GEN Genetic Engineering & Biotechnology News

Nov 15 2008 (Vol. 28, No. 20)

Feature Article

Synthetic Biology Finds a Niche in Fuel Alternatives

Advanced Engineering Tools Facilitate Production of Next-Generation Biofuels

Elizabeth Lipp

Synthetic biology refers to both the design and fabrication of biological components and systems that do not already exist in the natural world, and the redesign and fabrication of existing biological systems. As tools are developed to hone and refine this technology, researchers across multiple disciplines are finding novel applications for it.

"There is a lot of interest in this space—synthetic biology is important for a lot of reasons, explains Kareem Saad, vp of marketing and business development at Codon Devices. "Introducing engineering principles of design, modularization, and standardization to biology promises to revolutionize the way we make fuels and consumer products that rely less on crude oil and are less damaging to the environment, can be a game-changer."

While industries are taking advantage of the pharmaceutical applications of synthetic biology, immediate global concerns such as the economy, global warming, and creating renewable sources of energy have propelled synthetic biology to the forefront of research.

"Everyone is looking for the most economic solution," points out Sarad Parekh, Ph.D., vp R&D at SunEthanol. "Everyone will get there, because economics will drive it." But timing is crucial, and current oil reserves finite. Nevertheless, Jack D. Newman, co-founder and svp research at Amyris Biotechnology, notes that you can't schedule a breakthrough, no matter how much one is needed.

"There are things we can do now, there will be things we can do in three years, and then five years, and then ten years, but the truth is, we really don't know when the breakthrough we need is going to happen," adds Newman. "How fast can you get through proof of concept? You are dealing with compressed timelines. There is a lot of enthusiasm, but the breakthroughs will happen when they happen—it's very hard to predict."

Actually, finding the next generation of fuel presents a twofold problem: having a renewable source, and reducing our carbon footprint and emissions contributing to global warming.

Better Fermentation

One company that provides the raw material for the creation of biofuels is Agrivida, an agricultural biotech firm that creates renewable, biomass-based alternative fuels and raw materials. "We are working upstream, making plants that are more easily degradable, primarily switchgrass, sugar cane, and corn," states R. Michael Raab, founder and president. "We are focused on nonfood crops and crop residues that are degradable into fuel."

Agrivida's seed and process technologies allow the entire plant to be converted into biofuels as a result of improved liquefaction and saccharification characteristics. Liquefaction and saccharification are the steps by which corn is broken down into small sugars. These steps use common enzymes such as amylases and cellulases to break down the crop. “The result is a product that is more fermentable and cost effective to convert to fuel,” adds Raab.

Last year, Agrivida partnered with Codon Devices. During the first phase of the collaboration, Codon and Agrivida scientists successfully designed and engineered protein switches that can be used to activate an enzyme expressed in an inactive form. The successful effort to further develop Agrivida’s GreenGenes technology highlights the computational modeling and protein engineering components of Codon Devices’ BioLOGIC Engineering.

“Focusing on engineering biologically based products with partners is the direction we’re heading in,” explains Saad. “Our platform uses an integrated suite of sophisticated computational tools, high-throughput biological construction, and screening technologies to engineer proteins and pathways more rapidly and cost-effectively than other currently available technology.”

Next Generation of Biofuels

Gevo develops advanced biofuels technology based on butanol and its derivatives. “The magic isn’t in the biology alone,” according to Pat Gruber, Ph.D., CEO. “It’s in the chemistry, fermentation, processing, and genetic engineering all together; knowing what tools you need, and having the tools to make it happen.”

Dr. Gruber points out that three critical pieces of technology have helped Gevo produce these on a commercial scale. “We have a group that’s been working on this for 20 years or longer. Metabolic engineering of suitable host organisms make it possible to use carbon and energy efficiently for fuel production. Process engineering makes it possible to lower product separation costs and chemistry to produce valuable hydrocarbons.”

Gevo operates with economy in mind, Dr. Gruber insists—the main point being that partners should be able to use the equipment they have with a minimal retrofit. “That takes a lot of risk out of the capital equation,” he says. “One hundred percent of our raw costs go to product. We’ve solved the production issues. We have low capital cost. The combination of synthetic biology with chemistry does a good job of making this simple. We know that it works.”

Two other companies working in the metabolic engineering space are Mascoma and LS9. Mascoma recently received $26 million in DOE funding, which will be applied toward the development of a cellulosic fuel production facility that uses nonfood biomass to convert woodchips into fuel. Mascoma’s production facility is expected to produce 40 million gallons of ethanol and other valuable fuel products per year.

LS9 developed new metabolic pathways that efficiently convert fatty acids to a broad portfolio of petroleum replacements. It also discovered and engineered a new class of enzymes and their associated genes that catalyze the efficient conversion of fatty acids to hydrocarbons. They recombinantly produce hydrocarbons (oxygen-deficient biocrudes), fatty acid alkyl esters (biodiesel), and a variety of industrial chemicals from sugars via fatty acid biosynthesis.

The fatty acid biosynthetic pathway has evolved over millions of years to be nature’s energy-storage mechanism and is highly efficient in terms of energy conservation. The company believes that it is the most cost-, resource-, and energy-efficient pathway for producing hydrocarbon biofuels and petroleum-replacement products. LS9 has launched a pilot program this year and plans to be producing biofuel on a commercial scale in three to five years.

