Altered Yeast Strains Hold The Promise Of Expanded Biofuel Supplies

Indiana University
Indiana University Research and Technology Corp.

Most people don't spend a lot of time thinking about yeast, but in fact, it plays extremely important roles in our lives. A singlecelled fungi with hundreds of variations, it digests sugars in plant materials, in the process leavening flours into breads and fermenting grapes into wine, grains into beer and hard alcoholic beverages.

And, as it turns out, helping deal with the world's energy crisis. It's an essential component in the manufacture of ethanol, the biofuel made from renewable crops and added to gasoline to reduce the nation's dependence on oil.

If Mark Goebl, Ph.D., has his way, the genetically modified yeasts he's developed will dramatically expand the availability of ethanol. A professor of biochemistry and molecular biology at the Indiana University (IU) School of Medicine, he and several colleagues founded Xylogenics Inc. in Indianapolis to develop the technology.

“Right now,” he says, “we’re focused on helping corn ethanol manufacturers expand their production. In the long run, we see ourselves providing the missing element — more efficient yeast — that will make manufacturing cellulosic ethanol practical for biofuel companies. This will significantly increase the amount of ethanol that can be created.”

Ethanol, the most common type of biofuel, is an alcohol obtained by fermenting sugars and starches in plant materials. Although nearly all gasoline sold in the United States today is 10 percent ethanol, it’s corn ethanol, made from the starch in corn kernels, a limited source. The cob, stalks, leaves and other cellulosic material are often left on the ground as waste.

To Goebl, those cellulosic “waste” materials represent the opportunity to create new and much more abundant sources of ethanol. But it’s not practical yet.

“People we’ve talked to say the missing piece in cellulosic ethanol production is the yeast,” says Xylogenics Founder Mike Neibler. “The strains of yeast that are currently available work on the starch in corn kernels but not on the cellulosic material in other parts of the plant in a way that makes it financially feasible.

“And cellulosic ethanol is much harder to make than corn ethanol,” he adds. “You have to pretreat it, expose it to expensive enzymes to convert it to sugar and then add yeast to ferment it. Currently, yields are low — 7 to 8 percent.

“We expect our technology to help make it workable by increasing the production yield, speeding up the process and reducing enzyme needs.”

Understanding Yeast

As a cancer researcher, Goebl’s focus on cell division would seem to be far away from the subject of biofuels. However, yeast connects the two.

> *"Yeast is one of those organisms, like fruit flies, that constitutes a model system for studying biological processes, such as how cells grow and divide," he says. “As we worked with yeast for biological insights, we began to understand the things that yeast cells eat — and that one of those things could be cellulose.*

“Once we found that, we realized that it could be important for nonmedical uses. We kept studying it.” We is Goebl and three graduate assistants working with him in 2005-06: Ross Cocklin, Josh Heyen and Cary Woods. The issue is that yeast has an overwhelming preference for the simple sugar glucose — when it eats, it uses up every bit of glucose available before moving on to other sugars, even abundant ones like those in other plant materials. By working with the genome, they found that removing specific genes made cells able to use xylose and other key sugars in cellulosic materials at the same time as glucose. And, they found that the enzymes breaking down the complex sugars also became much more efficient.

“It took a while to understand, but once we did, making it happen wasn’t hard,” Goebl says. “The key part was figuring it out.” Notes David Wilhite, M.B.A., senior technology manager in IU’s Office of Technology Commercialization, “One day, Mark and his team were looking over their data and one of them had the thought that perhaps they ought to patent their findings.

“They brought their results to the technology office and we applied for the patent,” he says. “Forming a company made sense as a way to develop the technology as quickly as possible.”

The company was established in late 2008 with Goebl and his assistants as founding partners, and the technology licensed to it in mid-2009.

Goebl lauds Wilhite for his assistance. “David was instrumental in making our company happen, helping us through the legal steps, finding the right people, developing a business plan.” They named it Xylogenics for xylose, the second most abundant sugar in cellulosic material.

Goebl’s original research and his biofuel offshoot received support from the National Science Foundation. Ongoing research was supported by money raised once Xylogenics was formed.

