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# Biotechnology in the developing world: a case for increased investments in orphan crops $\stackrel{\star}{\sim}$

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#### Abstract

This article examines the opportunities for using several forms of modern biotechnology to improve orphan crops in developing countries. These crops, including tef, millets, cowpea, and indigenous vegetables, fruits, roots, and tubers, tend to be locally important, but receive little public or private investment. Recent advances in the fields of genetics and genomics provide a more unified understanding of the biology of plants. We summarize some important ways in which genetic technologies can be harnessed for orphan crops and provide examples of potential genetic and genomics research that is likely to benefit poor regions. Finally, we suggest policies that could help create incentives for application of advanced science to orphan crops.

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# Introduction

Most investments in agricultural biotechnology<sup>1</sup> have centered on widely consumed crops that are traded internationally, such as maize, rice, wheat, cotton, soybeans, and canola (James, 2001). Neither the public nor the private sector has invested significantly in genetic technologies in the more diverse minor or "orphan" crops that are often critical in the world's most disadvantaged regions.<sup>2</sup> Because orphan crops occupy smaller areas and have more limited markets, they are rarely a target of advanced science.

The dual purposes of this paper are to bring orphan crops to the fore and to explore the possibilities and limitations of extending advanced molecular science to them. Important new opportunities for improving orphan crops now exist in the tools gained through research on major crops and on model species, notably *Arabidopsis*. Recent achievements in the fields of genetics and genomics provide a more unified understanding of the biology of plants, which in turn can provide new opportunities for applying advanced science to orphan crops.

We focus our discussion on orphan crops for several reasons. They are not produced widely around the world, they are not traded to any significant extent in international markets, and they receive considerably less attention than the major crops from international or regional crop research organizations (such as CGIAR, the Consultative Group on International Agricultural Research).<sup>3</sup> Nevertheless, orphan crops are valued culturally, often adapted to harsh environments, nutritious, and diverse in terms of their genetic, agroclimatic, and economic niches. A large discrepancy exists between the potential role of orphan crops in improving food security and the small amount of attention they have received.

Justifying significant investments orphan crop improvement requires a shift in investment from individual crops to whole sets of crops with common genetic structures. This perspective permits a focus on a series of important technological questions. How important, for example, will genetic and genomic research on key species now being used as research models—such as rice, maize, *Arabidopsis* or the emerging legume model, *Medicago truncatula*—be for future improvements of orphan crops? In which cases will the spillover benefits from major to orphan crop research be greatest? Will it be necessary to organize technical efforts along lines delineated by plant families, such as grasses and legumes, or will results from model species apply broadly? Will research on mechanisms of plant responses to

<sup>&</sup>lt;sup>1</sup> "Biotechnology" as used in this paper encompasses transgenic technologies, tissue culture, advanced genetics, and genomics.

 $<sup>^{2}</sup>$  We have chosen to use the word "orphan" as opposed to "minor" to describe those crops that receive little scientific focus or funding relative to their importance for food security in the world's poorest regions, although both terms are used more broadly in the literature. We refer to "minor" crops as those other than the "major" food crops of wheat, rice, maize, and soybeans. We want to stress the fact that minor crops and their orphan subset typically play major roles in nutrition and food production stability at local or regional levels.

<sup>&</sup>lt;sup>3</sup> For further information on the CGIAR, see http://www.cgiar.org.

stress provide broadly applicable strategies for limiting crop loss? Will reciprocal benefits exist for the major crops from incremental investments in orphan crops, e.g., the identification of genes conferring drought tolerance? And most of all, will it be possible to integrate new plant traits and other findings into the ongoing, if limited, crop improvement efforts already underway in the less developed regions of the world?

A key issue in this process is identifying the correct balance of scientific investments between major and orphan crop development in poor countries so that the spillover effects from major crop research are maximized and the scientific foundations for orphan crop research are ensured. At the same time, attention must be paid to conventional breeding and delivery in both major and orphan crops. Crop improvement entails far more than biotechnology, and biotechnology entails far more than transgenic applications of Bt and herbicide resistance, which have been most commonly reviewed in the policy literature.

# Orphan crops in a development context

Population growth over the next 30 years will be concentrated almost exclusively in the developing countries, where more than 1 billion people currently live on less than US\$ 1 per day, more than 800 million people are undernourished, and 200 million children are underweight (Smil, 2000). This poverty is worst in rural areas where agriculture is the leading source of incomes and employment. The world's poorest regions are typically those where agricultural investments by the public and private sectors are extremely low. Unless some mechanisms can be found to stimulate agriculture, the outlook for these poor societies is bleak.

The role of agriculture in food security extends far beyond growth in crop yields and total production. Agriculture promotes food security primarily when it contributes to incomes and productive employment. Enhancing food security in the poorest regions requires investments in scientific research and training and the transfer of knowledge and technology to ensure wise management of resources and sustained capacity for growth. Moreover, food security dictates a focus on poor people's crops: subsistence and marketed crops grown in marginal areas where the poorest segments of the rural population are concentrated.

Few tabulations of the importance of orphan crops exist.<sup>4</sup> Table 1 is our attempt to provide several indicators for minor (including orphan) crops, especially in relation to the four major food crops.

Wheat, rice, maize and soybeans each occupy more than 70 million ha globally per year. Collectively, they cover 580 million ha and generate on the order of US\$ 300 billion in gross value annually.<sup>5</sup> Approximately two thirds of their combined area is within developing countries. Remarkably, these four crops also supply an

<sup>&</sup>lt;sup>4</sup> One of the better efforts can be found in CGIAR (1994).

<sup>&</sup>lt;sup>5</sup> For reasons having to do with FAO data availability for the minor crops, Table 1 uses 1995 price data in the value calculations.

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	World <sup>a</sup>				Developing	50				Sub-Saharan Africa	n Africa	
	Area 1000 Ha	Production (1000 Mt)	Price (1000 US\$/ Mg) <sup>b</sup>	Value (million US\$) <sup>c</sup>	Area (1000 Ha)	Production (1000 Mt)	Value (million US\$) <sup>d</sup>	Calories (cal/day)	Protein (g pro- tein/ day) <sup>c</sup>	Area (1000 Ha)	Calories (cal/day)	Protein (g pro- tein/ day) <sup>c</sup>
Major crops Wheat Rice (paddy) Maize Soybean	213.709 154.140 138.739 74.102	584.994 600.638 592.999 161.230	177 208 124 259	103.544 124.933 73.235 41.759	100.495 150.103 90.237 42.406	272.047 574.792 257.927 81.059	48.152 119.557 31.854 20.994	479 707 174 2.5	13.8 13.1 4.2 2.4	1.724 7.082 21.341 851	121 175 337 8	3.6 3.6 8.6 0.7
<i>Minor grains</i> Barley Oats		135.156 26.086	152 87	20.544 2.270	15.022 1.477	20.587 2.288	3.129 199	9	0.3	955 56	1 12	0.3
Millets Sorghum		26.282 57.965	131 119	3.431 6.898	34.234 37.848	24.408 42.486	3.187 5.056	34 44	0.9 13	19.939 21.469	137 202	3.3 6
Tef Rye Triticale Ouinoa	2.200 9.745 2.819 69	1.700 19.694 9.601 55	412 109 356	700 2.140 1.267 20	1.600 795 503 69	1.148 1.005 55	125 133 19	Q	υ	1.600	U	o
Fonio Buckwheat		261 3.154	164 111		354 807	261 1.383	43 153	×	0.3	354	31	0.8
<i>Pulses</i> Dry beans Broad bean	24.138 2.474	17.152 3.530	428 298	7.334	22.688 2.158	14.933 3.035	6.386 903	24	1.5 <sup>f</sup>	3.042 491	24	1.6 <sup>f</sup>
Dry peas Chickpea Cowpea, dry	6.048 9.969 9.868	10.791 7.840 2.970	253 480 208	2.734 3.761 619	2.416 9.367 9.829	2.298 7.150 2.920	582 3.430 609	S	0.3 <sup>g</sup>	498 397 9.650	c	$0.2^g$
r igcoupea Lentils Vetches	4.123 3.793 1.028	3.392 976	358 358 146	707 1.214 142	2.854 487	2.130 2.130 423	762 62	36	2.2 <sup>h</sup>	205 111 125	53	3.5 <sup>h</sup>

