Agriculture in the developing world: Connecting innovations in plant research to downstream applications

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Enhancing agricultural productivity in those areas of the world bypassed by the Green Revolution will require new approaches that provide incentives and funding mechanisms that promote the translation of new innovations in plant science into concrete benefits for poor farmers. Through better dialogue, plant breeders and laboratory scientists from both the public and private-sectors need to find solutions for the key constraints to crop production, many of which center around abiotic and biotic stresses. The revolution in plant genomics has opened up new perspectives and opportunities for plant breeders who can now apply molecular markers to assess and enhance diversity in their germplasm collections, to introgress valuable traits from new sources, and to identify genes that control key traits. Functional genomics is also providing another powerful route to the identification of such genes. The ability to introgress beneficial genes under the control of specific promoters through transgenic approaches is yet one more stepping stone in the path to targeted approaches to crop improvement, and the new sciences have identified a vast array of genes that have exciting potential for crop improvement. For a few crops with viable markets, such as maize and cotton, some of the traits developed by the private sector are already showing benefits for farmers of the developing world, but the public sector will need to develop new skills and overcome a number of hurdles to carry out similar efforts for other crops and traits useful to very poor farmers.

crop genomics

By the year 2015, all 191 members of the United Nations (UN) member states have pledged to meet eight important development goals. Of these, the first goal, to halve the proportion of people who suffer from hunger and whose income is less than one dollar per day, is most relevant to the plant science community. Because >70% of the extreme poor who suffer from hunger live in rural areas, the effort to enhance agricultural productivity will be a key factor in achieving this goal and is listed as a key goal by the UN Hunger Task Force (1).

This challenge comes at a time when the plant sciences are witnessing remarkable progress in understanding fundamental processes involved in plant growth and development. Complete genome sequences for the reference plant species *Arabidopsis thaliana* and, more recently, for rice and poplar are now available, with others sure to follow. Through a variety of functional genomics approaches, plant scientists are increasingly able to identify and characterize genes that control key processes, while breeders worldwide are beginning to recognize the power that genomics can bring to their efforts for crop improvement. Sadly, it is also a time when the growth rate of global crop and livestock production is on the decline, especially for farmers in sub-Saharan Africa, where per capita production is actually declining (2). Such a situation indicates the urgency of finding better ways to translate the new advances in the world of basic plant science into concrete successes in the field of global agriculture. From my own personal experience working most of my life in academia and now the past few years with the Rockefeller Foundation, I can testify to the existence of a fairly high degree of "disconnect" between those who work at the lab bench and those who work in the field. This article is an attempt to analyze both the constraints and the opportunities presented by the challenge to translate new discoveries in plant sciences into successes in agriculture for the benefit of the poor of the world.

Translational Biology in Support of Agriculture

Creating Links to Academia. Plant biologists, like all scientists in academia, are overworked human beings whose achievements are measured by success in teaching, service to their institutions, gaining funding to support their basic research efforts and, above all, using that funding to make discoveries that can be published in high-profile scientific journals. Although many have a real desire to see the fruits of their fundamental research translated into concrete benefits, they have little opportunity to interact with those involved in international agricultural development and even less opportunity to find sources of funding to support such interactions. Despite all of the complaints, scientists of the "North" do have strong and relatively stable sources of funding for basic plant research, in particular for plant genomics. On the other hand, donors who support work on global agriculture are largely constrained to fund downstream applications relevant to the developing world. What seem to be lacking are systems that promote and reward efforts to create a strong interface between fundamental and applied research in support of global agriculture.

The concept of "translational biology" has received attention in the field of health, where the focus is on the promotion of better collaborations between bench scientists and clinicians; in fact, there is even a *Journal of Translational Medicine* devoted to this type of collaborative work. There are a few indications that this concept is taking hold in the plant community as well. Within the U.S. Department of Agriculture's National Research Initiative, there is now a program for Coordinated Agricultural Projects that has sponsored conferences on translational genomics for crops such as cotton, soybean, and barley and intends to fund integrated projects that will help engage applied plant scientists to better use the tools of genomics for crop improvement. The focus is on U.S. agriculture but, if partners and funding sources could be identified, such efforts could also be of great benefit for the improvement of staple crops important to the developing world. The Developing Country Collaborations

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Abbreviations: GM, genetically modified; CGIAR, Consultative Group on International Agricultural Research.

See accompanying Profile on page 15736.

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Program at the National Science Foundation will support research collaboration between U.S. scientists and scientists in the developing world. The leadership of the 15 international research centers of the Consultative Group on International Agricultural Research (CGIAR) that are strategically located throughout the developing world also has created a Standing Panel for Mobilizing Science that aims to engage scientists from the "North" in issues of priority to their efforts. As part of its strategy for human capacity building, the Rockefeller Foundation, through its grantmaking in support of agriculture, often promotes collaborations between scientists in the developing world and those in advanced laboratories. Yet funds are woefully lacking to identify and carry out full-fledged projects that connect upstream science with serious downstream applications to agriculture. Recently, at a meeting of a joint U.S.-European Commission Task Force assembled to identify challenges for plant science in the next few decades, one recurring theme was the need to support more efforts designed to apply new discoveries to downstream efforts in crop improvement, perhaps through the establishment of specific programs that fund imaginative efforts in plant biotechnology. Certainly any efforts that provide incentives for meaningful collaborations are needed and should be promoted by the entire plant science community.

