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Genetic Engineering of Maize: A Report on Work in Progress

"Now we know for sure that it is possible to genetically engineer corn." That's how biotech analysts reacted when Monsanto and Dekalb Plant Genetics presented documented evidence last year on the breakthrough that everyone was waiting for: successful transformation of maize cells with a foreign gene and regeneration into complete plants that pass the new genes on to succeeding generations through the seed.[1] Transgenic maize plants are heralded as a major breakthrough because important cereal crops like maize and wheat have proven much more difficult to genetically engineer than broad-leaved crops like soya beans, tobacco and tomatoes. This issue of *RAFI Communique* takes a look at current R & D in genetic transformation of maize--the financial stakes and major players, goals of transformation, and prospects for commercialization. RAFI concludes that the current frenzy over genetic engineering of maize stands in stark contrast to the languishing efforts to conserve and utilize maize genetic resources worldwide.

Introduction

Zea mays L. (maize or corn) is the third most important crop after rice and wheat, supplying 20% of the world's total grain production. The widest range of genetic diversity of maize can be found in Latin America, where the crop originated.

Despite the importance of maize genetic resources for the future of plant breeding and biotechnology efforts in both industrialized nations and the developing world, it is estimated that only 5 percent of the over 260 races of maize accessions in germplasm banks have been tapped thus far for use in genetic improvement programs. With the advent of genetic engineering, the value of exotic germplasm is expected to increase. Recent reports on the status of the most important collections of maize germplasm, however, suggest that these invaluable genetic resources are disappearing at an alarming rate. (see box, "Disappearing Maize Genetic Resources," page 4.)

Financial Stakes

Maize, the single-most important commercial seed species, is considered the "the Holy Grail" of crop genetic engineering because it offers potential for enormous financial rewards to the global seed industry.

In eight countries comprising the largest market for commercial seed sales, 91.5% of all maize seed was commercially supplied.[2] Seed industry consultants estimate that the worldwide value of the maize seed market totalled (US) $2.5 billion in 1988, accounting for 24% of the entire commercial seed industry. Between 1988 and 1993, industry analysts predict that maize is projected to rise to 26.1% of all commercially-supplied seed--an estimated value of (US) $3.1 billion annually.

Given the potential financial rewards, it is not surprising that a large number of companies are researching new transformation technologies, with the ultimate goal of moving novel genes into commercially valuable inbred maize lines. Major players include both large transnational corporations and small biotech companies: Agracetus (Wisconsin, USA), Biotechnica International (Kansas, USA), Cargill (Minnesota, USA), Ciba-Geigy (Basel, Switzerland), Dekalb Plant Genetics (Illinois, USA), Monsanto (Missouri, USA), Pioneer Hi-bred Intl.(Iowa, USA), Plant Genetic Systems (Ghent, Bel-

□ P.O. Box 655 • Pittsboro, North Carolina 27312, USA • (919) 542-1396 • GEO4:RAFIUSA
□ Box 188 • Brandon, Manitoba R7A 5Y8 CANADA • (204) 727-8995 • North American Telex: 7601055RAFIUC • GEO4:RAFICAN
□ RAFI/IIZ • Wipplingerstr. 32 • A-1010 Vienna, AUSTRIA • 222/5334786 • Telex: 116629 IIZA

gium), Upjohn (Michigan, USA) and Sandoz (Basel, Switzerland). For more information, see "Company Profiles,", p. 4.

Goals of Transformation

Despite the hype and hubris surrounding genetic transformation of maize, the production of commercial hybrid seeds is a long-term, painstaking process. New commercial varieties with novel agronomic traits are still 5-15 years away. In the U.S., Ciba-Geigy, Monsanto, Biotechnica, Pioneer, Dekalb Plant Genetics, Garst Seed (ICI), Holden's Foundation Seeds, Inc. and Upjohn have already applied to and/or received approval from the U.S. Department of Agriculture to conduct field tests of transgenic maize. Ciba-Geigy also conducted one field test of transgenic maize in France. Long and short-term goals of transgenic maize plants include:

1) Herbicide tolerance -- The development of maize plants genetically engineered to withstand spraying of chemical weedkillers is an early goal of maize transformation. Dekalb plans field tests of maize containing a gene to resist the herbicide bialaphos (an herbicide marketed by Hoechst under the name Basta). Both Monsanto and Pioneer are developing maize with resistance to chlorsulfuron, and Upjohn and Holden's Seed are developing maize with tolerance for the herbicide glufosinate. In addition to the companies mentioned, others have transgenic, herbicide-tolerant maize varieties in the pipeline. Biotechnology analysts estimate that the U.S. market for maize-tolerant seed varieties is approximately $150 million annually.

