Minichromosomes Carry The Key To Improved Crops, Better Yields

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The projections are dire. "World Population in 2300," a report released by the United Nations' Expert Meeting on World Population in 2004, predicted that the planet's population will grow nearly 50 percent — to more than 9 billion people — by the year 2075.

"Reaping the Benefits," a study released by the United Kingdom's Royal Society in 2009, concluded that current food production systems will be unsustainable for future needs, with few opportunities for increasing crop-producing lands without inflicting environmental damage.

> *In the future, the ability to grow more — and better — crops on existing farmland will be essential to meet expanded population demands.*
>
> Daphne Preuss, CEO of Chromatin Inc.

By altering plants' genomes, today's researchers can improve production on limited acreage with crops that can be planted closer together and are more resistant to pests and diseases.

"But these plants have been developed by adding genes incrementally — a very slow process," she says. "The technology we have developed — minichromosomes — lets us add a larger number of genes simultaneously and breed varieties containing those changes much more quickly."

Laboratory Research

Minichromosome (or gene-stacking) technology grew from a discovery by Preuss while working with a small mustard plant called Arabidopsis thaliana in her laboratory at the University of Chicago, where she served as a professor of molecular genetics and cell biology.

"Daphne found a mutation with characteristics that let us develop a genetic mapping technique for plants," notes Gregory Copenhaver, Ph.D., who began working on the project with Preuss as a postdoctoral student in 1996. "We devised a technique for identifying the centromere, the spot on chromosomes that a cell grabs onto when it needs to move them during division. We were able to figure out how to catch hold of the centromere ourselves and use it to work with other plants."

Building Chromatin Inc.

The question was what to do with those discoveries. During the course of the 1990s, the University of Chicago secured the rights to them with a series of patents. "To take it beyond that," notes Heather Walsh, Ph.D., project manager in the university's Office of Technology and Intellectual Property, "Daphne and Greg believed they needed to commercialize it. But they felt that if gene-stacking was simply licensed to a single big organization, their work would be relegated to a limited set of plant products. They thought a smaller operation would be able to make the technology more broadly available for use with a multitude of crops."

Preuss and Copenhaver founded Chromatin Inc. in 2001, with the university licensing the technology to the new company. The name draws on the DNA and protein material that make up a cell's chromosomes.

Copenhaver put his pursuit of an academic career temporarily on hold to serve as president, eventually going back to academia as an associate professor with joint appointments in the Department of Biology and the Carolina Center for Genome Sciences at the University of North Carolina. He continues to serve Chromatin as a consultant, working through teleconferencing and monthly trips to Chicago.

Preuss, who has now left the University of Chicago, has been leading Chromatin for the past three years, serving as president and CEO of a company that has grown to more than 30 employees and facilities at several sites. In its primary DNA workshop in Chicago, the company builds and analyzes chromosomes. At labs in Urbana, Ill., researchers focus on plant growth and manipulating plant tissues and DNA.

Additionally, Chromatin operates field stations in other locations where higher yielding crops are bred. Among a series of additional patents secured by the company is one in 2007 granting it exclusive minichromosome rights in all plants.

Autonomous Chromosomes

"People have been able to alter plants by putting genes in chromosomes for several decades," Copenhaver says, "but that's essentially a random approach. When you place a new gene within a cell's nucleus you can't be sure where it's going to land. First, the gene must insert itself into an existing chromosome. The position it lands in may affect its functioning. Or, it might disrupt other genes during insertion."

As a consequence, researchers often have to work with thousands of plants in order to find a few that achieve the sought-after alteration. And since the point is that new traits have to be successfully passed on to succeeding generations, it's a long, labor-intensive — and expensive — process.

Preuss and Copenhaver thought a better approach would be to create their own chromosome, stack it with the genes they wanted and insert it into the cell.

"We were able to identify the centromere region in corn and work from there," Copenhaver says. "We tested a lot, using marker genes that fluoresce under ultraviolet light. We could see if the genes were being expressed and make sure they were autonomous — that they didn't insert themselves into existing chromosomes."

"Being autonomous solves a lot of problems," Preuss adds. "It makes it easier to pass on traits. It makes breeding new plants faster, better, cheaper and more predictable."

It's still an empirical process. As the Chromatin researchers build up a catalog of minichromosomes, they can compare traits and make better predictions as to what a combination of genes is going to do. Testing is still necessary but the ability to predict results shortens the process.

They reported their results in corn in the journal PLoS Genetics in the fall of 2007; the company has also had ongoing programs in a number of other crops, including soybean.

Corporate Licensing

Initial research was supported by funding from the university; private foundations; the National Science Foundation; and the Consortium for Plant Technology Research, a Department of Energy/industry funding collaboration. As a company, Chromatin was launched with venture capital and federal Small Business Innovation Research (SBIR) financing. It subsequently has gone through additional rounds of venture capital and SBIR funding. And, it receives revenues fromits licensing contracts with agricultural companies.

These include a 2007 collaborative agreement with agricultural giant Monsanto Co. allowing that organization to adapt Chromatin technology for its research crops. Also in 2007, Chromatin granted Syngenta Biology Inc. a nonexclusive license to use the technology for corn and soybeans.

Other agreements have followed — with Dow AgroSciences for research on combining Chromatin minichromosomes with Dow technology and with Bayer Crop-Science for its use in cotton plants. An exclusive agreement with Syngenta lets that company pursue minichromosome technology in sugarcane.

"Our first mission has been developing crops that leading agricultural companies are pursuing today — crops like soybeans that farmers can plant more closely together to increase yields, allow more efficient use of pesticides or are resistant to drought," Preuss says.

"In the future, minichromosomes can bring about improved types of crops — foods high in Omega 3 oils, cottons with different types of fibers, new medicines and biofuels," Preuss continues. "Manufacturers have been seeking to derive insulin from safflower plants and antibodies from aquatic plants. Crops like sugarcane and sawgrass offer the prospect of becoming very productive, efficient biofuel sources."

That's why the importance of minichromosomes' capacity for stacking unlimited numbers of genes can't be understated, Copenhaver says.

"Science's ability to discover new genes and be sure what they're doing has outstripped our ability to use them," he says. “Most companies have a lot more genes than they’ve been able to implement. This opens new doors for making important advances available to people.”

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