Table 1 Area, production, value and dietary contributions of major and orphan cons. Selected country groupings

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Roots/tubers Potato Sweet potato	19.940 9.112	328.051 138.849	157 88 52	51.504 12.219	9.436 9.009	139.018 137.004	21.826 12.056	37 39	0.8	692 2.016	10 33	0.2 0.4	
Cassava Taro (coco	17.032 1.470	176.764 8.885	53 154	$9.370 \\ 1.371$	17.032 1.451	176.784 8.651	$9.370 \\ 1.334$	56 7	0.4 0.1	11.038 1.293	266 37	2 0.5	
yam) Yams	4.050	38.304	130	4.980	4.041	38.102	4.953	10	0.2	3.905	78	1.2	
<i>Oil crops</i> Groundnut	24.291	34.516	344	11.872	23.612	32.745	11.263	22	1	9.373	39	1.7	
Sunflower	21.081	26.169	226	5.910	7.838	10.470	2.364			192		0.1	
Rapeseed	25.721 •70	39.518 600	292 736	11.540 162	14.324 650	18.104 18.7	5.287	1	0.1	25 70			
Sesame	7.158	0.50 2.807	340 340	954	7.158	-02 2.806	954	б	0.1	2.788	9	0.2	
Mustard	610	446	314	140	275	170	54						
Bananas and plantain	lantain												
Bananas	4.476	69.832			4.432	68.741		10	0.2	1.074	10	0.2	
Plantains	5.054	32.211			5.054	32.211		9	0.1	4.058	55	0.5	
Primary fruits 48.331	48.331	466.414			35.765	336.650		72	0.8	6.985	93	1	
Vegetables +melons	42.442	691.894			34.454	530.094		61	3.2	3.167	22	1.2	
<ul> <li><sup>a</sup> Source for entire table: FAOSTAT (2002), unless otherwise noted.</li> <li><sup>b</sup> Source for price data: FAOSTAT (2002), except for major crops (World Bank, 1997), roots and tubers (Scott et al., 2000), and tef (UNDP, 2002)</li> <li><sup>c</sup> Dietary data are for 1999. Contributions from each crop include net international trade, deductions for feed, seed, and waste, and stock changes.</li> <li><sup>d</sup> Source for exchange rate conversions: Oanda (2000).</li> <li><sup>e</sup> Numbers in bold refer to the total contribution of the six minor grains; further disaggregation of data is not possible from FAO sources.</li> </ul>	Source for entire table: Source for price data: F Dietary data are for 199 Source for exchange rat Numbers in bold refer t	FAOSTAT (2002), unless otherwise noted. FAOSTAT (2002), except for major crops (World Bank, 1997), roots and tubers (Scott et al., 2000), and tef (UNDP, 2002) 99. Contributions from each crop include net international trade, deductions for feed, seed, and waste, and stock changes. te conversions: Oanda (2000). to the total contribution of the six minor grains; further disaggregation of data is not possible from FAO sources.	2002), un 002), exce ions from s: Oanda ontributio	less otherwis ept for major n each crop in (2000). n of the six n	e noted. • crops (Wor aclude net in ninor grains	id Bank, 199 ternational t ; further disa	7), roots and rade, deduct iggregation o	1 tubers (S ions for fo	scott et al eed, seed, a not possibl	, 2000), and tu and waste, an le from FAO	ef (UNDP, d stock chi sources.	2002). Inges.	
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<sup>g</sup> All peas. <sup>h</sup> Other pulses.

average of about 1360 kcal of energy and 33 g of protein daily to individuals in poor counties. $^{6}$ 

Orphan crops also play a large role. Table 1 provides a long but incomplete list of food plants, and the list should be even longer. For example, millets are key crops for the poor in both Sub-Saharan Africa and South Asia; the 12 cultivated millet species in the table include finger millet (*Eleusine coracana*) and pearl millet (*Pennisetum glaucum*). In addition to grouping sets of species like the millets, Table 1 excludes several tree crops that are locally important in providing food security.

Twenty-seven orphan crops within developing countries occupy areas of between 0.5 and 38 million ha. None is on the scale of wheat, rice, or maize, yet they total some 250 million ha. In addition, there are 70 million additional hectares planted to fruits and vegetables. Using the prices shown in Table 1, the subset of minor crops, even without bananas, plantain, fruits and vegetables, has a combined value of nearly US\$ 100 billion within the developing nations.<sup>7</sup>

Orphan crops take on even more significance within regions. The data for Sub-Saharan Africa illustrate this point. Sorghum and millets are more important than rice and wheat, both in area (41 million ha versus 9 million ha) and in contributions to the diet. Similarly, roots and tubers play a dominant role, providing more than 400 kcal of energy per person per day.<sup>8</sup> Given that 38% of Sub-Saharan Africa's total population is undernourished and that the number of undernourished children in that region is forecast to increase by 39% by 2020 (Pinstrup-Anderson et al., 1999), the issue takes on added urgency.

Important questions remain regarding the types of investments that are needed for individual crops or crop groupings. Minimum investments in biotechnology approaches for individual orphan crops are likely to be at least as large as those for major crops for a particular trait. As a result, the economic incentives to invest initially in biotechnology for major crops seem clear. Once such investments have been made, however, incremental investments that extend the science to orphan crops could be extremely beneficial to some of the world's poorest populations, an opportunity often ignored.

<sup>&</sup>lt;sup>6</sup> Reference to "developing" or "poor" nations in this paper uses the FAO definition of "developing" (FAO, 2003). Minimum dietary standards are typically cited as being 2300 kcal of energy and 40 g of protein per day. See Smil (2000) for a review of the various estimates of nutritional requirements. The indirect contributions of energy and protein from these crops through the livestock sector would add further to the dietary data shown in Table 1.

<sup>&</sup>lt;sup>7</sup> Minor crop prices were obtained by averaging the local prices of India, Brazil, and Kenya, converted into dollars at the official exchange rate for 1995. If one or more of these countries did not have a price listing for the crop in question, the largest developing country producer was then substituted into the averaging process. Price data derived in this manner inevitably suffer from country-level sampling problems and from distortions arising from agricultural, trade, and exchange rate policies.

<sup>&</sup>lt;sup>8</sup> To push the disaggregation point one step further, tef, which is not large enough to warrant a separate line entry for all "Sub-Saharan Africa", provides 240 kcal of energy per person per day in Ethiopia.

## Molecular tools for germplasm improvement

Over the past few decades, large investments have been made in biotechnologies for the major crops in industrialized countries. Molecular approaches have been widely used to describe and manipulate crop genomes and to better understand the genes and biochemical pathways that govern traits such as yield, disease and pest resistance, abiotic stress tolerance, plant architecture, and quality. Many national agricultural research programs (NARs) in developing countries have also made some investment in molecular technologies as applied to the major crops, such as rice and maize, but the extent of that investment varies sharply across countries. Nations with strong NARs are generally those with strong economies, such as China, India, and Brazil. Even in those countries, however, biotechnology investments are rarely applied to orphan crops.

