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BIOTECHNOLOGY: SCIENTIFIC PANACEA OR RESEARCH BANDWAGON

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I am pleased to have been invited to participate in this symposium on biotechnology. For the past decade, I have followed the developments in biotechnology and molecular genetics with fascination and great anticipation. It is pleasing to see the first fruits of some of this research now beginning to enter commercial production.

Agricultural science, including genetics and plant breeding research, like many other areas of human endeavor, is subject to changing fashions and fads, generated from both within the scientific community and imposed upon it by external forces, especially the politically induced ones that affect the actions of financial donors.

Crop varietal improvement in the Americas, as well as in Europe and Asian countries, up until the first decade of this century was mainly achieved by selection of superior plants, commonly by farmers, from the so-called land races. By the second and third decade, many government, university, and private company breeding programs were established based on Mendelian genetics—involving controlled pollination (crossing) to create superior populations with great genetic diversity, from which selection of superior progeny were made from each successive segregating generation until uniform superior lines and varieties were developed.

Over the past seven decades, the conventional breeding programs have produced a vast number of varieties (and hybrids) each superior to the ones it replaced. The procession of increasingly superior crop varieties has contributed immensely to increasing grain yield, stability of harvest, and farm income. Surprisingly, though, the methodology currently used in breeding of self-pollinated crop species continues to be based largely on the same basic principles and methods and procedures that were used when it was established in the 1920s and 1930s. One important modification in methodology used in handling segregating populations and in selection of progeny, however, was the introduction of shuttle breeding and multi-location international yield testing (in Mexico) that produced the broadly-adapted, disease-resistant, high-yielding semidwarf Mexican spring wheat varieties that gave rise to the Green Revolution.

Surprisingly, there has been no major increase in the maximum genetic yield potential of the high yielding semidwarf wheat and rice varieties since those that served to launch the so-called Green Revolution of the 1960s-1970s. There has been,

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however, important improvement in resistance to insects and diseases.

World population now stands at 5.7 billion and is increasing at 1 billion more each decade. There is little new land suitable for agriculture that can be opened to cultivation in most countries of the world. Moreover with noisy anti-science groups and well financed vociferous extremists in the environmental movement, concerned about pollution of land, food, water and air by agrochemicals and destruction of forests and other habitats for wildlife, where will the needed increases in food and fiber production come from? Will the plant breeders, employing the conventional methods, that have been highly successful since World War II, be able to increase the maximum genetic yield potential of the varieties of the major crops fast enough to cope with the rapidly growing demand for food and fiber over the next three decades?

I must admit I am apprehensive. Consequently, I am convinced we must find new appropriate higher yielding technology to cope with the problems that now confront us. In my 50-plus year career, I have seen various scientific bandwagons come and go. In the 1930s and 1940s plant improvement by the development of polyploids (doubling of chromosomes) was promoted as the panacea. By the 1950s and 1960s, mutation genetics was the rage. In the 1970s and 1980s, anther culture, somatic tissue culture and farming systems research were the crazes. During the 1990s, biotechnology and genetic engineering, computer modeling of cropping systems, maximizing biodiversity, low-input sustainable agriculture, and participatory farmer research are the new buzzwords. While each of these lines of research has had or will have, some beneficial aspects, all have had one thing in common; some of their most aggressive proponents, certainly partly driven by the desire to secure more research funds, often have exaggerated the potential for benefits, especially in the near-term.

Currently, some scientific circles are proclaiming that major agricultural production benefits will soon be forthcoming from new superior crop varieties developed by biotechnology, cell and protoplast fusion, recombinant DNA, and a number of other molecular genetics engineering technologies. Scientific data, now available, do not justify many of these wide sweeping claims. Exaggeration of promising potential benefits from biotechnology is dangerous! For example, several years ago, at a Conference of Agricultural Research Directors for Latin American Countries (held at CIMMYT in Mexico), organized to discuss the agricultural research needs and priorities for the next decade, a brilliant molecular geneticist/biotechnologist, in the plenary session stated: "The only way that Latin American Countries' agricultural production can catch up with those of the USA, Canada, and Europe is to allocate all of our research funds to biotechnology." What a disaster it would be, were political leaders—Ministers of Agriculture and Finance and Heads of State—to follow such a reckless recommendation.