A Role for the Private Sector. Scientists in the private sector are much more adept at working in the interface between basic and applied biology. In contrast to academia, success for these scientists is measured in the development of real products that generate profits for the shareholders of their companies. Personal interactions with such scientists indicate to me that many, like their colleagues in the public sector, would welcome the opportunity to work with the public sector to apply some of their findings to benefit poor farmers, in addition to serving their traditional clients, who are large-scale farmers. This latter group has the resources to optimize the use of inputs, yields in good years can often approach true yield potentials, and intense competition exists among the various large private-sector seed companies to develop only those new technologies that can enhance farmer profits, even by relatively small margins. For developing world agriculture, the considerations are quite different. A large-scale farmer in subSaharan Africa can get a yield of 10 metric tons (MT) per hectare for maize, whereas a poor farmer using a comparable variety with little or no inputs will obtain a yield <2 MT per hectare (3). What may be considered small gains in yield for the large-scale farmer, therefore, can be a quite significant increase for crops grown under low-input conditions, so crop improvement strategies that focus on optimizing yield under stress and minimal inputs may be, at least in the short-to-medium term, more appropriate than those that focus on enhancement of yield potential under optimal conditions. Given these different agronomic scenarios, it is easy to imagine that a promising technology for disease control may sit on the shelf at a company yet have enormous potential in the developing world.

The emergence of supermarkets in many places in the developing world (4) demonstrates there can be real potential for markets that serve the poor. Poor farmers increasingly recognize the benefits of hybrid maize and other high-quality seed. Yet there is little doubt that the current cost of good-quality seed, especially in subSaharan Africa, poses a real constraint for poor farmers. When technology fees for genetically modified (GM) crops are added on, the risk of purchase can often be considered too high for a poor farmer who is also burdened with excessive fertilizer prices and unpredictable rainfall. Efforts directed at enhanced microcredit and/or two-tiered pricing schemes for small- vs. large-scale farmers (with reduced or eliminated technology fees, where applicable) could certainly help mitigate some of these risks.

Because seed markets for poor farmers will grow slowly, it is not realistic to expect the larger private-sector companies to spend much in the short term to optimize their products for small-farm environments. Similarly, it is clear that they will be targeting few if any crops beyond cotton, maize, canola, and soybean, even if they possess technologies that might be beneficial to other crops. At least for maize, where there are markets for both large- and small-scale farmers, the analogy with the development of vaccines and medicines for neglected diseases is not perfect, but it is still worth considering. Because of imaginative thinking, public pressure, and truly significant funding, public–private partnerships (PPPs) have indeed emerged in the health sector for the development of vaccines to fight HIV/AIDS and for the development of medicines against the diseases of the poor, such as tuberculosis and malaria (5). For PPPs in the health field, the Rockefeller Foundation was instrumental in helping partners identify the prime targets for development and the motives for both sectors to join the efforts, to sort out issues of intellectual property, and to facilitate acquisition of the substantial funding needed for such large efforts. We have no equivalents yet for agriculture, but very promising are several meetings held recently to explore possible mechanisms for companies like Monsanto and Dupont/PioneerHiBred to work with the public sector to ensure that new traits under development, like drought tolerance, will benefit both large- and small-scale farmers. Also welcome are some of the projects funded by the Gates Foundation Grand Challenges in Global Health and the USAID-sponsored ABSPII program, which involve collaborations among pubic- and private-sector scientists.

There is a vast difference between what happens in the fields of a farmer growing just one or two different crops on 500 hectares in Iowa and another growing many more different crops on <1 hectare in Africa. The former will use varieties developed from highly inbred lines adapted to temperate climates, sophisticated agronomic practices, and optimal amounts of fertilizer and pesticides and, at least in most years, will operate with reliable and adequate rainfall. The latter, usually a woman, may live in any one of a number of diverse agroecologies (3, 6). She will also grow many different crops that will minimize her risk, growing for example some maize and beans in case rainfall will be plentiful and perhaps sorghum, cassava, and cowpea in case of drought. Cost considerations will prevent her from using even marginally acceptable levels of fertilizer or pesticides. These differences almost guarantee that any crop bred in the "North" will not be adapted to her growing conditions. Thus, one model for public–private partnerships (PPP) could be based on the fact that development of beneficial traits such as disease and pest resistance or drought tolerance in major commercial crops may sometimes best be addressed by the private sector, whereas the public sector holds a wide range of locally adapted germplasm relevant to poor farmers. In such a PPP, the public sector supports efforts to transfer valuable private-sector traits/genes into a range of locally adapted varieties suitable for low-input agriculture, with the private sector concentrating on varieties that would be sold in the larger, more profitable, markets of large-scale farmers. In cases where there would be an overlap in varietal preference, imaginative two-tiered marketing schemes might be devised. Yet we must recognize that, looking beyond maize, for certain important crops like cassava, banana, legumes, sorghum, and the millets that are often traded informally, the burden for crop improvement will certainly fall to the public sector, although the private sector should be strongly encouraged to find ways to share relevant technologies and provide crucial advice.

