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Colloquium Paper

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Plant genomics: More than food for thought

STEVEN P. BRIGGS*

Pioneer Hi-Bred International, Inc., 7300 N.W. 62nd Avenue, Johnston, IA 50131

ABSTRACT **In all but the poorest countries of South Asia and Africa, the supply and quality of food will rise to meet the demand. Biotechnology, accelerated by genomics, will create wealth for both producers and consumers by reducing the cost and increasing the quality of food. Famine and malnutrition in the poorest countries may be alleviated by applying genomics or other tools of biotechnology to improving subsistence crops. The role of the public sector and the impact of patent law both could be great, but government policies on these issues are still unclear.**

Agricultural Plant Science

The goals of agricultural plant science are to increase crop productivity, increase the quality of agricultural products, and maintain the environment. Each of these goals has significant economic value. Increased productivity has accounted for nearly all of the added value in germ plasm until recently. Quality is rapidly replacing productivity as the most valuable property of germ plasm to improve. The corn market, for example, is moving from a homogenous commodities market to a segmented, specific-use market where the value of unique grain is preserved from the farm through to the end-user, similar to the wheat market. Maintaining productivity and quality under minimum tillage conditions, which reduce erosion and inputs, also is growing in importance. The real cost of agriculture to the environment will be increasingly factored into production costs. These goals are interrelated. The greatest environmental impact of agriculture is the use of land. Increased productivity directly reduces the amount of land needed.

The means by which these goals will be met include germplasm improvement, precision farming, and conservation tillage. Germ-plasm improvement is the focus of this article and is occurring by both conventional and molecular means. Precision farming is significantly adding to the profitability of producers by enabling optimized use of the land and inputs. For example, farm vehicles are increasingly equipped with global positioning systems and computers that create geographic databases of the fields. Soil qualities and crop yield are recorded at high resolution and reveal useful correlations that guide decisions about soil treatments and crop varieties. All of the inputs then can be tuned to maximize efficiency. Conservation tillage reduces erosion but also makes it more difficult for crops to yield well because of lower soil temperature and higher pest populations.

Germ-plasm improvement will continue to depend on nontransgenic methods that use sophisticated assays and molecular genetic markers. It is difficult to envisage a replacement for meiosis-based approaches to environmental adaptation. Nevertheless, gene technology will be the principal means by which value-added traits are created over the next several years. Genomics in particular will accelerate the discovery of genes that confer key traits, enabling their rapid improvement.

The Rationale for Biotechnology

The new wealth of the developing world has made possible the transition to a meat-based diet, with a consequent expansion in the demand for grain. The demand is expected to grow. The human population will increase to nearly double over the next 45 years (1). Taking improved diets into account, food production will have to triple. Worldwide production acreage probably will not change, although in some areas there will be decline because of urbanization and environmental degradation. There are vast potential acreages for grain production in South America, including 75 million acres in Argentina and 150 million acres in the central Cerrados Plateau of Brazil (2). The cost of bringing this land into production currently exceeds its value. However, much higher grain prices could result in its utilization.

The genetic supply industry will try to satisfy the growing demand by increasing the yield and quality of grain produced, possibly making an expanded acreage unnecessary. Yield increases over the past 45 years suggest that optimism is not unreasonable (3). During that time the population doubled, yield on the best land tripled, while acreage remained static. The feed-to-meat conversion efficiency also doubled, it now takes only 4 pounds of grain to produce 1 pound of pork, and further increases in this efficiency can be expected to contribute to future increases in productivity. Although it costs more to produce today's high yields, wealth has increased faster than the costs. Food accounts for half as much of our income today (11%) as it did 45 years ago. Past gains in productivity were achieved by improved mechanization and agricultural chemicals, in addition to genetic improvements. Future gains will depend increasingly on genetics, with some sectors of the agricultural chemical industry being replaced by genetics (e.g., insecticides and fungicides). It is encouraging to note that at the same time productivity was tripling soil erosion per ton of food produced was cut by two-thirds.

There is no reason to think that we are close to maximum possible yields. Annual yields of maize have increased by 1.5 bushels/acre since 1965. The best average U.S. maize yield was 138 bushels/acre in 1994 but the highest recorded yield is 370 bushels/acre. The theoretical yield limit of maize has been estimated to be 500 bushels/acre. Worldwide maize production could be increased significantly simply by switching from open-pollinated cultivars to hybrids, which currently account for approximately 65% of total maize acreage. Hybrids typically outyield cultivars by 2- to 4-fold.

Abbreviation: EST, expressed sequence tag.

*To whom reprint requests should be addressed. e-mail: briggs@phibred.com.

Under ideal growing conditions, elite maize hybrids provide surprisingly little advantage over much older germ plasm. But under stress, which is typical of growth on the farm, the difference becomes striking. The greater the stress, the greater the performance advantage of elite germ plasm. Essentially all of the yield gain from plant breeding has been caused by increased stress tolerance. The isolation of genes for stress tolerance is a high priority for plant science.