I am completely convinced that the developed nations should be investing aggressively in biotechnology/molecular genetics and genetic engineering for varietal improvement; but it must do so while continuing to give adequate balanced financial support to research on conventional breeding, agronomy, soils, physiology, plant pathology, entomology and cereal technology. However, I am skeptical about developing nations, with the present state of the art, investing much of their limited research funds for agricultural research in biotechnology. My fears of the danger of over-investing in a new bandwagon technology goes back to my experience in Asian countries during the 1960s, while introducing the high-yield, semidwarf Mexican wheat varieties into India, Pakistan, and Near East countries. The Mexican wheat varieties, which were developed by a conventional shuttle breeding program, together with a package of improved agronomic crop management practices permitting them to express their high genetic grain yield potential, were introduced commercially into many countries in the aforementioned regions. Their superiority in yield, rust resistance and breadth of adaptation was readily apparent and they spread like wild-fire across vast areas and revolutionized yield and production in what became known as the Green Revolution.

For nearly a decade, prior to the introduction of the Mexican wheats into Asian and North African countries, virtually all of the countries had been spending the majority of their limited budget for varietal improvement on the mutation genetics bandwagon. Mutation genetic breeding programs had been promoted as a panacea by the Atomic Energy Program of the United Nations in many countries. These programs were financed by matching funds from the U.N. Agency and the host country. The improved varieties that were produced by the mutation breeding programs (and conventional breeding programs), were unable to compete and were swept away by the Mexican Green Revolution varieties. Soon after the successful introduction of the Mexican varieties, the wheat breeding programs of these countries were reorganized using the Mexican shuttle breeding scheme. In the process the mutation breeding program died a lingering death, leaving in their wake only a lot of shattered dreams and "learned" scientific papers. I must admit, I reluctantly also got on the mutation breeding bandwagon for a couple of years, but fortunately, we (my Rockefeller Foundation—Mexican colleagues) abandoned the bandwagon before the conventional shuttle breeding program had been seriously weakened.

The Potential Role of Biotechnology for Increasing Plant and Animal Food Production

I am now convinced that what began as a biotechnology bandwagon some fifteen years ago, has developed some valuable scientifically well-founded methodologies, processes and products, which now need more active financial and organizational support to bring them to fruition in widespread food and fiber production. The tremendous potential benefits from a number of these fascinating biotechnological developments that are now approaching commercial applications, as I see them, are outlined in the remainder of this manuscript.

Biotechnology in its broadest sense, up to the present, has had its earliest and greatest positive impact on medicine and public health. Over the past fifteen years, molecular genetics, involving recombinant DNA technology, etc. have produced and effectively used:

a. the human somatotropin growth hormone (HST)
b. monoclonal antibodies
c. improved human insulin
d. interferon

e. several improved vaccines

Animal Biotechnology

1. Bovine somatotropin (BST)

In 1993, the Food and Drug Administration (FDA) approved bovine somatotropin (BST) for use to increase bovine (cow) milk production. In December 1994, there were 800,000 cows, 8 % of the USA herd of 9,500,000 cows, receiving Prosilac, the trade name for Monsanto Corp. BST. A surver by the U.S. Department of Agriculture in late 1994, found the nation's milk production had increased by 3 %, compared to 1993; and attributed this increase largely to BST. The BST supplementation increases milk production by 1) shifting to higher level of milk production, and 2) improving the persistency of lactation. On average, milk yield is increased by 4 to 6 kg/day, which is associated with about a 12% increase in production efficiency (increased in units of milk produced/feed units consumed). Bovine somatotropin has no adverse effect on the cow and no change in composition of the milk. The USDA reports that Prosilac has lowered the cost of milk production to $12.70/hundred pounds. Contrary to concern of economists for the small dairy farmers ability to utilize BST and his ability to survive economically, Monsanto reports that 40% of the Prosilac customers in 1994 were farmers with less than 75 cows.

