

Natural Enzyme Helps Farmers Feed The World

BioResources International Inc. North Carolina State University





At this writing, the world population counter on the website of BioResource International (BRI) reads 7,109,797,785 (but only for half a second). To feed a projected world population of 9.1 billion by 2050, the Food and Agriculture Organization of the United Nations estimates food production will need to increase by 70 percent.

Meeting the world's increasing food demands in economically and environmentally sustainable ways is a primary driver for BRI, an agriculture biotechnology company spun out of North Carolina State University (NCSU), and based in the Research Triangle Park in Durham, NC.

BRI's flagship product called Versazyme is a feed additive for poultry and swine that improves the digestibility of protein, which in turn lowers farmers' feed costs and reduces the environmental impact of animal waste.

"This could be a real world-changing technology that helps farmers be more efficient and provide more poultry and pork to people, especially in Brazil, India and China," says BRI co-founder, chair and CEO Giles Shih, Ph.D.

Stumbling on a Solution

Giles' father, Jason Shih, now retired professor of Poultry Science at NCSU, was studying new strategies for waste management and biogas production when he noticed that chicken feathers shed into manure and moved to a waste digester mysteriously disappeared during the digestion process, despite being made of a tough and insoluble protein called keratin. Curious about what bacterial process could break down keratin — the same protein found in nails, hooves and claws — the professor and a graduate student went on the hunt for the responsible microbe.

What they found was a unique strain of bacteria known as *Bacillus licheniformis* that secretes an enzyme called keratinase capable of degrading whole feathers. Jason and his research team isolated the bacteria and identified the gene-coding sequence for keratinase, ultimately filing six patents (with the help of NCSU's Office of Technology Transfer) around the discovery and its application improving poultry feather meal, a feed supplement made from chicken feathers.

Father and Son Team

Giles initially followed in his father's footsteps as an agriculture science major in college, but quickly switched to microbiology. He had just completed a doctorate in the field and was considering his career options when a venture capitalist called on him to help evaluate some technologies being spun out of academic research institutions into biotechnology companies.

"That was something I had never considered," says Giles, who broached the idea of licensing his father's patents from NCSU.

"My father has always been very applied in his work, and some of that has rubbed off on me," says Giles. "I had just finished my Ph.D. We thought, 'How much harder can it be to start a company?'"

The father and son team, along with a former graduate student of Jason's named Jeng-Jie (JJ) Wang, founded BRI in 1999 and licensed all six of Jason's patents in 2000.

"We each had different strengths that we brought to the table," says Giles. "My father serves as senior advisor, JJ as the technical expert and I do the day-to-day managing and capital raising. We had the science figured out, but the sales and marketing challenges were more difficult to overcome."

Best-Laid Plans

"Initially we thought we would create a better feather meal product," says Giles. "But in the course of research and development, we found that if you add the enzyme to chicken feed, the chickens grow faster and healthier, and the market for feed enzyme additives was far larger than the market for improved feather meal."

In 2001, the company tested Versazyme as a feed additive for improving the growth of chickens that are bred for meat production, otherwise known as broilers. The study found that broilers fed a low protein diet supplemented with the enzyme grew as large as birds fed a standard diet.

"Broilers require less feed, which lowers feed costs for farmers," says Giles.

The enzyme additive also has value for the hens producing eggs, or layers. With the Versazyme additive, farmers are able decrease the amount of protein in the layers' feed while maintaining their performance of one egg per day.

The company also discovered that the additive improves protein digestibility in swine, resulting in significant cost

savings in feed.

"It takes just six weeks to grow a chicken but as long as a year for pigs, so there is a potential for greater savings in feed costs," explains Giles.

Brewing Batches of Enzyme

BRI developed a way to produce mass quantities of the keratinase enzyme using fermentation technology. Today, this part of the manufacturing process is subcontracted to a vendor in Asia, which ferments the live organism in large tanks by adding nutrients such as starch and proteins and aerating the mixture. After two days, a drying process evaporates the liquid leaving behind a powdered form of the enzyme.

"The enzyme is grown in a fermentation broth similar to the process of brewing beer," says Giles.

The enzyme is then shipped to the United States, where it is blended with carrier and flow agents and packaged at a BRI facility in Apex, N.C. To distribute the finished product to its customers around the world, BRI chose Novus International, an animal health and nutrition company, as its global distribution partner in 2008.

Well-Timed Market Entry

The introduction of Versazyme to the market was well-timed.

"Farmers were looking for solutions like ours," says Giles. "Over the last 10 years, feed prices have gone up more than 100 percent. It's one of their biggest costs."

By increasing the chicken's ability to digest the protein in soybean meal — which along with corn, are the two main ingredients in animal feed — Versazyme enables farmers to reduce the amount of protein in their feed formulation by about 2 percent for an average savings of \$10 to \$15 per ton of feed.

"Our biggest demand is from countries outside the United States, because they have to import grains and soybeans," says Giles. "For example, China is a big growth opportunity for us."

In addition to feed costs, the disposal of animal waste and its environmental impact is a growing problem for large farming operations and nearby communities. Undigested nutrients in animal feed excreted in animal feces and urine find their way into the air and ground water, threatening both the ecosystem and human health.

Reducing Excess Emissions

"Incomplete digestion leads to nitrogen and phosphorous emissions that put excess ammonia into the environment," explains Giles. "Excessive phosphorus release from farms find its way into rivers and lakes, which in turn drives algae to grow very rapidly and consume oxygen in the water, causing fish to die in large numbers."

Giles said the U.S. Environmental Protection Agency is monitoring emissions out of large U.S. farming operations and considering mandates to reduce the release of byproducts into the environment. He added that the U.S. Food and Drug Administration is closely watching the use of growth-promoting antibiotics in animal feed, a practice banned in Europe within the last decade.

"Research done by investigators at NC State University has shown that adding Versazyme to the diets of layers can reduce the amount of nitrogen emissions in the manure," says Giles.

Upside Opportunity

Between 2008 and 2011, BRI went from producing a few hundred to a few thousand tons, posting revenue growth of 938 percent and earning the company a spot on Inc. magazine's 2012 list of the 500 fastest growing companies in the country.

"We've captured only a small percentage of the market, so there's a large upside opportunity for us," says Giles. "We credit much of our success to the support of NCSU and the department of Poultry Science, which we still collaborate with on trials, and an early grant and loan from North Carolina Biotechnology Center."

The biotechnology center was also an early supporter of Jason's research, awarding him with a \$166,000 institutional development grant to support a multiuser fermentation facility on the campus.

"We always tout BRI as one of our success stories," says Kelly B. Sexton, director of NCSU's Office of Technology Transfer. "Especially because they contribute economically to a business sector that's so important to our state."

Sexton says BRI is an example of a great partnership between a university and a startup.

"We've enjoyed an unusually good relationship with BRI because our goals have always aligned," she says. "We want them to be successful, and the company has continued to be supportive of the university."

From just 300 square feet of office space in the incubator (of NCSU's) Centennial Campus, BRI has grown into a 20employee company including an R&D facility where it is developing new products.

"We've pushed through the ups and downs and now we're profitable and growing," Giles says. "We have a product that creates jobs and impacts the world. And at the end of the day, I am proud to say we're helping to feed the world."

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