More than a decade of investment has developed powerful technologies for major crops, making genetic information for crop improvement more accessible. With this technology, DNA-based approaches have been applied in two broad areas of molecular breeding.<sup>9</sup> The first, marker-assisted breeding, is aimed at enhancing the power of conventional genetic analysis and manipulation. The second is transgenics.

The first step of molecular breeding uses molecular markers as tools to detect the extent and structure of genetic variation, providing insights into the diversity of crop varieties and potential contributions offered by their wild relatives. Diversity seen at this level can be used to inform the selection of parents with a high likelihood of producing novel progeny in a crossing program. Molecular tools are also used in the analysis of inheritance of key crop traits, including those that are subject to complex inheritance due to the involvement of numerous genes. Once the genetic basis of a trait is well understood, molecular tools can be used to select for specific desired genes or combinations of genes.

The second avenue involves the transfer of genes from one genotype to another. This approach, often referred to as "genetic engineering", may utilize man-made genes (usually constructed using elements from various biological sources), or natural alleles. Thus, truly novel traits can be added to a crop. The two broad areas of molecular breeding converge when genetic engineering is applied to enhance the efficiency with which native genes are moved within a gene pool.

# Positional approaches to genome analysis and molecular breeding

Evidence indicates that all plant genomes have a great deal in common in their gene content, biochemical pathways, and chromosome organization. Different plant taxa have different versions of the same genes at a given position or locus in a genome, but the order of loci is conserved to varying degrees across even

<sup>&</sup>lt;sup>9</sup> The term "molecular breeding" has been used traditionally to refer only to the use of markers. We expand the definition as explained in the sections that follow.

distantly related crops, a phenomenon known as synteny. Because plant genomes are somewhat similar, investment in "model" species, chosen because they are easily studied, has paid off. Models have been selected for each of the most important plant groups, and research has been accelerated through large-scale projects. For example, the flowering plants can be divided into two main groups: monocots and dicots. The former includes the grasses, which in turn include the major cereal crops. The latter include the legumes, many roots and tubers, and vegetable crops. The genome of the model dicot species *Arabidopsis thaliana* has been fully sequenced (Arabidopsis Genome Initiative, 2000), and a great deal of basic research has been done on this species. More recently, the draft genomic sequence of the rice (*Oryza sativa*) genome was made available, which is useful both for rice and its monocot relatives.

Ninety-eight percent of the proteins found in maize, wheat and barley are also found in rice (Goff et al., 2002). Although the progenitors of rice and *Arabidopsis* diverged 150 to 200 million years ago, more than 80% of the genes that have been documented in *Arabidopsis* have also been found to have related genes in rice (Bennetzen, 2002). The genes involved in many biochemical pathways and processes are very similar across the plant kingdom (e.g., Thorup et al., 2000). Functions such as gene regulation, general metabolism, nutrient acquisition, disease resistance, general defense, flowering time and flower development are largely conserved across taxa.

Comparative mapping studies have revealed that the genomes of plant species within families are syntenous—that gene order is conserved for chromosomal segments (Bennetzen and Freeling, 1998; Gale and Devos, 1998; Devos and Gale, 2000).<sup>10</sup> Given the similarities among crop genomes, particularly among plant species within a family, it seems possible that research on major crops or model species would benefit a substantial number of related crop species in the same families. The potential spillover benefits are likely to differ, however, across taxa and region depending on the particular biology of the species, the constraints faced by farmers, and seed systems.

## Genetic diversity: analysis, conservation and utilization

The use of molecular techniques for analysis of genetic diversity and the structure of germplasm, the first conceptual step in marker-assisted breeding, has been fruitful for many species. This type of research can lead to better conservation of crop genetic diversity, more efficient selection of accessions for phenotypic characterization, and the identification of useful variants for conventional plant breeding. Some molecular techniques (e.g., amplified fragment length polymorphism, or

<sup>&</sup>lt;sup>10</sup> For instance, an ancestral gene order can be inferred for the grass family, even though chromosomal rearrangements and duplication events have occurred. However, chromosomal colinearity is much weaker between monocots and dicots (Devos et. al., 1999; Bennetzen, 2000). Based on the sequences of rice and *Arabidopsis*, synteny was found to be low but detectable (Goff et al., 2002).

AFLP) can be applied to any species, without the need for crop-specific DNA sequence information. Such analysis can be conducted in any laboratory for which minimum levels of basic training, supplies and equipment are available. Even with the most seemingly straightforward techniques, however, it is difficult to achieve smooth and productive operations under the conditions encountered by many scientists in developing countries. Administrators often err in thinking that investment in facilities alone is sufficient for scientific success, and they neglect the substantial costs incurred for training, consumables, and the diversion of key personnel from field-based efforts. Even when researchers are able to produce good-quality molecular data, they may lack access to expertise in some of the analytical procedures needed to interpret the results.

This area of research provides a clear example of one in which spillovers from investments in facilities, human capital, and supplies for major crops could be quite large for orphan crops. Once researchers are well trained in the techniques and have the necessary equipment, they could apply their skills to a wider range of crops, or they could help to train others to analyze genetic diversity of orphan crops.

#### Marker-assisted selection (MAS)

Marker assisted selection (MAS) is the identification of DNA sequences located near genes that can be tracked to breed for traits that are difficult to observe. MAS can be relatively straightforward for genes conditioning large phenotypic effects, such as strong effects on disease resistance, and its use for germplasm improvement is beginning to prove successful for some types of field applications for major crops.<sup>11</sup> Two new rice varieties with bacterial blight resistance (derived from polymerase chain reaction (PCR-based MAS) were introduced commercially in Indonesia in 2002 (Toenniessen et al., 2003). Rice lines carrying multiple resistance genes are being produced by several national programs following technical investments at the International Rice Research Institute (IRRI) (e.g., Hittalmani et al., 2000). Strong national programs, such as those in China, are effectively using MAS in some cases, e.g., improvement of quality traits in rice (Zhou et al., 2003a,b) and improvement of fiber strength in cotton (Zhang et al., 2003).

In "single large-scale MAS", selected genes are fixed by marker-assisted selection, and the constitution of the rest of the genome is determined by conventional field-based breeding (Ribaut and Betran, 1999). This approach has been used to develop virus resistance in maize, rice, and beans (Singh et al., 2000). In recent cost analyses of marker-assisted versus conventional selection, the cost of

<sup>&</sup>lt;sup>11</sup> Substantial investments in MAS have been made by the Rockefeller Foundation, the International Rice Research Institute (IRRI), and the Asian Rice Biotechnology Network (ARBN). For maize and wheat, the International Center For Improvement of Maize and Wheat (CIMMYT) has also made large investments in the development and evaluation of MAS.

MAS for a recessive mutant gene associated with quality protein maize was found to compare favorably with the (difficult) conventional screen (Dreher et al., 2003).

As basic research on key plant traits advances and as marker technologies continue to become increasingly simple and powerful, more applications of MAS are anticipated with the potential benefit of faster varietal release. Morris et al. (2003) showed positive cost-benefit results of MAS, and there are many similar unpublished examples from the private sector. In the published literature the costbenefit results of MAS are mixed (Berloo and Stam, 1999; Bohn et al., 2001), and many publications only report work aimed at eventual application of MAS as opposed to field-level use of MAS for practical crop improvement (Young, 1999). Due to the relatively high cost of MAS compared to conventional field screening, MAS is likely to be practical for orphan crops in the poorest countries only if partnerships with well-funded research groups allow free use of existing technologies. It is important, therefore, to assess various traits and trait categories for which there has been some proof-of-concept in non-orphans for MAS before considering what would be required to move the benefits to a broader set of plant species.