Major Constraints to Crop Production

DeVries and Toenniessen (3) have analyzed in detail both the biotic and abiotic constraints that currently limit yield on many of the major crops of Africa, a list that overlaps considerably with other very poor regions of the world. Examples of major constraints are given below; succeeding sections will suggest strategies for translating current basic research efforts into downstream solutions for some of these constraints.

Abiotic Stresses. Nutrient-poor, degraded, and often acidic, soils limit crop production in many tropical regions. When coupled with the high cost of inorganic fertilizer, especially in Africa, much small-scale agriculture occurs under conditions of nutrient deprivation and/or metal ion toxicity. Limiting amounts of phosphorous and excessive levels of aluminum are characteristic problems of acidic soils (7). The unintended consequence of trying to do good by drilling large numbers of wells in Bangladesh and parts of India has resulted in extremely high rates of arsenic poisonings in humans, but the problem also extends to agriculture, where these wells have served as irrigation sources, resulting in high levels of arsenic in the food (8). Saline soils are found naturally in many locales and have been created in others by poorly managed irrigation. Most of the extreme poor depend upon rain-fed agriculture and, according to World Watch, drought is perhaps the biggest constraint to agricultural productivity worldwide. As recognized by the International Rice Research Institute, in many countries of Asia, depletion of groundwater resources, rising soil salinity, and the competing demands for water by agriculture and a growing urban sector are likely to result in a shift in cropping systems away from traditional paddy rice toward growth under aerobic conditions. This, in turn, calls for more drought-tolerant varieties, new strategies for weed control, and a much better understanding of how large-scale changes in cropping systems for major crops like rice will affect the global balance of C and N.

Biotic Stresses. Fungal diseases are a huge problem worldwide. The fungal stem rust (*Puccinia gravinis*) of wheat was effectively controlled through introgression, decades ago, of the Sr31 resistance gene by Norman Borlaug and colleagues (9) and has been remarkably durable, but a resistant strain of the rust has recently emerged in Africa and, in this age of globalization, represents a potential worldwide threat if not addressed in a timely fashion (9). Soybeans of Africa, Asia, and Latin America are heavily affected by rust (*Phakospora*), and North American varieties have had good resistance until recently as the pathogen has emerged in some areas. According to the International Potato Center, the late blight of potato (*Phytophthera*) is the single most costly biotic constraint to global food production. Powdery mildews affect a wide range of crops, including major cereals like wheat, sorghum, and millet; fungal anthracnose affects crops such as sorghum, beans, and cassava; leaf spot and root rots also plague beans and other important crops; turcicum and gray leaf spot diseases are serious pests of maize in Africa; blast disease is serious for rice; and Black Sigatoka limits banana production worldwide. Small farm environments seriously promote the development of fungi that lead to mycotoxin accumulations; better statistics are sadly needed, but the little we have suggests the health effects of mycotoxins on the poor are much more serious than recognized previously (e.g., see ref. 10). Bacterial diseases similarly cause large crop losses. Particularly deadly are diseases caused by the genus *Xanthomonas*, which include blights in rice and cotton and, more recently, banana wilt, a serious new disease of the African Highland Banana, the major staple crop of Uganda.

Viruses are no less a problem for many crops. Among the RNA viruses are papaya ringspot, cassava brown streak, and cucumber mosaic virus which affect many vegetables. In Africa, the ssDNA geminisviruses such as maize streak and cassava mosaic virus are particularly deadly; worldwide, others, such as tomato leaf curl and banana bunchy top, are also important. And finally, in certain parts of subSaharan Africa, the parasitic weed Striga can be one of the most serious constraints to the yields of crops such as maize, sorghum, and cowpea, whereas another parasitic weed, Orobanche, is an important pest to several crops in countries like Egypt and India.

This list of constraints is by no means comprehensive. To my mind, the best approach to identifying key constraints is to establish a much better dialogue with between bench scientists and those key breeders in the developing world who actually talk to farmers and understand local agriculture. One of the most rewarding experiences I have had in recent years was to organize a workshop that brought together breeders of African crops with some of the key scientists working on genes that control flowering time and plant architecture. When forced to avoid jargon specific to their trade and to resist talking just about their most recent great discovery, these two groups were excited to learn from each other and to identify some imaginative new approaches to crop improvement, some of which are now being funded by the Rockefeller Foundation.

Harnessing the New Sciences for Crop Improvement

Agriculture will never truly thrive in places like subSaharan Africa unless solutions are found for fundamental issues, such as lack of roads, weak input and output markets, the low level of general health and education of poor farmers, poorly functioning extension services, and gender inequity that places a disproportionate burden on women in agriculture, all critical issues that cannot be solved by biotechnology and are well beyond the scope of this article. Even in the specific area of crop improvement, there are great opportunities to apply conventional breeding that do not need to draw on the very latest discoveries in plant biology. One of the first rules of our Food Security Team at the Rockefeller Foundation is, “If the breeders can solve the problem, let them do it.” In places like subSaharan Africa, once breeders began tailoring their efforts to breeding targeted specifically to African conditions, it became apparent that significant crop improvement is possible through conventional approaches (11).