2) Insect resistance -- Several companies are experimenting with the introduction of insecticidal protein genes into maize. These include both *Bacillus thuringiensis* (B.t.) and the cowpea trypsin inhibitor gene (CpTI). One target is the European corn borer. Farmers in the U.S. and Western Europe spend $350 million annually on conventional chemicals that are only 50% effective against this caterpillar. Ecogen (Pennsylvania, USA) recently licensed some of its B.t. insecticidal genes to Pioneer Hi-bred. Pioneer also has agreements with Agricultural Genetics (Cambridge, UK) to obtain their proprietary CpTI gene. The world's largest maize breeder, Pioneer controls 34% of the $1.33 billion U.S. hybrid maize seed market.[3] Monsanto is also inserting B.t. genes into maize. There is concern that widespread use of B.t. in genetically-engineered maize could lead to rapid pest adaptation and eventual loss of these genes as effective biological controls. Just as with chemicals, heavy use of a single pesticide encourages the rapid emergence of resistant species. Will companies like Pioneer and Monsanto take steps to insure long-term conservation of insect resistant genes?

3) Male sterility -- Although hybrid maize has been available since the 1930s, Plant Genetic Systems has developed a new, proprietary technique which prevents self-pollination in plants. If the trait for male sterility can be introduced in maize, it could save seed producers $75 million a year in labor costs for detasseling (removal of male flowers from maize plants by hand).[4]

4) Corn oil improvement -- Genetic engineers also seek to manipulate the fatty acid content of vegetable oils to improve their nutritional qualities (see *RAFI Communique*, July, 1991). While maize oil is a small vegetable oil market in comparison to soya and palm oil, analysts predict that the value of the maize oil market could increase in value by 10% in the U.S. alone. (The U.S. market is valued at approximately $280 million annually.)[5]

5) Improving protein quality for animal feed -- In the U.S., approximately 5 billion bushels of maize, worth approximately $10 billion annually, is used to feed livestock.[6] Several companies are attempting to modify the proteins found in maize. If they can improve the nutritional quality of maize used for livestock feed, it would reduce the need for feed supplements (mostly soya bean meal) which cost approximately $5 billion annually. Biotechnica International recently field tested transgenic maize plants containing a gene for an amino acid that improves nutritional quality. Biotechnica believes this a $2 billion market opportunity.[7]

When to Expect Commercialization?

Scientists predict that transgenic maize with qualities such as insecticide resistance, herbicide tolerance or male sterility, manipulations involving the movement of just one or two genes, could be commercialized as early as 1995.[8] But the expression of most agronomically important traits are governed by more than one gene. Isolation, manipula-

tion and expression of these multigenic traits are exponentially more difficult and will take a lot longer.[9] Consider, for example, that the corn genome contains about 20,000 genes. At least 30 genes, which have yet to be identified, influence yield. In a very real sense, maize transformation is still in its infancy. Dr. Michael Fromm, a molecular biologist with Monsanto Co., told AgBiotechnology News:

"A lot of the ideal things that everyone would like are simply too complicated at this point. Disease resistance, drought resistance, yield enhancement, better quality of starch and amino acids, those are all very complicated traits. There are a lot of the single gene traits that we think we can do. The others are going to take awhile." [10]

Conclusion

The development of transgenic maize plants must be viewed in a larger, geo-political context, taking into account the continuing trend of global consolidation within the seed industry, where fewer, larger companies dominate the worldwide market for hybrid maize. In the next five years, transnational seed companies expect growth potential in Eastern Europe and elsewhere following fundamental structural changes in agriculture and the opening of new markets. Seed industry consultants predict that the value of the hybrid maize seed market will increase 25% between 1988 and 1993.[11] The unquestionably good business opportunity for the seed industry, however, may not translate into big advances for farmers--especially in the developing world.

A recent study by Carliene Brenner of the OECD Development Centre looks at the potential of new biotechnologies to increase both the supply and quality of maize as an essential food and/or feed crop in the Third World. She concludes that there are major obstacles to both domestic development of new maize biotechnologies as well as transfer of technology from abroad. According to Brenner:

"The lessons from maize illustrate that, in the short term at least...many developing countries will be unable to develop new plant biotechnologies domestically to any significant degree. Quite simply, they lack national financial, scientific and technological resources, public and private. This could have serious consequences for food self-sufficiency or competitiveness in international markets."[12]

Despite the breakthroughs in genetic transformation technology, it will be a long time before commercial, transgenic maize seed is developed which brings superior varieties with important agronomic qualities. At present, maize transformation research and development is dominated by large corporations, with research goals determined by private interests. The push for protection of intellectual property, and the built-in protection offered by hybrids, gives the seed industry an even tighter grip on control of the world's hybrid maize market. Ironically, the end result will likely be fewer options and greater vulnerability for farmers.