# Marker-assisted genetic analysis and improvement of complex traits

In viewing cases in which genetic research has allowed for progress in MAS, it is important to distinguish between two types of traits: those conditioned by single genes with large effects showing simple inheritance (qualitative traits), and those showing complex inheritance (quantitative traits). Important plant traits that frequently show simple inheritance include some resistances to diseases and insects and some important characters that relate to plant growth and development. It is relatively easy to locate these genes with precision, and in many cases such genes have been cloned. It is often straightforward to select for these genes in a conventional breeding program, in which case MAS does not necessarily offer substantial benefits. There are cases, however, in which markers are particularly beneficial; for example, when a disease resistance gene must be identified but the pathogen is not present at the breeding site, or when a gene is to be selected at the seedling stage for a trait that is only expressed later in development.

Most important traits are governed by multiple genes, each having relatively small effects. These "quantitative traits" have been difficult to understand and to manipulate in conventional crop breeding programs. The term QTL, quantitative trait locus or loci, refers to the chromosomal regions of genes that control quantitative traits. Beginning with studies published in the late 1980s (Paterson et al., 1988), molecular genetic approaches began to illuminate the genetic architecture of quantitative traits. By now, the chromosomal segments associated with many traits have been identified in a large number of studies (Kearsey and Farquhar, 1998). As estimated by Goff et al. (2002), about two thousand cereal QTLs have been mapped.

While so-called anonymous QTL-associated markers are sometimes used for marker-assisted selection in crop improvement, the utility of such markers can be limited by a high degree of imprecision in mapping desirable loci of small effects.<sup>12</sup> The identification of "candidate genes" makes it possible to localize desirable variants much more precisely. Candidate genes are genes known or suspected to be involved in conditioning the phenotype of interest, such as disease resistance. The inference that a particular gene contributes to a given trait may be strengthened if it maps to a chromosomal region that has been associated with the trait in QTL mapping experiments. Credible candidate genes co-localizing with QTLs have been identified for several traits, including quantitative disease resistance in rice (Wang et al., 2001), wheat (Faris et al., 1999), bean (Geffroy et al., 2000), and potato (Trognitz et al., 2002).

A number of research approaches have converged to allow some genes underlying QTLs to be cloned (Frary et al., 2000; Johanson et al., 2000; El-Assal et al., 2001), and to set the stage for future QTL cloning in others. This process permits both the identification of potentially useful variants of agronomically important genes and the precise selection of those alleles found to be most useful.<sup>13</sup> One of the approaches that puts QTL cloning within reach is the increasing availability of express sequence tags (ESTs), short segments of sequenced gene transcripts that provide information on genetic expression, function, and heritability. Tens or hundreds of thousands of ESTs are available for major crop species, but the number of sequences for orphan crops is quite meager (Fig. 1). Researchers can now use the combination of QTL mapping data and mapped EST data as a powerful tool for determining the genes that underlie quantitative traits.

Sequence data on expressed genes and on plant and crop genomes are rapidly accumulating and present powerful tools for plant science, provided that scientists are able to access and exploit the data efficiently. The sequence data sets are, in themselves, imposing and potentially cumbersome. But with the help of increasingly powerful and friendly databases (Yuan et al., 2001), biologists and breeders

<sup>&</sup>lt;sup>12</sup> Although MAS is made more challenging by the imprecise localization of the QTL and sometimes by inconsistent QTL expression, recent studies have provided encouraging evidence that MAS can be useful for enhancing quantitative traits under certain circumstances. For example, Han et al. (1997) used MAS to improve malting quality traits in barley, and Zhou et al. (2003a,b) showed the utility of MAS in breeding for quantitative disease resistance in wheat. Wissuwa et al. (2002) showed that a transfer of a single QTL region could contribute significantly to tolerance of phosphorous-deficient soils in rice. This result is particularly encouraging in the context of orphan cereals for the poorest countries, considering the extent to which phosphorous-deficient soils limit cereal production in Africa. The use of MAS to locate genes in wild relative, and to transfer the genes to cultivated crops to add stress tolerance or nutritional value, could greatly benefit resource-poor producers.

<sup>&</sup>lt;sup>13</sup> For instance, genes affecting flowering time in *Arabidopsis* and maize have recently been identified (El-Assal et al., 2001; Thornsberry et al., 2001). Flowering time is a quantitative trait that is important in allowing plants to adjust their life cycles, often in response to differing day lengths as they change with the seasons. Farmers frequently require shorter-duration crop varieties to fit into the increasingly intensive cropping systems or to avoid drought or pest stresses that can occur at certain times of year. The availability of the isolated genes could allow natural variation at loci affecting flowering time to be analyzed efficiently in a range of genotypes, enabling the identification of useful variants for future use.

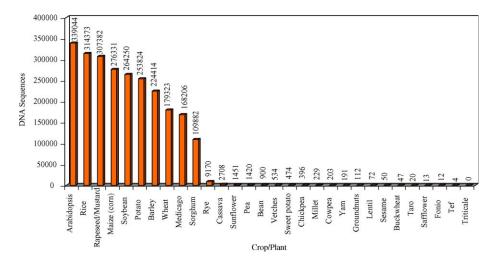


Fig. 1. Number of DNA sequences associated with genus same in the National Center for Biotechnology information (NCBI) database, 31 May 2002.

can now gain access to genetic information that allows them to identify and exploit natural variation for a wide variety of crops in ways that were previously not possible.

# Regulatory genes

The genetic complexity underlying quantitative traits often makes it difficult to seek trait-marker correlations that can be used for indirect selection. For instance, a great number of genes (hundreds or thousands) are involved in plant defense against insects and pathogens. This complexity may seem defeating, but it may be possible to improve complex traits by manipulating the genes that sit at the top of the regulatory hierarchy and control large numbers of other genes. In fact, there is growing evidence that many QTLs are explained by transcription factors—genes that control the expression of other genes. The identification and utilization of the "best" alleles of these genes is a promising avenue of research, both via MAS and via transgenic approaches. Transformation experiments enhancing the stressresponsive expression of a transcription factor that controls drought-related genes led to increased tolerance to drought, salt stress, and freezing in Arabidopsis (Kasuga et al., 1999). Similarly, overexpression of a regulatory factor involved in plant defense in transgenic Arabidopsis led to enhanced resistance to diverse pathogens (Cao et al., 1998; Friedrich et al., 2001). Some of the genes involved in regulation of the defense response are also implicated in responses to other stresses (Singh et al., 2002). The identification of these transcription factors seems likely to play a useful role in genetic improvement for a wide range of food crops.

## Transgenic delivery of crop protection traits

The use of direct gene transfer, the second tool for "molecular breeding" of crop traits, employs recombinant DNA technologies to insert one or more genes into the crop plant's genome.<sup>14</sup> While most transgenic research and applications have focused on a few major crops to date (James, 2001), the potential to extend applications of this technology to orphan crop improvement may be significant. Promising transgenic lines for about 20 different crops, including pepper, squash, and sweet potato, are currently being field tested by public research institutions in at least 10 developing countries (Toenniessen et al., 2003). These lines, which have been engineered for particular traits like virus resistance and pest control, could provide significant benefits to poor farmers who cannot afford chemical controls for crop loss.

# Genes used in direct gene transfer

A wide range of approaches employing transgenes is available for controlling herbivory, but by far the most extensively used method to date has been "Bt" technology (Dunwell, 2000)<sup>15</sup> Different Bt toxins are lethal to the immature or larval, herbivorous stages of lepidoptera (adults are the butterflies and moths), diptera (the flies, including mosquitoes), and coleoptera (the beetles, including weevils), many of which are major crop pests.