The Increasing Power of Molecular Breeding. With respect to the recent advances in the plant sciences, as the sequences of many plant genomes become known, the power of genomics for applied breeding has to be one of the most exciting advances of recent years. Extremely valuable to breeders in the national agricultural research systems is the ability to genotype their collections to get a clear picture of their diversity and how such diversity might be enhanced through sharing and access to global collections. The use of marker-assisted selection in cases where phenotyping presents a challenge or to trace introgression of known genes or important regions from wild relatives should also become part of every serious national breeding program.

Complete sequence information, maps, and a huge array of molecular markers exist for rice; with more sequence information for other crops, new techniques for assessing allelic diversity, and a better understanding of synteny (12), these are now being adapted for the breeding of other crops. Yet, for orphan crops like cowpea, common bean, the millets, tef, and cassava, we still have insufficient numbers of ESTs, bacterial artificial chromosome libraries, molecular maps, and markers (13). Programs such as the Generation Challenge Program and crop-specific initiatives such as Phaseomics are beginning to address these limitations, but a glance at the number of ESTs available for different organisms (www.ncbi.nlm.nih.gov/dbEST/dbEST_summary.html) indicates that more funds and efforts are clearly warranted. Good value can also be had through sequencing of the genomes of major plant pathogens. In addition, there are many challenges in creating the needed infrastructure, including high-throughput analysis systems and critical high-speed Internet access to the tools of bioinformatics; development of a pool of breeders well-versed in the use of these tools also still limits progress on this front. Networks in Asia that brought together rice (the Asian Rice Biotechnology Network, ARBN) and maize breeders (the Asian Maize Biotechnology Network, AMBIONET) to build capacity and better interactions among molecular breeders have been most successful; a similar fledgling network called AMMANET (African Molecular Marker Applications Network), which holds promise for African breeders, is another welcome development.

A new regional center in Nairobi called Biosciences for East and Central Africa (BECA) is intended to serve as a center of excellence for agricultural biotechnology that will interact with and serve the various universities and national agricultural research systems of the region. At BECA, the modern tools of genomics can be shared with breeding programs through training, provision of markers, high-throughput analysis coupled with a sophisticated bioinformatics platform, and joint efforts to genotype key crops and identify projects suitable for marker-assisted selection. For example, a recent meeting at BECA brought together 28 sorghum and millet breeders from national agricultural research systems representing 14 countries of the region and specialists in molecular breeding and genomics from the U.S., Europe, and the International Crops Research Institute for the Semi-Arid Tropics (ICRISAT). The purpose of the meeting was to learn about the genomics tools available to them from both public and private sources and to discuss and draft project proposals for application of marker-assisted selection in African sorghum and millet breeding programs. More extensive promotion of such collaborations and other forms of imaginative human capacity building is clearly warranted.

The use of molecular markers has helped highlight the importance of genes from wild relatives for use in crop improvement (14, 15) and, as evidenced by recent work on tomato improvement, the results can sometimes be spectacular (16). African farmers are showing real enthusiasm for new interspecific hybrids that combine the best of both Asian and African rices (17). For complex traits, the identification of quantitative trait loci (QTL) has advanced to a considerable degree, to the point where it is now becoming somewhat more feasible to identify specific genes that control the traits underlying the QTL (e.g., see ref. 18 and refs. therein). Advances in genomics should also be able to contribute new insights to our currently vague understanding of that most important of traits, heterosis (hybrid vigor). Can the recent work showing how inbred lines of maize differ strikingly in gene sequences (e.g., ref. 19) and gene expression patterns (20) provide some clues? Can such understanding help us determine whether there is good value in promoting the development of hybrid sorghum and millets for Africa and to explore further the potential of heterosis in many crops beyond maize? Certainly, development of hybrid seed is one way to promote viable seed markets for crops. But do we understand well enough the cost–benefit equations for small farmers with respect to purchase of high-quality seed (hybrid or not) vs. the saving of seed, and is the development of a strong private-sector seed business a necessary part of moving such farmers beyond the subsistence level? Such questions go beyond the realm of science into that of sociology and economics, but good answers clearly require input from the scientific community.

Are GM Crops the Answer? A fierce debate continues over the potential of GM crops to solve the problems of hunger in the developing world. At one extreme, proponents argue that these new technologies will be the panacea needed to solve hunger, whereas the other extreme argues that the technologies are unsafe to both humans and the environment and are being promoted simply as a means to further the interests of the large multinational companies that market them. Those arguments are not the focus of this article, except to say that most reasonable people understand the truth lies somewhere between these extremes and, at best, GM crops are only one of many approaches available to solve world hunger, and developing countries should be free to assess their worth within the context of their own needs and priorities. It can be argued that all new advances, including the undoubted success of the Green Revolution, can have their downsides. A recent example is the Roundup Ready soybean, which has been a huge success for the farmers of Argentina and Brazil but may be promoting a debatably dangerous trend toward monoculture and expansion of farming into valuable sites for biodiversity. Whatever one's opinion on these issues, there seems to be little doubt that the endless, and often shrill, GM debate has limited the development of crops that could be very relevant to poor farmers by reducing the number of donors willing to support such efforts, raising concerns over liability in companies considering the provision of their technologies for use in public-sector projects and creating confusion and uncertainty about whether to allow even simple testing of the efficacy of new transgenic crops in developing world countries. A key consequence of this debate has been to lower the level of engagement of skilled scientists in key laboratories who should be building better capacity in this field.