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NOTES

1. Biotechnica Intl. was the first company to announce genetic transformation of maize, but Monsanto and Dekalb first presented documented evidence at a Keystone meeting in April, 1990.
2. These and other statistics on value of maize seed market extracted from "Executive Summary from the Teweles Report II," published by L. William Teweles & Co. seed industry consultants, Milwaukee, Wisconsin, January, 1990. All statistics are for eight largest global seed markets, including: U.S., France, Japan, Brazil, Italy, Germany, U.K., Spain, Canada, Mexico, Argentina, Australia.
3. Anonymous, 1991, Genetic Technology News, May, p. 10.
4. Anonymous, 1990, "Genetically Engineered Corn: Breakthrough Brings Market Closer," Genetic Technology News, October, p. 8.
5. Ibid., p. 11.
6. Anonymous, Bioprocessing Technology, March, 1991, p.
7. Anonymous, 1991, "Genetically Modified Proteins," in Agbiotech Stock Letter, No. 38, September, p. 6.
8. Cutler, Karol, 1991, "The Current State of Corn Transformation: How is the Race Developing," AgBiotechnology News, January/February, p. 21.
9. Anonymous, 1990, "The Lowly Cowpea: A Boon to Agriculture?," Agricultural Genetics Report, Vol. 9, No. 2, p. 8.
10. Cutler, K., AgBiotechnology News, Jan/Feb., 1991, p. 21.
11. L. William Teweles & Co., 1990, "The World's Principal Seed Markets: Executive Summary," in Teweles Report II, January, p. xii.
12. Brenner, C., 1991, "Biotechnology in the Developing World: Lessons from Maize," The OECD Observer, p. 12.

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Disappearing Maize Genetic Resources

Maize breeders warn that Latin America's most important collections of maize germplasm in storage are "only marginally viable." In a recent article appearing in Diversity magazine, maize breeders Dr. Major M. Goodman and Juan M. Hernandez conclude that the status of maize genetic resources has deteriorated over the past 9 years, due to lack of funding for regeneration, evaluation and utilization of maize seed in storage. In 1983, of approximately 250 races of Latin American maize, eight races in storage became extinct, and 30 additional races were considered endangered. Today, 4 of the 30 endangered races have been replenished, but all 80 races from Bolivia, Ecuador and Venezuela have now become endangered. Goodman and Hernandez conclude that, "Without suitable regeneration facilities, without reliable funding, and with, at best, inconsistent interest in germplasm resources from the International Agricultural Resources Centers (IARCs), much responsibility for germplasm maintenance falls upon poorly-funded national (often Third World) programs."

Corporate Profiles
Leading Companies Involved in Genetically Engineered Maize

• **Agracetus** -- (Wisconsin, USA) Agracetus has used particle gun to transform maize. The company is a wholly-owned subsidiary of W.R. Grace (New York, USA). With 1990 annual sales of (US) $6.8 billion, W.R. Grace ranks #202 on Fortune magazine's list of the largest U.S. industrial corporations.

• **Biotechnica International** -- (Kansas, USA) Recently field tested genetically-engineered maize in four midwestern U.S. states. Plants contain a gene to improve lysine content, an essential amino acid that occurs at a relatively low level in corn. Biotechnica is a relatively small plant biotechnology company, but it has purchased 5 North American seed companies since 1987.

• **Cargill** (Minnesota, USA) -- Cargill is one of the largest, privately held corporations in the world. The company is a major buyer and seller of grain, and one of the top seed companies in the world (ranked # 5 in 1989).

• **Ciba-Geigy** (Basel, Switzerland) -- With annual sales of US $14 billion in 1990, Ciba-Geigy ranks # 80 on Fortune's list of the world's largest industrial corporations. According to an unconfirmed source, Ciba-Geigy's seed division is spending 80% of its R&D budget on maize transformation.

• **Dekalb Genetics Corp.** (Illinois, USA) -- The company controls an estimated 9% of the U.S. maize seed market. Dekalb used a particle gun to insert herbicide-tolerance gene into maize cells. Field-tested in U.S.

• **Hoechst** (Germany) - A leading agrichemical corporation, with 1990 sales of $28 billion. Little details are known about their work on maize transformation in U.S. and Europe.

• **Monsanto** (Missouri, USA) -- With 1990 annual sales of US $9 billion, the company ranks #146 on Fortune's list of world's largest industrial corporations. In 1989, Monsanto was ranked the leading plant biotechnology company, based on research expenditures.

• **Pioneer Hi-bred, Intl.** (Iowa, USA) -- The world's largest seed company, Pioneer controls 34% of the $1.33 billion U.S. hybrid maize seed market. Pioneer had 1990 seed revenues of $944 ml.

• **Plant Genetic Systems** (Ghent, Belgium) Has developed a proprietary technique for transforming plants with a gene for male sterility. In 1989, the company ranked 13th among world's top plant biotech companies, based on research expenditures.

• **Sandoz** (Basel, Switzerland) -- 1990 annual sales of US $8.9 billion, and is ranked 4th globally, in terms of research expenditures on plant biotechnology.

• **Upjohn** (Michigan, USA) -- Upjohn's subsidiary, Asgrow, is ranked the 4th largest seed company in the world. Upjohn had 1990 annual sales of US $3.0 billion.