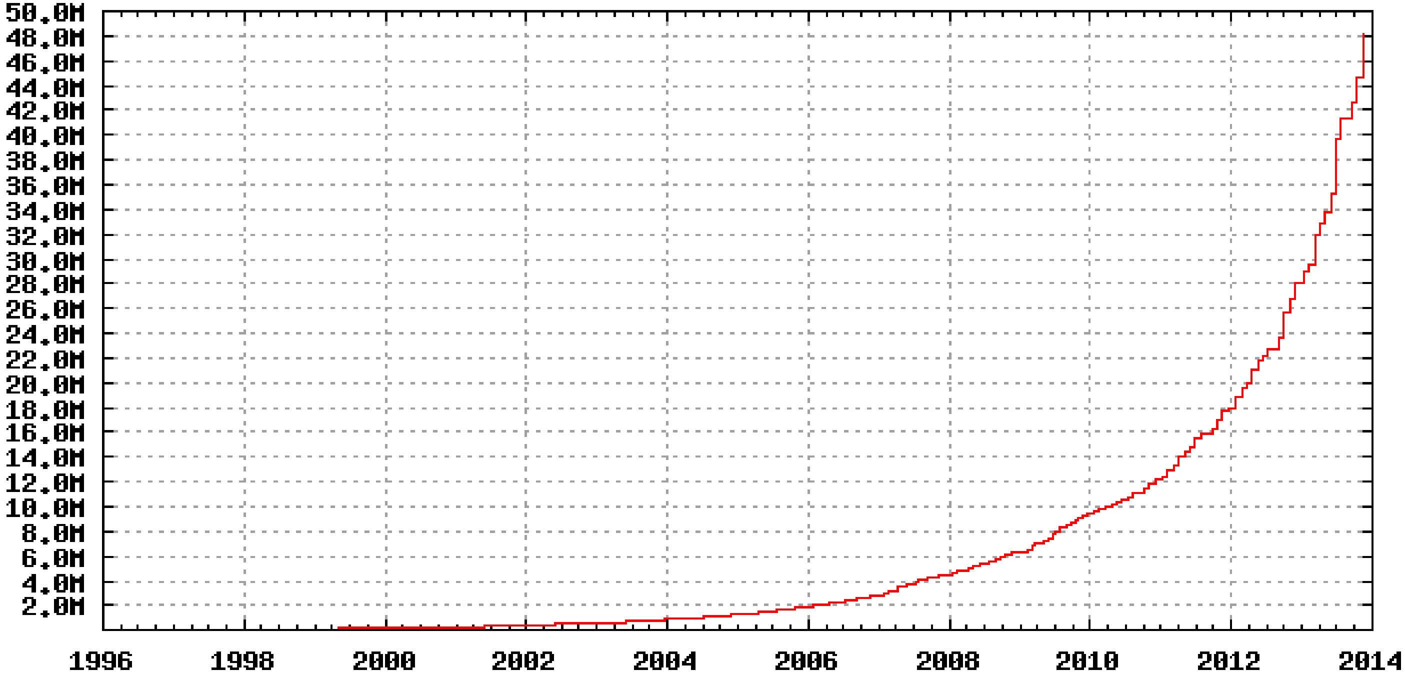
Synthetic Biology-Enabled Science

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

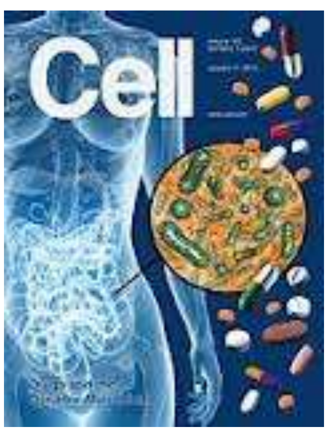
Top 200 Brand Name Drugs by US Retail Sales in 2010

Compiled and Produced by the Njardarson Group (The University of Arizona): Daniel J. Mack, Melissa L. Weinrich, Edon Vitaku, Jón T. Njarðarson

Harnessing nature's potential

Breakdown of plant material

Oil Degrading Enzymes



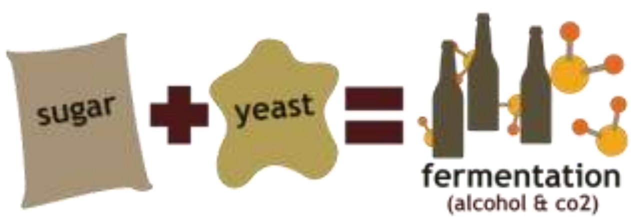
Regulate health and fight disease

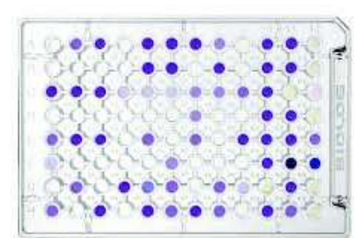
What exactly are we doing ?