Despite the fear of milk farmers and food merchants that the vicious ill-founded (contrary to scientific data) health hazard scare (that was propagandized by a small noisy anti-science and anti-technology crowd that the BST produced milk was dangerous to human health) would seriously adversely affect the sales of the BST produced milk this has not materialized; and this anti-propaganda is now largely ignored by the public.

At present, the use of BST in milk production has been approved for commercial use in Brazil, Bulgaria, Costa Rica, the Czech Republic, Jamaica, Mexico, Namibia, Russia, South Africa, the Ukraine and Zimbabwe. However, its approval for use in the European Community (EC) has been embargoed for another five years—apparently largely because of political considerations. Indirectly, the use of BST has a modest positive indirect effect on the environment since, because of an increase in production efficiency, it requires less feed for each unit of milk produced.

2. Porcine somatotropin (PST)

The evaluation of porcine somatotropin is in the final stages of wide scale field testing. It is assumed by many that PST will be approved for commercial use by the FDA either in late 1995, or early 1996. Extensive research data indicates PST increases growth rate of pigs by 10 to 15% and improves productive efficiency by 15 to 35% (increase of body weight gain/unit of feed consumed). Moreover, it decrases adipose tissue mass by 80%, while increasing muscle growth by 50%. Producing leaner fresh pork will benefit consumers who wish to reduce intake of total fat and saturated fatty acids (SFA) and thereby, reduce risk of chronic diseases.

Saturated fatty acids elevate plasma-total and low-density lipoprotein-cholesterol levels and hence reduce the risk factor from heart diseases.

Plant Biotechnological Progress

1. Insect resistance employing genes from *Bacillus thuringiensis* (BT)

a. Transgenic cotton

Plants carrying the BT gene are in the fifth year of extensive field test. The transgenic BT varieties have provided excellent protection against cotton bollworm, tobacco budworm and pink bollworm for the past four years. It is expected that transgenic BT cotton will be approved for commercical planting in 1996. The fact that transgenic BT cotton varieties provide excellent control, not only of the three above mentioned very destructive insects, but also of several other less important lepidopteran insects, will be a boon to cotton production. Moreover, when transgenic BT varieties are used as a component part of an integrated pest control management program, including appropriate control of boll weevil (which is not controlled by the BT gene), it may usher in a new era of achieving effective control of cotton insects while greatly reducing the amount of insecticides.

b. Transgenic BT potato

Recently, Monsanto Corp. has obtained approval from the U.S. government, after five years of extensive field trials, for the commercial release of a BT potato variety, which effectively controls the Colorado Patato beetle. This insect is the most serious insect pest of potato throughout the USA, Europe and the former USSR.

c. Transgenic BT maize

On August 10, 1995, Mycogen Corporation and CIBA Seeds, a division of CIBA Geigy Ltd., received approval from the United States government to sell transgenic BT hybrid maize seed. For the past five years, in widespread experimental plantings on farms in different parts of the US corn belt, transgenic BT maize hybrids have provided excellent protection against the European corn borer (the most important insect pest of maize) and also against several other lepidopteran insects of maize.

It is almost certain that before the end of 1995, transgenic BT resistant varieties or hybrids of cotton, potato and maize, will all be approved by the FDA and the USDA, for commercial production in 1996. This event may usher in a new era, whereby widespread effective insect control may be obtained on three of the world's most important food and fiber crops while at the same time greatly reducing the consumption of insecticides.

This potentially revolutionary giant step toward achieving better insect control with the use of less insecticides, however, raises the question is this control real and durable—or is it ephemeral? Will insects soon overcome the resistance of the transgenic BT genes as they repeatedly have been able to do over the last three decades whenever new highly effective insecticides were introduced and widely used? No one knows, at this time, if the insect pests will quickly develop resistance and the ability to damage these transgenic BT varieties. I would not be surprised if they did—drawing on my fifty plus years of experience in battling the three shifty fungal rust pathogens of wheat. Although we have maintained stable resistance—worldwide since 1952 (43 years)—against the stem rust organism (*Puccinia graminis tritici*), the resistance of wheat varieties to stripe rust (*Puccinia striformis*) and leaf rust (*Puccinia rubigo-vera tritici*) seldom survive more than five to eight years. Why the difference? No one knows! And so it may also be, with the current transgenic BT varieties and other future transgenic genes for insect and disease resistance and control. Only time will tell.

