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Synthetic Biology Emerges as Key to Biofuels Future

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Amaizing Microbes

Synthetic Biology Emerges as Key to Biofuels Future

By Amanda Lyle
BioWorld Perspectives Managing Editor

Converting cellulose quickly and cheaply into biofuel may be feasible any day now — what remains to be seen is who will be the first to use synthetic biology to create an organism capable of such a dramatic step.

“There is no technical barrier to synthesizing plants and animals, it will happen as soon as anyone pays for it,” said Drew Endy, an engineering professor at the Massachusetts Institute of Technology, as quoted in ETC *Group’s Extreme Genetic Engineering: An Introduction to Synthetic Biology*.

The Boston Globe called synthetic biology a science “so new that even Harvard does not yet offer a formal course in it.” (One is now planned for later in 2008.) Although a new field, companies engaged in synthetic biology (also called synbio, synthetic genomics or systems biology) are springing up rapidly, and the industry is already solidifying.

According to Brent Erickson, vice president of the Industrial and Environmental Section at the Biotechnology Industry Organization (BIO), synbio is still in its infancy, but it seems to be growing quickly in terms of importance to both healthcare and industrial spaces.

Although there are synthetic biology applications in healthcare, some of the most exciting developments are in industrial biotech. Using synbio for biofuels could result in increased efficiency and decreased cost — the keys to biofuels becoming a transportation fuel reality.

It takes much more energy to break down cellulose (from switchgrass, corn stover and wood) than it does to break down the sugars commonly converted to ethanol. Successfully engineering microbes will open up a variety of feedstocks for use in renewable fuels. According to ETC Group’s report *Extreme Genetic Engineering*, “The synthetic biology approach is to custom design a microorganism that can perform multiple tasks, incorporating built-in cellulose-degrading machinery, enzymes that break down glucose, and metabolic pathways that optimize the efficient conversion of cellulosic biomass into biofuel.”

Synbio researchers are scanning microbes and enzymes to see how they can be modified and combined to perform new tasks, such as converting cellulose into biofuel. They are engineering microbes and enzymes that already break down plant matter to be able to do it more efficiently, and to be able to convert it to other substances.

Some of the initial efforts in synbio focused on Clostridia such as *Clostridium acetobutylicum*. This bacterium can ferment sugars into butanol and ethanol, and could perhaps be modified to secrete cellulases. *C. acetobutylicum* and other Clostridia can digest lignin, cellulose fiber, starch, sugar and other biomass.

The U.S. government and venture capitalists have already poured millions into the industry. June 2004 brought the world's first synbio conference. Housed at the University of California, Berkeley, SynBERC is a multi-institutional research effort. BP plc in November 2007 announced $500 million for an Energy Biosciences Institute (EBI) for research on biotechnology's use in the production of biofuels; part of the research will be focused on the use of synthetic biology in the production of lignocellulosic fuels.
The majority of research is being conducted by private companies.

Amyris Biotechnologies Inc. was founded by Jay Keasling, a UC Berkeley professor who has been called "the world's most famous synthetic biologist."

The company is engineering microbes to produce biofuels. In addition to a project it has for artemisnin for the treatment of malaria, Amyris is working on gasoline and diesel substitutes. Its focus is on the creation of new metabolic pathways in microbes.

Pasadena, Calif.-based Gevo Inc. is using *E. coli* to produce butanol, a process it licensed from James Liao, a chemical engineer at the University of California, Los Angeles. Unlike ethanol, the fuel does not mix with water, so it can be transported in the existing petroleum transportation infrastructure.

E. coli does not naturally produce butanol, but it can be modified to produce it, and it has the added benefit of fast growth. To make it work, scientists diverted some of *E. coli's* metabolites (keto acids) into alcohol production. They inserted a gene from a microbe that is often used in cheese production, as well as a gene derived from yeast that coverts the organic compound aldehyde into butanol. Further tweaking allowed for increased efficiency.

According to Gevo, another added benefit of this process is that the biochemical pathway for the creation of isobutanol can be transferred to other microbes. Gevo is currently investigating other microorganisms for feasibility in biofuels production. For commercialization, the process must still become faster and the microbes must increase their tolerance to isobutanol, which can be toxic to them.

San Carlos, Calif.-based LS9 Inc. is engineering bacteria, with hopes of incorporating gene pathways that are used by other organisms, which can make hydrocarbons for fuels. When bacteria consume sugars, they naturally convert them into fatty acids, which in turn, are quite similar molecularly to diesel fuel. A few changes to these bacteria, and diesel-producing strains are created.

Unlike ethanol, hydrocarbon fuels would be able to use existing transportation infrastructure and engines. In addition, the company's final product has 50 percent more energy content than ethanol.

LS9 DesignerBiofuels are customized to be similar to petroleum fuels. The company has created industrial microbes that can convert feedstocks to "drop in compatible" hydrocarbon-based fuels. This allows LS9 to control the structure of its fuels, as well as how they function.

CEO Robert Walsh spent 26 years at Shell before going to LS9, which was founded in 2005 by Stanford University plant biologist Chris Somerville and Harvard University geneticist George Church.

Synthetic Genomics Inc., based in La Jolla, Calif., aims to create synthetic microbes that can inexpensively convert cellulose into fuel. These "bugs" would be able to excrete fuels like ethanol and hydrogen.

The company's president, Aristedes Patrinos, was an associate director at the U.S. Department of Energy's Office of Biological and Environmental Research, and is credited for the mention of switchgrass in former President George W. Bush's 2006 State of the Union address.

J. Craig Venter was the first person to sequence the entire genome of a living organism (*Hemophilus influenza* in 1995). He and his team were also the first to create a virus from scratch. In June 2007, he added another achievement: the first bacterial genome transplantation that changed one species into another.

In January 2008, a team of researchers from the J. Craig Venter Institute announced they had created the largest man-made DNA structure, which was created by synthesizing and assembling the base pair genome of *Mycoplasma genitalium* JCVI-1.0. It was created by chemically making DNA fragments, them using homologous recombination to build the chromosome from large subassemblies. Venter's company, Synthetic Genomics, funded the research.

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