About 80% of maize and 100% of soybeans produced in the U.S. are used for animal feed. By increasing the energy content or nutritional value of these grains, the amount used for feed is proportionately decreased. Decreasing the amount of feed needed is tantamount to increasing the yield. High-oil corn has a significantly increased energy density. Currently, such corn is produced by conventional means. Several genes have been isolated that may enable the production of transgenic crops with higher oil content or modified oil types.

The ability to make large, qualitative or quantitative improvements by using transgenic methods provides the rationale for biotechnology in agriculture. Genomics is vital to this ability because it can greatly accelerate the discovery of genes for transformation.

First-Generation Products

Crop protection encompasses insect, herbicide, and disease resistance. The first large-scale commercial use of transgenic crops was for improved crop protection traits, primarily insect and herbicide resistance. These and other, smaller-scale, products were the first to market because they are conferred by single genes. The next generation of improved traits will include disease resistance, male sterility (for hybrid seed production), and grain quality. These traits may be conferred by multiple genes whose products cause major changes in cell physiology. Stacking multiple traits into a single cultivar will be a challenge.

It's easy to see the value of crop protection and male sterility to seed companies and farmers: the costs of production are reduced. Improved grain quality likewise lowers the cost of meat production. Eventually, these improvements translate into reduced prices at the grocery store, a greater capacity to feed the world, and a reduced impact on the environment. But will there be other near-term benefits of agricultural biotechnology to consumers? The answer is clearly yes, with one targeted area for improvement being food safety.

Most of the world's grain supplies are seriously contaminated with mycotoxins. These secondary metabolites are produced by fungi that infect the developing grain. By harvest time, mycotoxin levels often are dangerously high. Poor storage conditions may permit the continued growth of fungi and accumulation of mycotoxins after harvest. Aflatoxin was one of the first mycotoxins described and is the most widely known. Yet, aflatoxin contamination is sporadic and occurs in a narrow range of food products. Of much greater impact are mycotoxins such as fumonisin B1 and deoxynivalenol. Field tests are underway at Pioneer that demonstrate that crops can be engineered to degrade mycotoxins. The resulting increased safety of both food and animal feed will cause a significant reduction in human health costs and the costs of meat production.

Finally, changes are being engineered that will markedly increase the availability of nutrients in the grain. This increase will provide the obvious nutritional benefit but it also will provide a less obvious, but perhaps more important, environmental benefit. Nutrients, such as phosphorous, that pass through the animal are a major pollution problem. Low-phytate grain allows most of the grain's phosphorous to be used by animals instead of being excreted. These improved products will be on the market soon and should contribute significantly to making agriculture sustainable.

One lesson learned from the first generation of products is that qualitative improvements produced by using transgenes are commercially viable only if the genes are placed into elite germ plasm, so that the myriad of other traits that are necessary for a good product are also present. The seed industry is highly competitive. Seed performance is judged by the total value it brings to the farmer at harvest. Therefore, transgenes must be viewed as improvements rather than replacements for elite germ plasm.

The Role of Genomics in Agriculture

The success of transgenic crops has erased the last vestiges of doubt about the value of agricultural biotechnology and triggered large-scale investments in plant genomics.

The term genomics has a rapidly evolving definition. Genomics is a science that's defined by technology. The first genomics technology that was practiced on a large scale was sequencing the 5′ ends of cDNAs, to produce expressed sequence tags (ESTs). ESTs provide a cost-effective and rapid approach to describing the collection of genes that define an organism. EST sequencing remains the method of choice for genome-level surveys of eukaryotic organisms.

DNA sequence information unites biology. Determination of an EST sequence permits an immediate search of sequence databases for similarity to sequences with known functions from any organism. The information content of an EST database primarily is derived from links with other databases. Discovery of function in one organism provides insight to related sequences in all organisms. Inexpensive, fast DNA sequencing has replaced expensive, slow experimentation. This makes sequencing attractive to companies that develop gene-based products, such as transgenic crops. All of the large genetic supply organizations have in-house genomics programs or access to proprietary databases.

Creating an EST database of our major crops should be the top priority for agricultural plant genomics. In contrast, complete genome sequencing is currently only practical for microbes with small genomes, with the exception of a few large, international efforts to sequence the yeast, human, nematode, fruit fly, and mouse-ear cress genomes. The sequence of the latter, also known as *Arabidopsis thaliana*, will be invaluable for both science and the development of agricultural products. Contributing to the timely completion of the *Arabidopsis* sequencing project should be the second-highest priority for agricultural plant genomics.

The Value of Agricultural Plant Genomics to Society

Genomics will accelerate the application of gene technology to agriculture. As previously described, this technology will enhance food security, by increasing productivity, and food safety, by eliminating mycotoxins. There is a third benefit, derived from the first two: increased wealth. By accelerating the application of technology, genomics significantly increases the value of seeds and agricultural products. This increase adds much wealth to the customers, company owners, employees, and citizens of the nations in which genetic supply companies operate, and to both producing and importing nations whose food costs consequently are decreased.