2. Transgenic biotechnology in control of plant diseases

The development of transgenic plants for the potential control of viral and fungal diseases is not nearly as far developed, at present, as it is for either transgenic control of insects, or for the transgenic protection of cultivars of crop varieties against herbicides. Nevertheless, there are very promising examples of specific virus coat genes in transgenic plants that confer considerable protection against other viruses or fungi in a number of crop species. For example, a benign transgenic protein coat viral gene introduced into Burbank potato confers considerable resistance to the important virulent potato X virus (PVX) and Y virus (PVY). Recently, a transgenic rice plant containing a chitinase gene (from a soil bacterium) has been reported to manifest considerable resistance to sheath blight, caused by the fungus *Rhizoctonia solani*. Currently, a considerable number of other promising disease-resistant genes are being incorporated into transgenic crop species for evaluation of their disease control potential.

3. The use of transgenic crop varieties in weed control programs

Over the past five years, considerable progress has been made toward development of transgenic plants of cotton, maize, oilseed rape, soybeans, sugar beet, and wheat, with tolerance to a number of herbicides.

Two different approaches are being made to achieve this objective. One is to increase the tolerance of the host-crop plant to a herbicide. Soybean and canola have been made tolerant to the herbicide Roundup by introducing DNA coding for overproduction of the herbicide-resistant analogs of 5-enolpyruvylshikimate-3-phosphate synthase, the chemical target of the Roundup activity. In a similar way, resistance to sulfonylurea, the active ingredient in the herbicides Glean and Oust, is being incorporated into canola and cotton by the introduction of mutant acetolactate synthase.

The second approach is diametrically opposite to the aforementioned. It consists of developing transgenic plants containing bacterial genes for encoding enzymes that inactivate the herbicide. Transgenic varieties of canola, maize, soybean and wheat have been developed that are resistant to *Basta*. They have an enzyme that inactivates by acetylation of the active ingredient gluphosinate present in the herbicide. In a similar way, transgenic plants of cotton, with resistance to bromoxynil, have been developed. These plants are resistant to bromoxynil because of the inactivation of its active ingredient by nitrile hydrolysis. A considerable number of transgenic plants of important crop species, with tolerance to herbicides are now under widespread field evaluation.

I would like to advise a word of caution about where to use the DNA transfer and gene engineering technologies, so as to achieve its maximum benefit. It is important that the genes for disease and insect resistance and to resistance to herbicides be incorporated into the best high yielding commercial varieties and hybrids. If they are incorporated into a variety of modest yield potential, they will not be grown by the farmers and the research effort will be of little value.

4. Increasing yield

Up to present time, it has been generally assumed that increases in yield of crop varieties and hybrids are controlled by a large number of genes with additive effects. The same has generally been thought to be the case in animal genetics and improvement. However, the work of recent years shows that there may also be a few genes that are sort of "master genes" that affect the interaction—either directly or indirectly—of several physiological processes that influence yield. For example, the bovine and porcine somatotropin genes are apparently such "master genes." The former not only affects the total production of milk during the lactation cycle, but it also affects the efficiency of production unit of milk produced for unit of feed intake. Similarily the porcine somatotropin gene increases rate of weight gain, improves feed efficiency while reducing the amount of lipoprotein and increasing muscle tissue. In the case of wheat, the *Rht1* and *Rht2* dwarfing genes (from Norin 10) used to develop the high yieding dwarf Mexican spring wheat appear to act in a similar way. Originally it was thought that the principal and main effect was to improve the standability (reduce lodging) by reducing straw length and harvest index. It now appears, that these genes also acted like a "master gene" for at the same time they reduce plant height, they also increase tillering and number of fertile florets and number of grains per spike. Molecular genetics may be a new window through which to search for master genes by eliminating or reducing the confounding effects of other genes.