Beyond the use of Bt, several additional insecticidal products are produced by plants, animals, and microbes that are also being evaluated for the control of herbivory. For example, many plants store large amounts of specialized proteins in their seeds (called storage proteins), and some of these proteins have insecticidal properties. Insects that consume plant seeds are particularly dependent on their ability to digest seed proteins using one or more proteases, and these inhibitors have been engineered into other plants to interfere with the feeding of insects on leaves and flowers (Hilder et al., 1992). Protease inhibitors have also found to be effective against some of the plant pathogenic nematodes.

A number of enzymes have also been tested for their possible use as insect resistance determinants. One of these enzyme groups is the chitinases, which target an essential structure of macromolecules (chitin) in insects and fungi (Ding et al., 1998). Three additional groups of enzymes (conifer monoterpene synthases, bacterial cytokinin biosynthesis enzymes, and cholesterol oxidase) have been designed to modify the chemistry of the plant in ways that make it less palatable as an insect food source.

<sup>&</sup>lt;sup>14</sup> This paper does not address the ecological and health risks of transgenic crops, although the authors acknowledge that these risks must be considered if foreign gene insertion is used as a crop protection strategy. For further reference on ecological risks see Wolfenbarger and Phifer (2000) and Gura (2001). On the health side, some lectins can provoke an allergic response in some people. For reference, see Board on Agriculture and Natural Resources (2000) and Lewis and Thrall (2000).

<sup>&</sup>lt;sup>15</sup> "Bt" refers to the genus (*Bacillus*) and the species (*thuringiensis*) of a soil bacterium that naturally makes a protein toxin that when ingested is lethal to insect herbivores.

Finally, in many crops, especially the grains, a major product stored in seeds is starch. Insect pests of these crops depend on their ability to digest starch using the enzymes  $\alpha$ - and  $\beta$ -amylases. Some plants encode a gene for an inhibitor of  $\alpha$ - and  $\beta$ -amylase; these genes have been used in a variety of cases to produce insect resistant plants (Ishimoto et al., 1996).

Transgenic approaches for reducing crop losses from disease have also been widely explored, with significant success in the area of plant viruses. Reports of success on transgenic technologies for controlling plant viruses abound in the literature and encompass numerous crops including rice, wheat, maize, barley, perennial rye, legumes, potato, sweet potato, several temperate vegetable species, and papaya. Plant viruses represent a major biotic constraint on agricultural production; viral symptoms commonly include stunting, reduced yields, or death. Viruses are usually transmitted to plants via insect, beetle, nematode, or other types of vectors, and as a result, resistance is often the only effective form of viral control in agricultural systems. While genetic resistance exists in many crops, it is not always well understood or identified. For orphan crops in particular, even the most basic knowledge of resources for genetic resistance is typically lacking.

Reports from the mid-1980s confirmed that when portions of plant viral genomes, such as the viral coat protein gene, were transferred and expressed in a plant genome, resistance to the virus was observed (Nelson et al., 1986). Since these reports were released, many types of sequences from both RNA and DNA plant viruses have been expressed in a diverse set of crops resulting in resistance to a wide array of pathogens (Kavanagh and Spillane, 1995; Pappu et al., 1995). More recently, scientists have turned their attention to resistance resulting from expression of genes from other sources, including mammalian antibodies (Ziegler et al., 2000), anti-viral compounds (Smirnov et al., 1997), and sequences that act to silence viral genes or silence host genes necessary for viral infection (Baulcombe, 1999; Dutilleul and Laine, 2001). To date, however, resistant varieties resulting from "second-generation" strategies (i.e., those involving gene silencing or expression of non-viral sequences) are not yet in use.

Nonetheless, future strategies to limit crop losses to viral disease will most likely encompass upstream research on sequences that silence plant genes and on direct gene transfer to move plant genes beyond the boundaries defined by sexual hybridization.<sup>16</sup>

# Implementation of transgenic approaches in orphan crops

Genetic engineering for insect or virus resistances is a so-called "implementation technology", meaning that once the genes are available, they must be combined using an "enabling technology" required to move the genes into target crops. Thus, in principle the sequences used that encode the "pesticidal" activity, combined with appropriate regulatory sequences that work in the target crop, can be used in any

<sup>&</sup>lt;sup>16</sup> Many cloned plant resistance genes function in plant species that cannot be hybridized with the species in which the gene originated (e.g., Erickson et al., 1999).

crop plant. In this way, genes isolated originally for use in a major crop such as wheat or soybeans can be readily modified for use in orphan crops.

The technical challenges for scientists applying these technologies to orphan crops are threefold. The first challenge relates to the extent of knowledge about the sensitivity of the pathogens or pests of orphan crops to forms of control that have been useful in developed countries with temperate environments. Very little information on the usefulness of known transgenic approaches is yet available for many of the crops listed in Table 1, and the initial costs of developing this information can be significant for the lesser-studied orphan crops. For example, work in India on insect resistance for chickpea showed that the proteins encoded by the previously isolated proteinase inhibitor genes were at best marginally effective against insect pests of chickpea (Harsulkar et al., 1999). The researchers then turned to isolation of orthologous genes from crop plants such as Asian winged bean to find more effective proteinase inhibitors. The second challenge concerns the availability of techniques for transferring genes into orphan crops. In some cases, the transferability of gene transfer methods has been fairly easy and direct from model species to orphan crops. But in other cases, significant new and expensive work has been needed to modify-or to develop entirely new-transformation technologies for these crops. And finally, a major limitation of the use of these promising technologies in the orphan crops to date is the paucity of approaches that can be successfully applied to the control of diseases caused by bacteria, fungi, the oomycetes, and nematodes.

#### **Genomics-guided transgenes**

Genomics approaches and transgenic technology converge when natural allelic variation is utilized through direct gene transfer. Useful alleles can be transferred from a wild relative of a crop by conventional breeding, but it may be difficult or even impossible to recover the desired plant type in a reasonable period of time. Using "genomics-guided transgenes" (GGT), native genes or homologous genes from closely related species that modify a plant's metabolism in a manner similar to natural or induced mutations are used for direct gene transfer (Strauss, 2003). Dominant alleles that confer important agronomic traits of interest (e.g., pest and disease control, drought tolerance) but that are scarce in breeding populations can be identified and inserted into breeding lines, based on knowledge gained from model gene studies. An example of this approach is the use of the Xa21 gene, which provides resistance to the bacterial blight disease of rice. Xa21 was originally transferred from a wild relative to cultivated rice by conventional breeding (Khush et al., 1989). The gene has been moved among genotypes by MAS (e.g., Reddy et al., 1997; Singh et al., 2001) and has also been cloned and utilized through genetic engineering (Zhai et al., 2000). GGT can comprise a wide diversity of genes, although many of the modified traits using this approach to date were already familiar, such as male sterility, seedless fruits, delayed spoilage, and dwarf stature (Strauss, 2003).

# Transferring the benefits to orphan crops

Given the range of molecular tools, what are the promising applications for orphan crops? The answers can best be explored when related major crops have received substantial research investment. The most obvious example is the grass family, or Gramineae, the most economically important plant family. There are around 10,000 graminaceous species, which include the world's most important cereal crops. Knowledge of the taxonomic structure (reflecting presumed evolutionary relationships) facilitates the use of information from the more studied species to the orphans. There are five sub-families in the grass family. Rice is a member of the ehrhartoid sub-family and has the smallest genome. The pooids include wheat, barley and rye. The panicoids include maize, sorghum, and pearl millet, all of which are important staples in sub-Saharan Africa and other areas. The chloridoids include the Ethiopian staple tef, as well as finger millet. The bambusoids include bamboo.