Unlike natural resources, wealth is a product of society; it can increase without limit. Increased wealth is the key to improved living standards. There are opportunities for solving some short-term agricultural problems in the developing world by using genomics, and these opportunities should be met. However, self-sufficiency in food production is probably not the best way for many developing nations to increase their living standards. Instead, they should purchase low-cost food from the most efficient producers and devote their resources to increasing wealth through the production of goods and services for which they are uniquely suited. The major impediment to this path is poor government and social strife. In large parts of South Asia and Africa, society barely functions. In these areas, improved crop varieties for subsistence agriculture may help alleviate misery. But this is a form of emergency aid, not a path to economic growth.

Wealth in the developing world is increasing rapidly. Consider that the middle class, defined as having an annual income greater than US$30,000, is larger in India (250 million) than in the U.S. It makes more sense for an Indian to work in biotechnology or the computer industry, where world-class competition is possible, than to practice subsistence or low-yield agriculture. Parts of Indian agriculture are extremely productive and should be built on. But a goal of food self-sufficiency seems to make no more sense for India or China than for the U.S. to be energy self-sufficient. If every nation harnesses its own unique strengths and trades them with each other, all will become more wealthy. The barrier to this is a fear of war, which will diminish as nations become mutually dependent.

Funding for Agricultural Plant Genomics

Society probably has made no better investment than in agricultural research. The consistent abundance of low-cost, high-quality food that has resulted from this research stands in contrast to the health-care profession, where, despite a far greater research investment, costs have skyrocketed and availability has declined.

Agricultural research has suffered from its own success. Politicians have concluded that the problem of agriculture has been solved and further research is unnecessary. Agricultural research now accounts for only 2% of the U.S. federal research and development budget, despite a 35% rate of return to society. Combined federal and state research expenditures have been flat at $2.5 billion for the past 20 years while private investment has grown rapidly, accounting for 60% of total expenditures by 1995. More than 20% of the research budget at state universities is from industry. The value of agriculture to society in the U.S. dwarfs its investment. Eighteen percent of American jobs are tied directly or indirectly to agriculture, as is 15% of the gross domestic product. Over 30% of U.S. agricultural products are exported, at a value of $56.5 billion; this is twice the value of our agricultural imports. Importantly, of the products we export, 60% are processed; only 40% are commodities, and this fraction is declining. The added value from processing is being captured in the U.S., along with the associated jobs.

Agricultural plant genomics should be publicly funded for several reasons. First, the DNA sequence of plants is necessary for continued low-cost, rapid progress to understand crops. As such, it is an essential resource for scientists in both the public and private sectors. Second, industry needs the public sector to create innovative methods for structuring and analyzing databases, which can't be done without access to genomics resources. Third, genomics is an equalizer in the research world. Anyone with a computer can contribute interpretations of the data or methods for analysis. The limitations are primarily intellectual rather than financial. This expands the population of investigators who can contribute significantly to world-class plant science. Fourth, genomics is a natural organizing principle for team-based research. As we try to solve larger problems, teams have become essential.

Intellectual Property Rights

Aside from their educational obligations, most research universities today have a mission that is similar to that of commercial technology vendors: create technology and intellectual property for the purpose of licensing, to enrich the institution and the inventors. The differences between companies and universities are the tax status and the traditional license-free privilege to practice patented inventions. As universities become direct competitors with companies, the release of know-how and materials from companies is drying up, and enforcement of patent rights on universities is increasing. The free exchange of knowledge and materials that has enabled science to be so productive is being choked off, even between universities. This is especially damaging when it is the tools of invention that are restricted, not just the process and products of manufacture. For example, agrobacterium transformation methods are the subject of intense legal disputes. Whoever ends up owning the transformation process and its products will be in a position to block all inventors who use transformation to discover genes or gene functions. It's likely that there would be more plant biotechnology companies starting up if the tools of invention were freely available.

It is imperative that publicly funded genomics databases be equally accessible to everyone. If one group was given privileged access, then industry would be forced to compete by duplicating the databases. This principle has served the Human Genome Project well. The central problem with intellectual property law and genomics is the ability to own compositions of matter for self-replicating, natural substances, such as genes, and particularly ESTs. If DNA were not self-replicating then treating DNA and its products as just another collection of purified substances would be fine. But we have a situation where an "invention" that provides trivial enablement grants composition claims to all future inventions. This has been debated at length but little progress has been made. We are witnessing the Gene Rush of the '90s. One of the legacies will be a failure to adequately exploit genes because of composition claims held by disinterested parties.

Conclusions

The governments of the industrialized nations should invest in public genomics research, with immediate data deposition policies. Funds should be increased for improving crop germ plasm in the poorest nations, as humanitarian aid. Patent laws affecting genomics must be clarified. The future looks bright for both consumers and producers of food, except in the poorest nations.

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