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

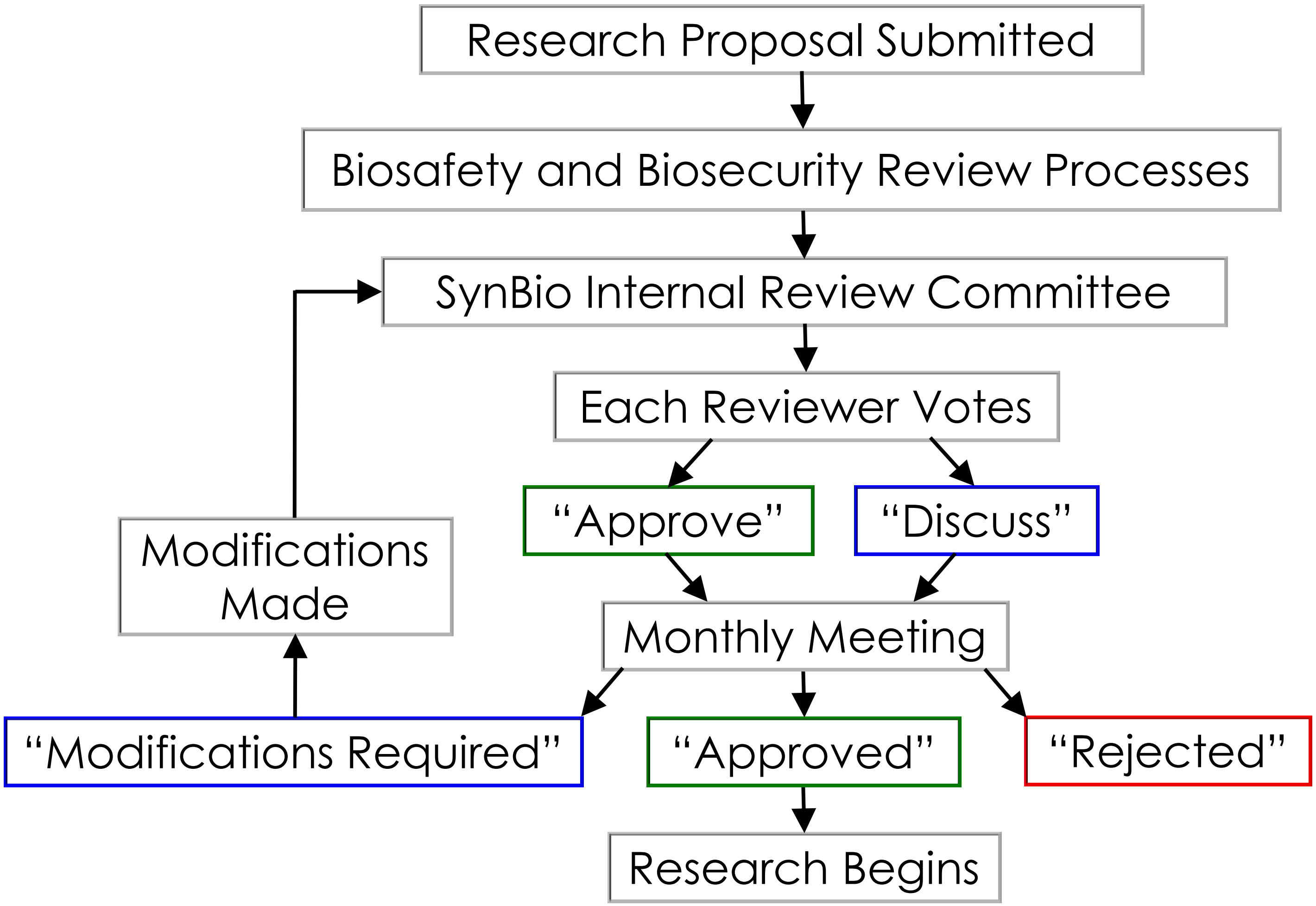
SynBio Internal Review Committee

- 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 faciliate replication

Review Process



Web-based Review System