



GROWING PROFITS WITH MICROBES

Agriculture industry seizes on beneficial fungi and bacteria to help **THWART DISEASE** and increase productivity

MARC S. REISCH, C&EN NORTHEAST NEWS BUREAU

HUGH GRANT, chairman of the agribusiness giant Monsanto, calls microbes “the next major platform in agriculture that will drive yield and productivity beyond the seed itself.” And seed treatments incorporating those microbes, he says, are “the biggest near-term opportunity.”

Those declarations came at a press conference last December at which Monsanto and fermentation expert Novozymes revealed a strategic alliance focused on microbial pesticides and growth-enhancing seed treatments. Monsanto estimated the global market for such remedies at about \$1.5 billion annually and growing quickly.

The two big firms are not the first to see opportunities in microbial products. Over the past few years, seed, crop protection, and fertilizer firms including FMC, Bayer, and Agrium have formed microbe-motivated alliances or acquired smaller companies with microbial technologies.

Start-up firms—among them investor-backed ventures such as BioConsortia, Marrone Bio Innovations, Green & Grow, and Advanced Biological Marketing—also

see opportunities in a field that until recently attracted little attention outside of the organic farming community. All see a fledgling business that could become another pillar of the agricultural industry along with fertilizers, pesticides, and seeds.

By creating a symbiotic relationship with roots and seeds, microbes confer benefits that make plants more efficient and productive. The high cost of developing new chemical pesticides, rising insect and weed resistance to chemical treatments, and growing regulatory pressures to limit chemicals in the environment all figure into the recently found interest in beneficial microbes.

“Everyone in the agriculture industry is looking at ways to improve yield, lower water use, and increase fertilizer uptake,” points out Marcus Meadows-Smith, chief executive officer of BioConsortia, a Cali-

BOUNTIFUL FMC microbiologists Xinxin Zhang (left) and Kristin West harvest roots of corn plants whose growth has been enhanced by a microbial stimulant.

fornia-based start-up that identifies and develops beneficial microbes.

Rhizobacteria and mycorrhizal fungi, for instance, form a relationship with plant roots that can increase crop biomass, sugar content, and

disease resistance, he notes. With the right microbes, scientists can “positively impact almost any plant phenotype,” he adds.

However, microbes, some of which are harmful, are no panacea. The benefits some microbes bring will vary with the health and variety of bacteria, fungi, and other microorganisms already in the soil, warns **Robert Harwood, CEO of CPL Business Consultants**, an Oxfordshire, England-based agricultural consulting firm.

Beneficial microbes are the probiotics of the plant world. Just as yogurt makers add bacteria such as *Lactobacillus* to promote human health and well-being, beneficial microbes are intended to enhance plant vigor and productivity.

Microbial treatments “could work well where soil is depleted because of flooding or drought,” Harwood says. But where the soil is healthy, treatments may have little effect, just as a healthy person is unlikely to

What is happening now is nothing short of the “industrialization of microbes.”

benefit much from probiotic supplements, he suggests.

Exceptions do exist, Harwood acknowledges. No matter the soil condition, adding nitrogen-fixing rhizobacteria helps leguminous plants take up more nitrogen. Inoculated into the soil with the seeds, the bacteria form a symbiotic relationship with plants such as soybeans and peanuts that helps them access the nutrient.

Even when soil would benefit from microbes, the challenge is getting them to work predictably, Harwood notes. Microbes' performance can vary depending on soil composition, temperature, and moisture, as well as the type of plant to which they are applied, he says.

BUT CROP PROTECTION firms say they can select and breed microbes that will perform reliably whatever the plant or soil condition. At least that's the intent of a year-old alliance between crop chemical maker FMC and fermentation expert Chr. Hansen.

Mark A. Douglas, president of FMC's Agricultural Solutions business, says the continuing regulatory pressure on pesticides figured into FMC's decision to form the alliance. At the time, FMC also bought the Center for Agricultural & Environmental Biosolutions, the microbial research unit of North Carolina think tank RTI International.

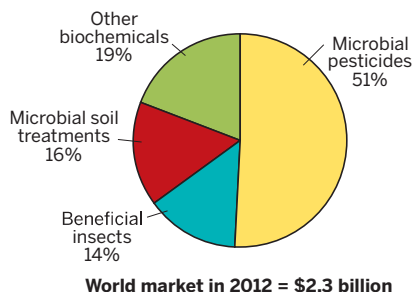
Both actions provide FMC with an opportunity to combine traditional synthetic chemistry with microbials, Douglas says.

FMC and Hansen had earlier partnered to develop Nemix C, a blend of *Bacillus subtilis* and *Bacillus licheniformis* that treats sugarcane roots. Recently released in Brazil, Nemix C helps the plants resist attack from nematodes and increases yield. Nemix C "has characteristics that would allow us to use it on other crops," Douglas says.

The first commercial products to come out of the new alliance will be in 2015, Douglas says. He expects the partners to ring up "multi hundreds of millions of dollars" in annual sales by the end of the decade.

Other big agricultural firms such as Bayer are also looking to microbes for productivity improvement and disease and insect control. Beneficial microbes are "a major platform for us at Bayer Research," along with chemicals

SMALL START Soil treatments are now just a modest slice of the agrobiologicals market.



SOURCE: Monsanto

and seed traits, says Jonathan Margolis, head of biologics research at the firm.

Bayer bought AgroGreen, a supplier of bionematicides and biofungicides, in 2009 as well as filamentous fungi expert Prophyta in 2013. Earlier this year it acquired Biagro Group, an Argentina-based maker of inoculants and growth-promoting microorganisms. Margolis himself joined Bayer in 2012 when Bayer bought AgraQuest, a maker of bioinsecticides and plant-growth-enhancing soil treatments.