Within the grass family, genomes vary substantially. While the genomes show similarities in gene organization, there is evidence of significant variation in genes, chromosomes and genomes. Based on a framework of restriction fragment polymorphism (RFLP) maps, the cereal chromosomes show gross synteny. At a finer level, however, there are many deviations from synteny, such that the predictive power between taxa ranges generally between 50 and 75% (Gaut, 2002). Even between maize lines, the gene content of a given chromosomal region vary (Fu and Dooner, 2002).

Some of the genes affecting important traits such as seed size, seed dispersal, and flowering time have been shown to exist in corresponding sites in the genomes of rice, sorghum and maize (Paterson et al., 1995). Several QTLs conditioning resistance to the blast disease pathogen were found to exist in the same locations in both rice and barley (Chen et al., 2003). In many cases, therefore, knowing the location of a gene or group of genes affecting a key trait in one species will be useful for efficient identification of genes that are of interest for another trait. If the actual genes are known, then the gene discovery process is less dependent on synteny, as the genes can be traced by sequence similarity.

Similar examples are found for a range of plant families. For instance, the Solanaceae include many vegetable species that are extremely important as food and cash crops. For tomato, a substantial amount of genetic and genomic information is now available. The situation for potato and pepper is intermediate. The chromosomes of these species are syntenous, and the genes for various characters have been found to reside at syntenous locations. For various African indigenous vegetables (AIVs) in the Solanaceae, there is virtually no information available, but information from the better-studied solanaceous crops would doubtless be an asset if an investment were made in the AIVs. A similar situation exists for the legume family. The correspondence between model species and orphan crops to traits of interest is illustrated in Table 2. This mapping, while only partial, helps to identify niches of opportunity for biotechnology spillovers into orphan crops. Much greater

Crop family	Model species	Example of orphan and regional niche	Most limiting constraints
Grasses	Rice has sequenced genome Wheat has the largest number of ESTs Maize and sorghum have sub- stantial sequence information	Millets, tef Africa, S. Asia	Drought, disease suscepti- bility, low yields
Legumes	Medicago will have sequenced genome	Groundnut, pigeonpea, cowpea Africa, S. Asia	Pest and disease suscepti- bility, low-P soils
Solanaceae	Tomato is best researched	Eggplant, leafy vege- tables, peppers Africa, Asia	Virus susceptibility

Table 2 Some potential spillover niches

challenges exist for orphan crops like quinoa and some roots and tubers that have no close model or major crop relatives.

Despite identifiable niches, the task of implementing biotechnology approaches to germplasm improvement is not simple, particularly in poor regions. The process of analyzing the diversity of genes related to a trait of interest, and identifying and marking the useful alleles for selection, requires good access to current scientific literature and the internet, with at least modest bioinformatics capacity. The best promise for implementing a specific biotechnology strategy for germplasm development in orphan crops holds when research on a particular trait is pursued across a group of related species, one or more of which is not an orphan. The most rapid progress is likely to be made when there is a model crop in the same family as the orphan crop. Circumstances will vary greatly across crops and countries. Nevertheless, three examples of promising applications of biotechnology for orphan crops are shown in the boxes that follow (Boxes 1–3). These examples help to illustrate the practical aspects of our suggestions.

A key question remains: does it make sense economically to invest in these technologies? Our analytic task in answering this question would be easier if there were a half-dozen case studies of orphan crops that were (or could be) analyzed.<sup>17</sup> Such studies may be possible soon, but not now. Instead, we offer some broad parameters to gauge the potential.

As a start, it is helpful to assess a couple of promising technologies: Bt for sweet potato weevil resistance, and the use of comparative genomics within the grass family for marker assisted selection of blast resistance in finger millet. With the progress already made in Bt and blast resistance in major crops (e.g., maize and rice, respectively), an annual investment of US\$ 500,000 over a 10-year period (US\$ 5 million total) could well lead to success for these orphan crops. What would be the potential pay-off for achieving such gains?

<sup>&</sup>lt;sup>17</sup> A useful analysis for sweet potato has been done by Qain (1999).

# Box 1: Sweet potato in Uganda

Sweet potato is not among the world's top 10 food crops, yet it ranks third in Uganda (FAO, 2003). Because its storage roots are rich in carbohydrates, riboflavin, and calcium, sweet potato is an important source of nutrition among poor, rural households. Sweet potato underpins farm level food security in Uganda as a dominant reserve staple and has replaced or supplemented cassava and bananas (two other important starches in the Ugandan diet) in large areas. In spite of its present importance for food security, sweet potato receives relatively little research attention in Uganda or in developing countries.

A high potential for sweet potato yield improvement exists but remains unrealized. In the United States, estimated potential fresh storage root yield is about 70 tons/ha against the average global yield of 14 tons/ha. The average yield for Uganda is around 4 tons/ha, while yields recorded at experimental sites are over 40 tons/ha for some varieties (Turyamureeba et al., 1997; FAO, 2003). Some of the major production and utilization constraints facing developing countries like Uganda may be overcome or at least mitigated by advances in modern science (Qain, 2000).

Crop damage caused by the sweet potato weevil is a very severe problem. There is low heritable natural resistance to sweet potato weevils in the sweet potato germplasm pool. Chemical and cultural control measures are also ineffective, mainly because weevils burrow into the sweet potato tuber. Genes encoding insect-specific toxin proteins have been isolated from the bacterium *Bacillus thuringiensis* and transferred into several major and orphan crops (e.g., maize, cowpea) to confer resistance to certain insect pests. Researchers are now proposing to introduce these genes into sweet potato cultivars to confer resistance to the sweet potato weevil. Qain (1999) has estimated that this technology could increase incomes by 38–40% and reduce unit costs by 20% per ha throughout Africa.

Lack of high-yielding cultivars with consumer-acceptable traits represents both a challenge and an opportunity. Because sweet potato is perennial, polyploid and vegetatively propagated, the progress of conventional breeding is relatively slow. Biotechnology can accelerate improvement, especially of starch/dry matter ratios, weevil control, and virus resistance (Okada et al., 2001). Transformation and regeneration technologies are being used, and researchers have regenerated sweet potato plants from the leafstalk, or petiole. Researchers hope to produce transgenic plants soon with enhanced starch content and resistance to the sweet potato weevil. Conventional breeding can still be used for certain traits, such as increasing vitamin A content.

In the sweet potato case, weevils are known to reduce yields by 60%, and in some cases by 100%. Average yields, currently at 4.4 tons/ha, would thus rise to over 7 tons/ha with fully effective resistance. Viewing potential success more

# Box 2: Millets in Africa and South Asia

Millets are a diverse group of cereals comprising several genera. Grown primarily by poor farmers in Africa and South Asia, they are also important in areas of other continents. Of the total area of near 40 million ha, about half are devoted to pearl millet. Another 30% of the millet area is grown to foxtail and proso millets, and another 10% to finger millet. While the millets are included in the mandate of the international agricultural research system (CGIAR), only 2% of the system's resources have been devoted to millets in recent years (CGIAR, 2000).

Pearl millet is one of the world's hardiest crops. It serves as the staple food for millions of people living in marginal areas of the Sahel in West Africa, where environmental stresses, particularly hot and dry conditions, limit the production of other crops. While pearl millet is tolerant to harsh environments, West African pearl millet farmers suffer large and chronic crop losses from pests and diseases. Fortunately, tremendous genetic diversity for pearl millet is present in West Africa (Tostain et al., 1987; Tostain and Marchais, 1989). Pearl millet germplasm is rich in resistance to downy mildew, the crop's most destructive and widespread disease (Singh et al., 1997). Wild relatives of pearl millet carry resistance to the parasitic weed *Striga* (Wilson et al., 2000) and other pests. Experience has shown that resistance must be managed carefully. Single-cross hybrids have repeatedly been devastated by downy mildew epidemics just 1 or 2 years after release due to rapid adaptation by the downy mildew pathogen (Hash et al., 1997). This problem has not arisen when genetically diverse populations are deployed.