Building a Company

“We established the company at the worst time possible — the height of the recession,” notes Neibler, a chemical engineer by training whose background includes expertise in startup companies — Xylogenics is his sixth.

“My first job was to get funding,” he says. “I had a list of 200 prospects. It’s amazing how many nos I heard, that, ‘The technology looks good, the business plan looks good, we’re not investing right now.’

“We couldn’t have survived if we hadn’t gotten seed money from the School of Medicine. We finally got some funding from the Irish Angels, a group of Notre Dame University alumni.”

Initially, the new company was based at the School of Medicine, with Neibler the only employee. Goebl describes himself as “either one of the owners, or a volunteer.” Heyen, having earned his doctorate, has joined the company as a full-time employee, and the organization has moved into offices in IU’s incubator, the Emerging Technology Center. Cocklin is pursuing postdoctoral studies in plant genomics and Woods is finishing up his doctorate.

“Our strategy is to be a research and development company, to sublicense intellectual property,” Neibler says. “We’ve had people in Indiana, seeing the prospect of jobs, urge us to establish a manufacturing operation. But we don’t feel it would be economically feasible. It would change the nature of what we’re trying to do, and it would certainly delay introduction of our product for several years.”

Instead, the company sought to form an alliance with one of the largest companies that serve the global yeast market. In mid- 2010 they finalized an agreement with Milwaukee-based Lallemand Ethanol Technology to work on commercializing genetically enhanced ethanol-producing yeasts. Their first efforts will focus on new corn ethanol technology. Lallemand will utilize Xylogenics technology to manufacture and market modified yeast.

Cellulosic Ethanol Still in the Future

“When we started out, our vision was about the next generation of ethanol, cellulosic ethanol,” Neibler notes. “It still is, but, in the short-term, we found we could make a contribution to the production of corn ethanol.

“We went to a couple of corn ethanol manufacturers and talked to them. After looking at their operations, we saw ways we could increase their production by 3 to 5 percent. We didn’t consider it a huge number, but when we told them they practically fell out of their chairs. For them, it was a big deal.”

Specifically, Goebl points out, they saw a way to speed production time with Xylogenics yeast by 25 percent while using less enzyme. It’s a savings that turns a 40-million-gallon capacity into a 50-million-gallon capacity.

Since currently there are some 200 manufacturers producing corn ethanol and none at all producing cellulosic ethanol, focusing on corn ethanol makes sense. Revenue from that business can support research on cellulosic ethanol technology, with the expectation that the cellulosic industry will come of age in the foreseeable future. Several large corporations are presently constructing cellulosic manufacturing plants, anticipating cellulosic ethanol becoming a profitable product in the futureand prepared to live with losses while the technology develops.

To Goebl, the ability to process sugars other than glucose is essential in making ethanol a practical reality. Brazil, which relies heavily on glucose in sugarcane for ethanol production, can't produce enough of it. The United States has just approved usage of 15 percent ethanol for cars made since 2003, a 50 percent increase over the current level.

Goebl sees xylose as an important part of the future. Unused in corn ethanol production, it constitutes 25 percent of the sugars in corn stalks and leaves — currently treated as waste in corn ethanol agriculture — and represents an opportunity to significantly expand ethanol production. Neibler notes that corn kernels constitute a somewhat limited source for ethanol in its current form, since space to plant new corn acreage is limited, he says.

The Xylogenics team isn't solely committed to corn waste — sorghum, wheat and rye are all potential sources. Neibler speaks admiringly of switchgrass, the native grass that once covered the Midwestern prairies, which grows well, can be harvested twice a year, doesn't need pesticides or insecticides and is a great absorber of carbon dioxide.

For that matter, while ethanol occupies its attention at present, the company is looking at other potential yeast-related opportunities — including baking, brewing, distilling, and biochemical and biopharma production.

In the meantime, Neibler notes, the benefits of a shift to cellulosic ethanol will be enormous, including reduced dependence on foreign oil, lower carbon dioxide emissions, job creation and stimulation for the economy.

"The industry is waiting for advances in the fermentation process. That's us. We feel we can be a game changer."

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