Helping to propel interest in microbial treatments are new techniques to produce them "at scale and inexpensively," Margolis says. What is happening now, he adds, is nothing short of the "industrialization of microbes."

Using the techniques and know-how acquired in the AgroGreen acquisition, Bayer now sells Poncho/Votivo, a seed treatment that prevents early-season damage to seedlings and allows roots to develop before pests can strike. It combines a systemic insecticide and a *Bacillus thuringiensis* additive to provide corn, soybeans, and cotton with protection against black cutworm, wireworm, and aphids.

Margolis's boss at AgraQuest was Meadows-Smith, who sold the California-based firm to Bayer for \$425 million. Now at the helm of BioConsortia, Meadows-Smith has a goal to serve as a beneficial microbes R&D partner for big players. He hopes to start registering products for commercialization in 2016.

The firm recently raised \$15 million in funding from venture capitalists Khosla Ventures and Otter Capital. It also just opened a lab in Davis, Calif., with 15 researchers. The new facility complements a similar-sized operation in New Zealand, where the firm got its start.

INSTEAD OF ISOLATING individual microbes as others do, BioConsortia researchers develop a consortia of microbes by observing which ones affiliate with plants and improve yields, increase fertilizer uptake, or confer pest resistance, Meadows-Smith says. "Our model puts microbe research on its head. We select the phenotype, and the plant selects the microbes," he says.

Perhaps hedging its bets, Otter Capital is backing another beneficial microbe start-up, Green & Grow. Because researchers are just beginning to understand how microbes work in the soil and affect plant growth, "even a small firm can provide a significant amount of value," says Gary M. Nijak Jr., chief research officer of the Austin, Texas-based firm.

All told, Green & Grow has raised \$12 million from investors. The money will help the company advance and prove its technology, which is based on metabolites and stimulants derived and separated from microbes.

The firm's original technology was licensed from the Army Corps of Engineers, explains Chief Operating Officer Gregg Spivey. The corps was looking for a microbially derived soil stabilizer but didn't find one that met

BIOCONSORTIA



DISHY A collection of fungi and bacteria that could boost plant growth.

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its needs. Founders of the firm thought the product could help plant growth when they noticed material used for the engineering projects seemed to make vegetation thrive.

Nijak is hoping that agricultural chemical companies will combine Green & Grow's metabolites with their traditional insecticides, herbicides, and fungicides. “Many of the older chemicals are starting to lose efficacy,” he says.

AgriCen, which recently sold a controlling interest in itself to fertilizer maker Agrium, markets microbially derived products that aid fertilizer uptake in crops and enhance plant vitality. “It's not necessarily the microbes doing the heavy work, but the bioproducts they produce,” explains Brian Cornelious, director of applied sciences at AgriCen.

The firm's Accomplish LM and Titan PBA products are “biochemical fertilizer catalysts” that come from a blend of bacteria and fungi, according to Cornelious. Accomplish mixes with liquid fertilizers, whereas Titan blends with dry fertilizer and “makes phosphorus and nitrogen tied up in the soil more available to plants,” he says.

Investments by major firms such as Agrium, Bayer, and FMC in microbials are a validation of microbial research at academic institutions dating back more than 30 years, says Gary Harman, chief scientific officer of Advanced Biological Marketing (ABM), a privately held firm with several million dollars in annual microbial product sales. “Suddenly the big firms are getting into the microbial market where they had never been before. That's mostly because it is difficult and increasingly expensive to trial and register chemical pesticides,” he says.

A report from research analyst Michael E. Cox at the investment firm Piper Jaffray bears out Harman's assertion. In the report, published last year, Cox noted that it takes 10 years and \$260 million to bring a traditional agrochemical to market. A beneficial microbe can get on the market in two years at a cost of \$3 million.

Harman began work in 1980 on the fungi *Trichoderma* to control plant diseases while he was a professor at Cornell University. Cornell later licensed several *Trichoderma* strains he developed to small firms, including ABM. Harman retired from Cornell last year.

Starting around 2000, “the whole world has opened up for us since we've been able to measure gene expression,” Harman says. Originally, he thought *Trichoderma* only affected other fungi. But using new genomic tools he discovered that adding *Trichoderma* to plant roots made plant genes “function at higher levels.” The effects were greatest in the leaves and stems.

AMONG THE PRODUCTS ABM licensed from Harman's lab is a *Trichoderma*-based root inoculant for corn known as SabrEX. In return for starches and sugar from the plant, the microbes in SabrEX exude enzymes and proteins that help the plant develop a more robust root system, improve resistance to disease, and use water and nitrogen more efficiently, Harman says. Farmers can expect an average 8.5-bushel-per-acre yield increase when they use SabrEX, he claims.

Alison Stewart is a *Trichoderma* re-

searcher formerly at New Zealand's Lincoln University who is now chief technology officer of the bioproducts firm Marrone Bio Innovations. She also sees promise ahead for microbial plant treatments. Investments from large companies “will give farmers more confidence that these products will deliver,” Stewart says.

Marrone already sells products that aid plant growth, among them a plant extract that staves off soil-borne disease. It is also evaluating six new microbial inoculants offering benefits that include enhanced root growth and increased nitrogen and phosphorus uptake, Stewart says.

Some beneficial microbes will be niche products that will work only in certain soils or under certain conditions, she says. But within the next 10 years, she predicts, “some will also be blockbusters” that will put microbes on farmers' shopping lists along with fertilizers, pesticides, and seeds. ■

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