At the present time, virtually all agricultural scientists are specialists. This is especially true in the fields of molecular genetics, DNA transfer, and genetic engineering. But it is also becoming increasingly true of the other disciplines that bear on agricultural production. If we are to make the best possible progress in increasing yield of product and the safety of harvest (disease and insect resistance), as well as improving product quality, it will require much closer collaboration than we have had in the past between molecular biotechnologists, genetic engineers, geneticists, cytologists and plant breeders, agronomists, soil scientists, plant physiologists, entomologists, plant pathologists and cereal chemists. Unless this happens, we will not be identifying the potentials of the outstanding products coming from the new biotechnology and from conventional breeding programs. We will need to know, as early as possible, what the real maximum potential genetic grain (or fiber) yield, disease and insect resistance and consumer quality characteristics of the products are of the new plant genotypes. This can only be determined by growing them under optimum or near-optimum conditions under a range of different environments. This will require close collaboration of an interdiscipline team of scientists. I frequently have expressed my concern about the inadequacy of application of scientific knowledge to the improvement of agriculture and the alleviation of hunger with these words:

"No matter how excellent research done in one scientific discipline, its application in isolation will have little positive impact on crop or animal production. What is needed are venturesome scientists who can work across disciplines to produce appropriate technology and who have the courage and charisma to make their case with the political leaders to bring these advances to fruition."

Summing Up

Currently results of 15 years of biotechnological research are beginning to arrive at the commercial stage of application. This is most fortunate for the world has before it a most challenging and difficult situation. At the present time, world population stands at 5.7 billion and it is increasing at approximately 1 billion more each decade. The situation on the food front is further complicated by the fact that in most countries of the world, there is little additional suitable land available for cultivation, which means that to meet the growing food needs, most of the increase in production within the next three decades will have to come from increasing yield on the land now under cultivation. There are exceptions in the case of problem soils where there are abiotic stresses, toxicities or deficiencies, to which biotechnology can make contributions, but most of the yield and food production increases of the future will have to come from increasing the yield on the land now under cultivation. Moreover, with this great challenge before us, the application of science and technology will become more and more difficult, especially in the affluent nations, where there are strong, small but vociferous and highly effective well financed anti-science, anti-technology groups, who slow up the adaptation of new technology, whether it be developed from biotechnology or from conventional methods of breeding. Moreover, there is among this group some who are loudly opposed to the use of agricultural chemicals, who in discussions, lump together synthetic fertilizers, insecticides, herbicides, and fungicides, as though they all were of the same order of toxicity. There are other groups who are largely concenerned about endangered species. The interaction of all of such groups make it very difficult to launch new approaches for increasing agriculture and food production.

All young scientists should be aware of the danger of extremists who disregard or play down the importance of scientific facts and to rely too much on emotion and pseudo-science. Pseudo-science is dangerous! Recall that pseudo-agricultural science promoted by Dr. T. D. Lysenco contributed greatly to the destruction of the Soviet Union.

Finally

Let me emphasize to you students, that you utilize wisely and fully these golden years at the university to develop to the fullest the potential genetic talents you have inherited from your parents, grandparents, great-grandparents, etc. Don't waste them; don't be satisfied with mediocrity. Read and study! Read and study across many scientific disciplines to prepare yourself well for a fruitful scientific career! The world needs outstanding dynamic leaders. Reach for the stars! Although you will never reach the stars, if you exert yourself sufficiently you will get some stardust on your hands. With that as a catalyst, you will be surprised what you will be able to accomplish for yourself, your family and for the well-being of mankind in the broadest context. Moreover, remember that education should be a lifelong, continuing process, as was so poignantly put by the late Will Durant, the philosopher-historian, when he cautioned us to distinguish between knowledge and wisdom: "In my youth, I stressed freedom and in my old age (79 years) I stress order. I have made the great discovery that freedom (liberty) is a product of order, not of chaos. Sixty-two years ago (when I was 19) I knew everything and my father knew nothing. When I was 29, I was surprised to see how much my father had learned in the past ten years. Now I know nothing. So in effect, education is a progressive discovery of our own ignorance." Perhaps Will Rogers, the late Oklahoma country styled philosopher-humorist, said it even better in fewer words: "we're all ignorant, the only thing is that we are ignorant about different things." To this I might add, as we become more and more specialized, our ignorance become more and more expansive.

Now "goodbye, good luck and keep reaching for the stars!"

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