Progress has been made towards the development of molecular tools for pearl millet (Liu et al., 1994; Allouis et al., 2001). Devos et al. (2000) aligned the rice and millet chromosomes, and found substantial chromosomal rearrangements among rice, pearl millet and foxtail millet. QTLs for downy mildew have been mapped (Jones et al., 1995). The downy mildew resistance genes identified to date were found to exhibit race-specific resistance (Jones et al., 1995; Whitcombe and Hash, 2000); this work may indicate the resistance conditioned by these loci will be rapidly overcome through pathogen evolution. It is unclear whether the pearl millet gene pool contains additional forms of quantitative resistance that are more likely to contribute to durable resistance.

Comparative genomics could also lead to varietal improvements in other millets, such as finger millet. Finger millet is a subsistence crop grown by farmers in India and East and Central Africa, particularly in rainfed and drought-prone areas. Its grain has high nutritional value and excellent storage qualities; it thus serves as an important famine food. Yields are constrained mainly by blast disease and drought. The use of molecular maps to identify the location of blast resistance genes in rice (McCouch et al., 1994; Wang et al., 1994; Hittalmani et al., 2000) could aid in the selection of blast resistant varieties of finger millet.

## Box 3: Tef in Ethiopia

Ethiopia is the third largest country in Africa and one of the world's most famine prone nations. Tef (*Eragrostis tef*) is indigenous to Ethiopia and is the primary cereal for the country's 68 million residents. With annual grain production of 1.6 million tons, it constitutes about 22% of Ethiopia's gross cereal production (IARO, 2002). Nonetheless, the average yield, at about one ton per hectare, has been stagnant, constrained primarily by lodging, and there are no cultivars with high yield potential.

Conventional research on tef has been pursued in Ethiopia during the past 40 years with limited funding and very few scientists. Today tef research can benefit from the revolution in genetic technologies developed for major cereal crops, such as rice, through comparative genetic analysis. A high-density, comparative genetic map of tef and rice is currently being constructed to facilitate the transfer of information about genes controlling important traits. Research is also focused on identifying genes controlling agronomic traits of interest, such as lodging resistance, and on assessing within-species allelic diversity (http://mcknight.ccrp.cornell.edu/projects/tef/).

A preliminary RFLP linkage map has been produced for tef (Zhang et al., 2001) using a set of grass anchor probes (Van Deynze et al., 1998). Most of these anchor probes were obtained from rice and had been well characterized as mapping tools. Preliminary results indicate that tef linkage groups are found to align with six chromosomes of rice, and marker order is maintained between rice and tef in small local regions (Kantety et al., 2000). More information should lead to the identification of reliable QTLs for lodging resistance and other useful agronomic traits, which in turn could lead to the application of marker-assisted selection in tef breeding.

Lodging resistance in tef is being investigated using model crop information on genes such as those that affect plant height (e.g., dwarfing genes) and stem toughness (e.g., those that contribute to lignin biosynthesis). ESTs from rice and maize that are associated with the intermediates of the lignin biosynthetic pathway are being placed on the framework map of the tef chromosomes. Both the tef QTL study and studies in other model crops are being used to identify the candidate genes important for lodging resistance. Finally, the cloned dwarfing genes of important cereals (such as wheat) provide an option to produce transgenic materials that incorporate the semi-dwarf and non-lodging character from the donor species.

conservatively, a 25% increase in yields from weevil resistance would raise the average to 5.5 tons/ha. Given a sweet potato area of 570,000 ha in Uganda (FAO, 2003) and a price of US\$ 88/ton (Scott et al., 2000), the gain from achieving Bt-derived weevil resistance on half the area (a conservative estimate)

would be over US\$ 27 million per year. If the technology could be distributed throughout the Sub-Saharan Africa on one-half of the sweet potato areas (1.25 million ha), the gross annual benefits would be about US\$ 121 million. We assume that twice the initial investment would be needed to move the resistant cultivars into the field in Uganda (US\$ 10 million), and that five times the initial amount would be needed to disseminate the technology throughout the Sub-Saharan region (US\$ 25 million). Even with these expenditures, the net payoffs would still be large. Moreover, because sweet potato is a vegetatively propagated crop, the biosafety risks of introducing Bt in this case would be much lower than for maize or cotton.

Investing in marker assisted selection for blast resistance in finger millet could also prove successful within the next decade, particularly given the gains made in identifying genes and QTLs for blast resistance in rice. Finger millet yields are typically reduced by 35% or more as result of neck and finger blast.<sup>18</sup> Successful breeding for blast resistance could increase average yields from 1.3 ton/ha currently to over 1.75 ton/ha. A more conservative estimate of potential success would be to achieve a 15% gain in yields from resistance (to 1.5 tons/ha on average) on one-half of the total area. Given an area of 3 million ha planted to finger millet in India, another 1 million ha in Africa,<sup>19</sup> and a price of US\$ 96/ton<sup>20</sup> (FAO, 2003), the gross annual benefits would be more than US\$ 38 million globally (almost US\$ 29 million per year for India and US\$ 9 million per year for Africa). Again, even if large costs were incurred to move the technology into the field (e.g., US\$ 25 million initially, and a smaller long-term flow each year), the net pay-offs would still be large.

Greater challenges exist with a crop like tef, where the technology path leading to the creation of dwarf varieties is more obscure. In all cases, however, there are benefits associated with the investments, including the enhancement of scientific capabilities and human capital development. The probability of success, the potential financial returns, the collateral benefits, and the constraints on technology adoption should all be weighed.

#### From laboratory to field

Success in the laboratory or experimental plot still needs to be integrated into a much broader scientific process in order to be successful in rural communities. A technological continuum exists for germplasm improvement, which ranges from simple selection techniques, to conventional breeding approaches with farmer participation, to biotechnology developments in advanced laboratories. Unfortunately,

<sup>&</sup>lt;sup>18</sup> Leaf blast also occurs but rarely causes severe damage.

<sup>&</sup>lt;sup>19</sup> Area data for finger millet are estimates. See National Research Council, Lost Crops of Africa (1996) and ICRISAT (http://www.icrisat.org/web/asp/mainsection).

 $<sup>^{20}</sup>$  The 1995 price for millet in India is used as an indicator price, converted to dollars at the official exchange rate.

the continuing decline in funds for practical crop improvement, particularly in the international public sector (Knight, 2003), results in a fair amount of investment in research, and a weak application to practical problems. Applying molecular techniques to basic research in plant biology has led to a much deeper understanding of the genetics of key traits, but not always to a clear idea of how plants can be improved.

Appropriate use of biotechnology depends on the agricultural problem at hand, the biological properties of the crop, and the economic and social infrastructure that supports crop research. The best chances for harnessing the gains from biotechnology exist when the science is integrated into breeding efforts, farm management, and seed production and distribution. Even with integration, the benefits from advanced science depend critically on the institutional, human capital, economic, and political context of the recipient countries (Naylor et al., 2002).

Useful generalizations about potential field-level applications of biotechnology for orphan crops are made difficult by the great diversity of crops and socioeconomic settings. Nevertheless, orphan crop improvement is likely to benefit from attention in three areas: dispelling the myth that biotechnology is equivalent only to genetic engineering applications of Bt insect resistance and herbicide resistance; creating new incentives for public–private partnerships; and fostering new institutional arrangements that combine efforts across whole sets of major and orphan crops.

