Can genetic engineering deliver a natural microbial fertilizer for crops?

At the turn of the previous century, German scientists Fritz Haber and Carl Bosch got all the credit for finding a way to convert atmospheric nitrogen (in its very stable N2 form) into a charged ion that could be “fixed” or applied as a chemical fertilizer. Both eventually were awarded the Nobel Prize in chemistry for their efforts.

At almost exactly the same time, Dutch microbiologist Martinus Beijerinck discovered how certain bacteria do the same thing naturally.

Beijerinck never got the Nobel. And until now, the Haber-Bosch process has been the only way to create enough volumes of nitrogen fertilizer to meet global demand. But Beijerinck (not known for his sense of humor or self-reflection), may get the last hurrah.

That’s because Haber-Bosch takes a tremendous amount of energy to catalyze the reaction from nitrogen to nitrate (or ammonia) ions, using very high temperatures and pressures. That energy often comes from fossil fuels. In addition, the use of applied nitrogen has had severe (and growing) ecological repercussions: It’s inefficient, and much of works its way, through runoff, into streams, rivers and the ocean. This has created well-known “dead zones” such as the Mississippi River Delta in the US, the coasts of Korea and Japan, and parts of the Baltic Sea. Nitrous oxide, one product of fixing, is 300 times more potent a greenhouse gas than carbon dioxide.

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Scientists are now looking at genetics to see if they can take the ability of the bacteria Beijerinck studied, which even today only “fix” nitrogen in certain legumes, like peanuts, soybeans and peas (hence the need for applied nitrogen in crops like wheat, corn, oats or rice). If they can recreate the fixing process in other cells, then those cells could literally create their own fertilizer as they grow and propagate.

That won’t be easy. There are at least 20 genes involved in nitrogen fixation, and while the Haber-Bosch process takes a great deal of energy, so does “natural” fixation—about 16 moles (the standard unit comparing units of atoms, molecules, and the like) of adenosine triphosphate (ATP), the energy-containing molecule in all cells, are needed to reduce one mole of nitrogen to nitrate. A successful fixation would need to harness cellular signaling, receptors and target genes that are precisely regulated and respond even to small changes in environmental conditions to, in some cases, recreate the cycles and reactions that result in nitrogen fixing.

But a number of efforts to genetically fix nitrogen are starting to pay off, thanks to more precise identification of DNA sequences and better gene-editing techniques. Breeding (in the biological sense) has helped, too.

Pivot Bio, which began in 2011 with Karsten Temme and Alvin Tamsir, who were looking at how bacteria fixed nitrogen when they were graduate students at the University of California, Berkeley. After failing to genetically produce plants that could fertilize themselves, their work met up with the work of Sharon Doty, a forest science professor at the University of Washington, who was looking at how poplar trees were able to get at nitrogen.

The answer was a nitrogen-fixing rhizobia bacteria that persisted in slime surrounding the trees roots. Instead of looking at the plants, Temme and Tamsir started looking at tweaking the nitrogen-fixing bacteria. The company has been working with farmers nationwide, and is collecting thousands of nitrogen-fixing bacteria that could be bred to fertilize non-auto-fixing plants. Pivot is keeping much of how it is doing this on a proprietary basis, but the company website says their "genetic fine-tuning" isn't transgenic. According to an article in SynBioBeta, the company is:

> [S]tudying the intricacies of nitrogen fixation—the process of breaking nitrogen down into ammonia— when they came across these hibernating microbes. Together, they developed a method to re-enable the microbes' nitrogen-fixing genes. With these microbes, Pivot Bio can grow biological nitrogen fixation to the scale of modern agriculture.
> But it's not enough to genetically tweak microbes. Each plant species prefers different types. Pivot Bio's team started with corn. They tested thousands of samples from corn fields across the US to find out which microbes corn likes best. When paired correctly, the microbes live directly on the corns' roots.

According to the company's patent filed with the US Patent and Trademark Office, the final product is not transgenic. Instead, the company writes, its method involves:

> Exposing the plant to a plurality of bacteria. Each member of the plurality comprises one or more genetic variations introduced into one or more genes or non-coding polynucleotides of the bacteria's nitrogen fixation or assimilation genetic regulatory network, such that the bacteria are capable of fixing atmospheric nitrogen in the presence of exogenous nitrogen. The bacteria are not intergeneric microorganisms.

Its promise just got a big boost of $70 million from Breakthrough Energy Ventures, a venture capitalist fund headed by Bill Gates and others.

Another company making headway in nitrogen fixing is Joyn, an alliance between Bayer and Ginkgo Bioworks. This company, which started with $100 million, is using synthetic biology technology on more than 100,000 strains of microbes supplied by Bayer to look at tweaking nitrogen-fixing organisms. According to Joyn's website:

> While there are many microbes that can fix nitrogen in the soil, these bacteria need to be engineered to increase the amount of biological nitrogen fertilizer they produce before they can make a meaningful impact for growers and the environment. We engineer the DNA of these naturally nitrogen-fixing bacteria using synthetic biology, enabling them to provide nitrogen to plants more efficiently.

Gingko has been at work in synthetic biology for years now, taking organisms like yeast, bacteria and algae to use sequences of DNA that can produce enzymes and other molecules at higher volumes. Joyn recently moved into a 160,000 square foot lab in Sacramento, California, devoted to experiments on creating a wider array of effective bacteria that could fix nitrogen.

A third is Indigo Ag, based in Boston, which has raised nearly $700 million since it started in 2014. The company first looked at developing tolerance to drought, and has 19 commercial microbial products to its name. Indigo works by screening microbiome and microbes that seems promising and then using computer software to predict microbial interactions with crop plants. They can then coat seeds with the right microbes to aid in growth enhancement, ability to grow in adverse conditions, and, of course fix nitrogen.

Any of these developments, if applicable to the field (and pass regulatory hurdles), would be revolutionary. Even small increases in nitrogen availability from nitrogen-fixing cereal crops would result in large yield increases—a particular benefit to the developing world. And farmers could at least reduce the 24 billion pounds of fertilizer they use every year, replacing the Haber-Bosch-enabled chemicals with microbes.

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