Doing Well by Doing Good

According to Newman, part of Amryis' aim is to quickly deliver its renewable fuels to market and rapidly achieve the scale needed to make a difference globally, with plans for commercially available fuel by 2011. "No Compromise™ fuels are renewable fuels that demand no sacrifice in performance or penalty in price, and offer a superior environmental profile by reducing lifecycle emissions of 80% or more compared to petroleum fuels," he explains.

The No Compromise fuels will be developed using Amyris' GreenLane technology. Using sugar cane produced in Brazil, Amyris has developed a technology platform that enables it to redesign yeast organisms to act as living factories that can transform sugarcane into hydrocarbon renewable fuels such as Amyris' renewable diesel and jet fuel. They will be delivered to consumers using existing petroleum distribution infrastructure and will work in today's engines, the firm claims.

For right now, fatty acid ester is being used and its not the best fuel available. Ethanol is not really energy-dense enough for jet fuel. "In creating diesel from sugar cane, we've discovered that cellulose looks promising. Our pilot plant in Emeryville (CA) will open next month, and we will break ground in Brazil later this year. We plan to produce on a commercial scale by the beginning of 2011," according to Newman.

Green Chemistry

Codexis' technology enables solutions for cost-effective, efficient, and environmentally sound production of pharmaceuticals, transportation fuels, and industrial chemicals, reports David Anton, Ph.D., vp, bioindustrials R&D. The company focuses on biocatalysts—enzymes or microbes that initiate or accelerate chemical reactions. At Codexis, biocatalysis is used to design faster, less costly, and greener chemistry-based manufacturing processes in the life science and energy industries.

According to Dr. Anton, Codexis' technology makes it possible to customize enzymes capable of selectively and efficiently performing a desired chemical process that doesn't exist in nature.

"DNA shuffling is part of a directed evolution program to manipulate the DNA blueprint of an enzyme," explains Dr. Anton. "Starting with a diverse set of genes that encode for variations of the enzyme catalyst, Codexis recombines or shuffles these DNA sequences to create new variants. Using sophisticated high-throughput screening methods, novel biocatalysts with desired improvements are selected and these improved variants can then be put through the process again until a highly efficient biocatalyst is created that meets or exceeds targeted performance characteristics."

Dr. Anton adds that bioinformatics plays a big role in creating biofuels. "The company's technology platform includes millions of mutated enzymes and a dozen or more different reaction platforms. We can screen compounds against actual enzymes and our databases."

Bioinformatics capabilities allow Codexis' scientists to accelerate its directed evolution process by predicting the amount of gene shuffling and specific mutations needed, along with the likelihood and length of time for reaching a target.

"I am a practical person," continues Dr. Anton. "Academic pursuits are all well and good, but biofuels are something that we need today, and this is a good way to put the knowledge and tools to use. We are doing something that the market needs. When we are successful, there will be billions of gallons of fuel, and it will be renewable."

The company has aggressive milestones with Shell, its partner in developing next-generation nonfood transportation biofuels, and “we’ve been meeting them. We opened a new facility in Hungary earlier this year focused on large-scale fermentation. There is excellent academic infrastructure support in that region that supports our efforts. This is key in driving this to scale and moving this forward,” Dr. anton adds.

Superbug Cleans Up

SunEthanol was recently awarded a $750,000 Phase II Small Business Technology Transfer Program contract. This award, made as a follow-up for successfully completing a year-long Phase I grant, will allow SunEthanol to continue pioneering a process that converts plant waste into clean ethanol fuel in one simple step, saving time and money over the traditional two-step cellulosic conversion process, the company claims.

This latest DOE contract will help SunEthanol commercialize its Complete Cellulosic Conversion process. The company is developing a simplified cellulose-to-ethanol process, centered around its novel Q Microbe™, to decrease the cost of ethanol production from a variety of renewable feedstocks such as corn stover and other plant wastes.

“We have the benefit of having a really unique organism, a new microbe that is giving us a good starting point—this native organism is so primed for the job,” notes Dr. Parekh. “The Q Microbe™ has exhibited a 20-fold increase in efficiency since the beginning of this year.”

Dr. Parekh explains that the enhanced QMicrobe is able to liquefy and process plant wastes quickly and efficiently. “What’s unique about the QMicrobe is that you do not need to add external enzymes to modify. This expresses all the properties to produce ethanol. We’re researching and developing the commercial possibilities.”

Dr. Parekh also notes that collaboration is key, and the ultimate benefit will be the commercialization. “Ethanol will not be supplied by one player only. We do have an advantage in having the QMicrobe—we believe that the current technology can be mature and commercialized in a year or two.”

Looking Ahead

In finding alternatives, time is of the essence. Most of these companies are launching their pilot programs now, with the average time to market being three to four years.

“A lot of what we are doing is not that hard and for a long time there wasn’t really a demand,” comments Dr. Gruber.

“Industrial biotechnology is not that common. But now, there are a lot of people working on this. People know how to do this, have been doing it for a long time, and now that a lot of people are working on this it is easier to make progress much faster.”

HOME | SUBSCRIBE