#### Dispelling the myths

Many people in the policy community—and in the general public—believe that agricultural biotechnology encompasses only transgenic approaches to insect and weed resistance. This focus on GMOs (particularly involving Bt and herbicide resistance) has pitted consumers against industry, Europe against the US, and environmentalists against each other as they debate the relative costs of pesticide use and genetic engineering. While the debates are valid in their own right, they overlook the fact that many new genetics and genomics techniques do not involve the insertion of foreign genes into plants. The use of molecular tools to understand the genetic basis of crop traits for indirect selection and breeding is beginning to offer an alternative to traditional transgenics. These technologies will help alleviate some of the constraints surrounding intellectual property rights and biosafety that limit the dissemination of GMOs in developing countries. Many developing countries have been reticent to employ GMOs, lest their use interfere with trade and aid (Paarlberg, 2000; Conway, 2003).

It is the responsibility of agricultural policy analysts and practitioners to help redirect policy and public discussions on the future of biotechnology. The debate should focus foremost on the needs of poor farmers and consumers, and the tradeoffs they face. To the extent that conventional breeding can be facilitated by advanced genetics techniques, biotechnology should be encouraged as one tool in the agricultural development package.

# Public-private partnerships

If newer forms of biotechnology are to be applied, and especially those involving spillovers from one crop to another, partnerships will be necessary. Many partnerships exist and can be built upon, especially among universities and national agricultural research institutions (NARs).<sup>21</sup> Two types of linkages that transcend the traditional university-NAR relationships are also likely to be key: honest broker organizations that bring together needs and skill sets, and the private sector that is the home for much of the relevant technology.<sup>22</sup> The private sector is also essential in moving crops from the lab to the field. In many cases, the public sector has a comparative advantage in discovery, while the private sector has a comparative advantage in overcoming regulatory barriers and distributing seeds.

Creating new public-private partnerships will be essential for managing intellectual property issues. Ten companies, which own more than three-fourths of the agricultural patents in the US, are likely to be central in many of the biotechnology applications (Graf et al., 2001). Significantly, Dow, DuPont, Monsanto and Syngenta have already agreed to provide seed varieties, patent rights, and laboratory knowledge to African countries through the African Agricultural Technology Foundation (AATF) (Gillis, 2003).<sup>23</sup> The resulting spillovers into orphan crops could be especially important, although for this to happen, AATF will probably first need to succeed with a major crop such as maize. The private sector controls patents on transformation technologies for genetic manipulation as well as on the products themselves. In order for some of the newer forms of transgenics applications to work (i.e., those that do not involve Bt), patent rights on these transformation technologies will have to be relinquished not only for research, but also commercialization. The Center for the Application of Molecular Biology to International Agriculture (CAMBIA) has a major focus on securing patent rights for the public sector, particularly in developing countries.<sup>24</sup> In addition, a consortium of US universities convened by The Rockefeller and McKnight Foundations has recently launched an initiative called the Public-Sector Intellectual Property Resource for Agriculture (PIPRA), designed to make agricultural technologies accessible for humanitarian uses in developing countries (Atkinson et al., 2003).

Intellectual property is not the only factor discouraging private and public partnerships. For much of Africa and parts of Asia and Latin America, the lack of biosafety protocols and their enforcement creates serious problems of legal liability (Cohen and Paarlberg, 2002). Without such protocols, external public and private

<sup>&</sup>lt;sup>21</sup> While a complete listing of ongoing relationships has not been compiled, many can be inferred from DeVries and Toenniessen's informative volume on African crops (2001).

<sup>&</sup>lt;sup>22</sup> See Falcon and Fowler (2002) for a review of recent developments in intellectual property rights as applied to germplasm.

<sup>&</sup>lt;sup>23</sup> AATF is based in Nairobi and supported by the Rockefeller Foundation. Its primary function is to match biotechnology innovations with local needs in African countries.

<sup>&</sup>lt;sup>24</sup> See http://www.cambia.org.

organizations will be exceedingly reluctant to become involved with orphan (or major) crops, and for very good reasons. No responsible organization wants to be a party to, for example, an "escaped" pathogen or an inserted gene that outcrosses into a weedy relative. Remy et al. (1998) report, for example, that transformed bananas resistant to two devastating diseases in Rwanda and Burundi have been developed in Belgium. Because of the lack of biosafety protocols, the transformations remain in the laboratory.

Issues of intellectual property rights and biosafety are not confined to the transfer of science to orphan crops; major crop improvement programs face similar problems in developing countries. From a policy perspective, new programs will need to be developed in the legal and safety areas—in many cases with the help of external aid and consultation—to facilitate the adoption of technology and its use in farmers' fields. In terms of policy priorities, the establishment of legal and safety measures is often more important that allocating additional funds to biotechnology for crop research, lest new technologies simply remain on the shelf. These constraints will likely be much lower when molecular markers and mapping techniques aid conventional crop breeding. Nonetheless, private sector cooperation may still be helpful in distributing seeds.

# New institutional arrangements

For major crops, such as wheat and rice, much of the linking of research with farmers has been performed by Centers of the CGIAR. Limited inroads on millets, cassava, bananas, and a few other crops have been made by additional CGIAR Centers, but there are large numbers of orphan crops where virtually nothing has been done. It is on this point that the new AATF instituted by the Rockefeller Foundation holds considerable promise. Its mission is to help design the relevant templates, protocols, and procedures that will lower the transaction costs of applying biotechnology to major and orphan crops in Africa. By doing so, it will provide a model for other regions. The McKnight Foundation's Collaborative Crop Research Program is also aimed at enhancing the transfer of science from major to orphan crops and training scientists from poor countries in advanced genetics and genomics methods. Finally, the biotechnology programs being developed and promoted in Dutch, Swiss, and US aid agencies are contributing to progress in orphan crops. Special programs and new incentives within the scientific and development communities should be further encouraged to achieve widespread spillover benefits for poor farmers.

# The bottom line

It is useful to ask if an additional US\$ 100 million annually might be spent productively on new approaches to orphan crop improvement. At first glance, that number seems very large, but it is not. Pardey and Beintama (2001) estimate that global agricultural R and D totaled about US\$ 33 billion in 1995. About 35% of this total was spent in developing countries, almost all of which was in the public sector. Only about 10% of the developing country total was in sub-Saharan Africa, where expenditures per agricultural worker were less than US\$ 10, as contrasted to the approximately US\$ 600 per agricultural worker spent in developed countries.

Another financial window on agricultural R and D is provided by the CGIAR. System funding has been level nominally at about US\$ 350 million per year for the past decade. A thirty-year perspective on rice and wheat is also revealing. Over that period, CGIAR centers alone spent well over US\$ 500 million (each) on rice and wheat (CGIAR, 2003). Currently, some two-thirds of all the wheat and rice grown by developing countries trace at least one parent back to a CGIAR Center, primarily to IRRI for rice and to CIMMYT for wheat. The large areas of coverage, when combined with the consequent yield increments, produced phenomenal rates of return, the likes of which are rarely seen in any investment (Evenson and Gollin, 2003).

The question remains whether smaller new investments can draw upon the research experiences in rice, wheat, maize, and other major and model crops to provide equally high rates of return for orphan crops. We believe the answer is yes. Indeed, at the margin, US\$ 10 million invested in a crop like finger millet may return more than a comparable amount invested in rice. At a minimum, we believe the case is strong enough for aid agencies, progressive foundations, and science funding organizations to shoulder the investment risks.

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