Most of the discussions on GM crops are much too narrowly framed and focus just on the current situation, wherein only four major GM crops, with only two traits, represent the bulk of the GM market today. These traits are insect and/or herbicide resistance in soybeans, maize, canola, and cotton, a very limited repertoire that was designed by the private sector for use in large-scale agriculture. First, I shall discuss the extent to which this limited repertoire may be suitable and beneficial for use in the developing world. Then I shall make the argument that there are many other opportunities for crop improvement besides the current GM crops that could be developed by taking a more imaginative look at the recent advances in gene discovery.

The Relevance of Current GM Traits and Crops for the Developing World. In subSaharan Africa, maize is clearly the major staple human food crop in many countries, and cotton is grown as a commercial crop even by the poor in countries like Mali, South Africa, India, and China. For these crops, a strong commercial market for GM seed is developing that, at least in principle, targets both large- and small-scale farmers. Accumulating evidence indicates that the current GM crops can clearly prove beneficial to small as well as large farmers. Varieties of cotton with the toxin gene from *Bacillus thuringiensis* (*Bt*) are proving their worth to poor farmers in South Africa (21) as well as parts of Asia (22, 23), and *Bt* rice is performing well in late-stage trials in China (24). The benefits of these crops can be quite different depending upon circumstances. In China, where yields of conventional cotton and rice are maintained through heavy use of pesticides, the benefits are in savings on the costs of these inputs and on the health of workers from pesticide poisoning and protection of the environment through the use of fewer chemicals. In South Africa and India, where costs of pesticides are prohibitive for the poorest farmers, the benefits are more clearly seen in substantial yield increases when pests are controlled through *Bt* technology. However, quite worrisome for the developing world is the serious issue of illegal seed movement and/or sales for GM crops, which occur widely in countries like Brazil, India, and China, which has lowered the incentive of the private sector to continue their involvement, weakened the private seed sector within these countries, and also lowered the quality of seed available to farmers (e.g., see ref. 25).

In contrast to *Bt*, where the trait is embedded in the seed, herbicide tolerance is a trait more beneficial to large-scale farmers who can afford to buy chemical inputs. Yet, several developments may require some rethinking of this belief. One of these is the increasing shift in Asia from growing rice in paddies that provide good weed control to aerobic conditions. In Africa, cost considerations, as well as the variety of crops grown on a single small plot, make the idea of herbicide tolerance seem less attractive for small-scale farmers. Yet, as shown in Argentina, herbicide-tolerant crops certainly favor the development of no-till agriculture, which can control erosion, save water, and sometimes allow for double-cropping; furthermore, in Africa, hand-weeding occupies much of a farmer's time and, with the severe labor shortages developing as a result of the HIV/AIDS epidemic, the science community should perhaps think about promoting cropping systems that save the time and energy of the farmer.

All these facts indicate there definitely can be a positive role for the private sector for the sale of seed for these major crops with these traits in at least some areas of the developing world. Experience tells us that if farmers benefit, if they have the cash, or if they can be helped through microcredit schemes, and if strong regulatory systems are in place (as in the U.S., Argentina, and South Africa), they will buy such quality seed. But if governments, as was the case in Brazil with the Roundup Ready soybean, delay approval of a GM crop that farmers clearly want, the farmers often find a way to get it illegally, compromising both the quality of seed available, the viability of private seed sector, and the ability of a government to provide adequate regulation.

In terms of strategy, one has to strongly question whether the public sector should waste its precious resources developing any product that duplicates what the private sector can make available. However, similar benefits could be imagined for these same traits in a number of crops that are traditionally outside the formal seed sector and of no interest to the large private-sector companies. Targets where *Bt* genes could potentially be used to address the constraints of poor farmers include the pod borers that attack cowpea and pigeon pea; the stem borers of rice, weevils, and/or nematodes that attack banana or sweet potato; the diamondback moth that affects cabbage; or the fruit and shoot borers of eggplant. For maize, the larger grain borer has become a serious storage pest for maize in Eastern Africa and is a target trait not likely to be addressed by the private sector (26). Techniques now exist for transformation of all of these crops, although some would certainly benefit from further optimization. Genes have clearly been identified to control most Lepidopteran pests such as the moths and pod, stem, and fruit borers. Searches are still ongoing to identify the most effective *Bts* that may control Coleopteran pests like large grain borer, weevils, and nematodes; these are cases where the application of gene shuffling techniques may be important for enhancing effectiveness.

Moving Beyond *Bt* and Herbicide Tolerance. The plant science community is discovering a vast array of genes that control all aspects of plant growth and development. Although GM crops based on many of these other genes may have little or no commercial potential, they can have a much different value when considered for certain crops important to the developing world. The creation of nutritionally enhanced crops such as Golden Rice is an obvious example (27, 28), but it should be possible also to enhance mineral content and improve the digestibility of crops like sorghum and to eliminate toxic compounds such as the cyanogenic glycosides of cassava. Although perhaps not quite ready for downstream application, the recent work on the identification of new genes that control phosphorous utilization or tolerance to aluminum offers future promise (7). Also worthy of more intense study are the arbuscular mycorrhizal fungi that form symbiotic relationships with >80% of all plant species and certainly contribute to the more efficient extraction of nutrients from the soil (29). A major problem in working with these has been the inability to culture these fungi in the absence of the host; in this regard, an exciting breakthrough is the recent identification of strigolactones as key stimulants of fungal development, which are secreted from plant roots in response to low phosphate; this work may also have significance for research on the parasitic weed Striga, because similar compounds also stimulate Striga seed germination (29, 30).

Through the classic studies of coat-protein-mediated resistance (31) and, more recently, using RNA interference, we know it is entirely feasible to control RNA viruses such as ringspot, which attacks papaya (32); similar approaches can potentially be used with great benefit for the brown streak virus of cassava or against cucumber mosaic virus, which affects many vegetable crops. The ssDNA geminiviruses that cause devastating diseases of cassava, maize, banana, and tomato, because they do not involve an RNA-based intermediate for replication, were thought not to be controllable by this approach, but recent evidence suggests they may nevertheless be targets for posttranscriptional gene silencing (33); other targets for control are also being explored (e.g., refs. 34 and 35).

Bacterial and fungal diseases represent an enormous challenge, because they cause such huge losses to farmers who lack the labor and skills needed for good field management and the money for effective pesticides (36). Breeding for resistance can clearly solve some of these problems, but development of pathogen resistance is a persistent problem, so the plant community needs to unite to come up with more and better strategies to achieve durable forms of resistance, a goal I would list as one the highest priorities for future plant research for the developing world.

I think there is no field in plant biology that has a collection of more imaginative scientists than those who have discovered such an amazing amount of information about pathways invoked upon the response of plants to pathogens or insects. Surely the field can benefit from continued work on the complex events involved in early recognition, including further identification of interacting proteins and the role of proteolysis in the process (37, 38), and on the connections between and relative importance of basal and induced defense systems (38). For both breeding and transgenic approaches that target resistance (*R*) or avirulence (*AVR*) genes, a clearer understanding of the nature of the fitness costs of both the *R* genes of the plant (39) and *AVR* genes in the pathogen (40) is one avenue worthy of additional exploration. It is clear that the simple idea of constitutive overexpression of key genes in resistance pathways often leads to loss of plant vigor and yield penalties (41). At first glance, the idea of inducible overexpression of key transcription factors that control a range of downstream responses seems attractive for disease resistance (42) and may represent one of the best approaches for other complex traits, such as drought tolerance (43). Equally critical to the success of this approach would seem to be the type of promoter selected. Unfortunately, for all transgenic work, the pubic sector is woefully lacking in a suite of good promoters for both eudicot and monocot species that are tissue-specific, developmentally regulated, and/or inducible by environmental cues like stress, disease, or cheap and safe chemicals. But the use of transcription factors for the control of diseases may be more problematic than originally imagined because of the complexity of the response pathways and the discovery of negative crosstalk that sometimes occurs between the salicylic acid-regulated pathway for disease resistance and the jasmonate–ethylene-regulated pathways important for insect resistance (44). One key regulator that intersects both of these pathways is the *NPR1* gene (45); understanding ways to modulate its location and/or function in either pathway might therefore provide one way to control at least one type of negative crosstalk. Yet this is one field where it seems the more we learn, the more complicated the challenge, and one longs for another magic bullet similar to the Bt genes that control insects so well and so durably. Perhaps scientists need to think more about creating, through molecular design, some imaginative killer genes like Bt that could target specific groups of plant pathogens.

We should also be able to draw on the fascinating findings from the world of plant development to improve certain crops. At the meeting that brought together bench and field scientists, breeders told molecular biologists that cassava is very poor at flowering and, even worse, two varieties one wants to cross often do not flower at the same time in the same breeding station. From this emerged a project to attempt to create cassava for breeding purposes that has a flower-inducing gene under the control of an ethanol-inducible promoter. Ideas also emerged for projects that could aim to dwarf the ungainly East African Highland Banana or the favorite cereal crop of Ethiopia called tef, to enhance drought tolerance through stress-induced changes in root architecture, and to ask whether RNA interference technology might be used to control the parasitic weed Striga by sending, through host–parasite connections, an engineered small RNA from maize to directly target a critical Striga gene. References too numerous to cite here indicate we now should be able, perhaps with single-gene changes, to control traits like tillering in cereals; alter root or shoot branching patterns; control the timing and extent of flowering and/or alter vernalization requirements; change seed size or number; control seed shattering; and perhaps even think about altering flower color, scent, structure, and/or time of opening to prevent gene flow by pollinating insects. In Africa, children are made to stay home from school to scare away the birds that steal exposed grains of crops like sorghum; perhaps a mutant gene like "Tassel Sheath" of maize might be transferred to sorghum to mimic the advantages found in the enclosed grain of maize. Finally, the new insights emerging daily on how microRNAs control development (46) should offer many other new approaches to changing plant form and function. The above are only some examples of what might be done today, given current technologies, and only hint at what might be done in the future when additional insights become available, although they do not take into account cost–benefit analyses for any given projects or other roadblocks that might need to be considered.

One recent impressive *tour de force* study with rice involving genes controlling development is instructive for the current debate about whether molecular breeding should be favored over a transgenic approach. Using all the tools of modern breeding, Ashikari *et al*. (18) identified a strong quantitative trait locus (QTL) that controls grain number, cloned the gene (a cytokinin oxidase) in an effort that involved the analysis of 13,000 F_2 plants, and created transgenic plants with a larger grain number by overexpression of the gene. Having learned much about this gene and its relationship to other members of the same gene family through the transgenic approach, the authors (18) then returned to breeding to pyramid the locus for an enhanced grain number with that surrounding the semidwarf gene (*sd1*), resulting in a plant that should substantially enhance grain yield. Ashikari *et al*. (18) have impressively shown what can be accomplished through molecular breeding, particularly as one approach to the identification of candidate genes; however, one has to ask whether, once specific genes are identified (as they were for both the cytokinin oxidase and the dwarfing gene), it would not make more sense to pursue a targeted transgenic approach for pyramiding the genes. In the end, the goals of breeding and transgenic research are the same, the introgression of good alleles for crop improvement. With breeding, linkage disequilibrium is a reality that often (but certainly not always) can result in the transfer of unfavorable genes along with the targeted good gene, whereas the transgenic approach eliminates this problem. Once candidate genes (and/or or key alleles of promoters of genes) are verified for traits of interest, either through QTL or functional genomics approaches, it would seem the most obvious route for trait improvement should be to move each good allele (and, if two or more, preferably linked to each other) selectively to the crop. Even from a regulatory point of view, this should be more attractive, because one knows exactly what is being transferred. Unfortunately, under the current regulatory climate, any new variety containing one or two new genes produced through breeding can find an easy path to approval and release, whereas the same variety with the very same new genes produced through transgenic approaches may be held up for years, if not forever, awaiting the approvals necessary for release to farmers.

Roadblocks Facing the Public Sector

Learning to Think Like the Private Sector. Technically, GM crops such as those suggested above could be developed now through concerted public-sector efforts. In fact, the public sector seems to be hard at work in many places doing transgenic research for the developing world (47), yet many of these projects are still in the very early stages of exploration, and one wonders whether any has a strong chance of every reaching the fields of poor farmers. It is no accident that there have been only two successful transgenic crops [*Bt* cotton (22) and virus-resistant papaya (32)] developed through public-sector efforts. There are plenty of public-sector scientists who can create transgenic plants in their laboratories. What has been sadly lacking in the public sector is an understanding of how to make strategic assessments of which projects can have the highest impact; how to choose the best varieties for transformation and to design the best constructs to ensure the freedom to operate and gain regulatory approval; the recognition of the need to generate very large numbers of transformants to ensure high levels of expression and the stability of the inserts and to determine the optimal promoter; and a clear plan for the stewardship, uptake, and dissemination of new varieties.

For all these issues, there could be no better mentor than the scientists of the private sector who deal with these issues on a routine basis. One way to foster such mentoring would be to engage the interest of the Private Sector Committee for CGIAR, the mission of which is to foster better interactions between private-sector science and that conducted in the CGIAR system. Such a committee might be able to arrange for private-sector consultants for any transgenic crop development projects that do not compete with private-sector interests and are undertaken by CGIAR scientists and their collaborators in national agricultural research systems around the world. But there must be a serious resolve on the part of public-sector scientists to move beyond just proof of concept with a few transgenic events, and they will also need adequate resources and infrastructure for such efforts. I would also argue that, because the approaches for many different crops are similar, it would make sense for the CGIAR centers to come together to form one serious biotechnology unit where a team of skilled and interactive scientists can work together in an environment that provides the kinds of high-throughput capabilities and ability to do easy field testing that are needed for these types of efforts.

Dealing with Intellectual Property and Regulatory Issues. With respect to freedom to operate (FTO), several new initiatives are under way to try to address these issues (48). For the benefit of African agriculture, the relatively new African Agricultural Technology Foundation has been established by Africans to help negotiate access to private-sector technologies and to assist with stewardship issues. Access to public-sector technologies should become increasingly easy to obtain due to the interest in new models for licensing of technologies by organizations like the

Public Intellectual Property Resource for Agriculture and the Biological Innovation for an Open Society (BIOS) initiative of CAMBIA (49). I would urge all scientists to become familiar with the goals of Public Intellectual Property Resource for Agriculture (PIPRA) and to make sure that licensing policy for any patented invention of theirs is done to keep available rights for the use of that discovery for humanitarian purposes. Scientists should also study the strategy for the open-source licensing proposed by the BIOS initiative; as an example of how this may work, Richard Jefferson, the founder of this initiative, has agreed to make discoveries such as his recent development of an alternative to *Agrobacterium*-mediated transformation freely available under an open-source model in which users are free to use the technology but must keep all improvements within the public domain (49). The exciting new work on the modeling of complex interactive networks, such as that being done with *Caenorhabditis elegans* (50), might be an example of the type of activity that *Arabidopsis* gurus could take up as a highly interactive project where data are freely shared and based upon open-source concepts. Another attractive and rather obvious solution to the problem of FTO is to build the scientific capacity for transformation work within the developing country, where key patents often have not been registered, so genes can be amplified and plants transformed with limited FTO issues.

Regarding regulatory approval, so much has been written on this topic that there is little need to go over the same ground again here. Clearly, developing countries need to make their own decisions on these issues and learn from the experience of others while developing their own responsible means of regulation that takes into account and weighs benefits as well as risks. There seems now virtually no reason at all to insist on elaborate repeats of trials that have been done in vast numbers of other locations for a crop like *Bt* cotton, especially for countries where farmers are clamoring to grow it to remain competitive. For the developing world, the key would seem to be to find ways to make field trials responsible but as low in cost as possible; otherwise, no public-sector effort will be able to participate. One way to keep costs lower is to promote standards that are accepted not just in one country but in the entire region where growth of the crop is predicted. Another issue that has not been addressed sufficiently is the big difference between carrying out a limited field trial to test for the efficacy of a transgenic event and, depending upon the crop and the trait, more extensive trials that might be needed before final approval for release to farmers. Because it is expected that not all GM projects will yield useful products (in particular those developed by the relatively inexperienced public sector!), developing countries should find ways to allow limited efficacy trials under appropriately contained conditions that are simple in design to keep costs low but responsible in concept. Only when events are deemed worthy of further development and depending upon the crop and trait in question would it be necessary to invoke more extensive trials on a final chosen event. Bradford *et al.* (51) have outlined other very sensible ways good science can be combined with common sense to enhance the efficiency of regulation without compromising safety. One is to exempt selected transgenes and classes of transgenic modification from regulation where extensive data are already in place indicating they are safe. Another suggestion is to create regulatory classes in proportion to potential risk. One can offer examples relevant to the developing world. Even though cowpea and sorghum outcross with wild relatives in Africa, there would seem to be little or no risk to gene flow if the gene were one that enhanced lysine or β-carotene content, whereas introduction of herbicide tolerance might be considered a greater risk that needs some assessment. The idea of using transgenic food crops to produce pharmaceuticals involves a different class of risks and seems of dubious value when nonfood plants might just as well be used. Bradford *et al.* (51) also recommend eliminating the current method of "event-specific approvals." Currently in the U.S., each independent transgenic event must be submitted for approval, although it can later be crossed into other varieties. If this practice becomes widely mandated in the developing world, it will be extremely difficult to deal with when developing GM crops like cassava and banana that, for a variety of reasons, are difficult to breed but relatively easy to transform. This type of regulation was instituted in the early days of GM crops when it was thought that position effects might show a strong influence on gene behavior, but there is little or no evidence that this has been the case. The complexity of these issues emphasizes it is essential that all regulatory agencies have some staff that understand the science involved to make sensible decisions.

Some Special Challenges. A far greater challenge may be to find responsible mechanisms for dissemination and monitoring of crops for which there is no well developed seed sector. Because there is a growing demand for hybrid maize among small farmers, hybrid GM maize already has, through private-sector seed companies, a mechanism in place for distribution and monitoring. Open-pollinated varieties of maize and other crops that outcross widely and/or where seed is saved from year to year, represent a bigger challenge, and one could argue that traits like Bt or herbicide tolerance that may transfer through outcrossing to the same non-GM crop or to wild relatives would be better restricted to hybrids that can be monitored by those who sell the seed. One can, of course, argue that non-GM crops with traits for disease, insect, and herbicide resistance have been around for years and require no regulatory approval; transfer of genes from these to wild species has posed little or no problems; and GM crops for other traits like improved nutritional quality fall into a class that poses essentially no risk to the environment. A more serious issue from a scientific perspective is that any new trait can become diluted out and lose efficacy in crops with a high degree of outcrossing and where seed is saved and reused by farmers. For vegetatively propagated crops, the use of tissue culture to provide more vigorous virus-free plantings has expanded widely for crops like banana, cassava, potato, and sweet potato. Farmers, even in Africa, are finding good value in the purchase of some of these, especially banana, suggesting that distribution of these types of GM crops might be responsibly managed through similar tissue culture operations. What is clear is that a serious analysis for each crop in each locale will be needed, and perhaps the only good news in the slowness of the public sector to develop such crops is that we still have time to create the proper roadmap for distribution and monitoring of any future crops developed.

Conclusion

The challenges surely are great, but the opportunities are there to harness the innovations of the worldwide plant science community and put them to use for the public good. The genomics revolution is creating its own revolution in plant breeding that cannot be ignored, nor should we avoid stepping up to the plate with courage when it comes to GM crops. The best argument we can make that GM crops can have value for the poor is simply to produce a few winners that such farmers really need and can benefit from. Sadly, we have very few examples at present, but if we really believe in this approach, we need fewer roadblocks and a clearer roadmap than we have had so far to reach that goal. And for all approaches to crop improvement, we clearly need more efforts that promote meaningful dialogs between bench and field scientists, better systems of reward within academia for such collaborative efforts and, perhaps most critical of all, substantial new sources of funding for serious projects that aim to apply the exciting innovations in plant science to problems faced by poor farmers throughout the world.

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