

# Promethean Science

**Agricultural Biotechnology,  
the Environment, and the Poor**

*Ismail Serageldin and G. J. Persley*



CONSULTATIVE GROUP ON INTERNATIONAL AGRICULTURAL RESEARCH

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*For John J. Doyle,  
whose vision inspires us still*

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## **The CGIAR...**

The Consultative Group on International Agricultural Research (CGIAR) is an informal association of 58 public and private sector members supporting 16 international agricultural research centers. The CGIAR's mission is to contribute to food security and poverty eradication in developing countries through research, partnership, capacity building, and policy support, promoting sustainable agricultural development based on the environmentally sound management of natural resources. The World Bank, Food and Agriculture Organization (FAO), United Nations Development Programme (UNDP), and United Nations Environment Programme (UNEP) serve as cosponsors.

## **The Authors...**

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## Authors' Preface

Prometheus, according to Greek mythology, was a Titan, responsible for introducing fire to humans, a remarkable innovation at the time, but having benefits and risks, depending on its use. Promethean has since come to mean *dangerously original and creative*.

This book is a companion to the larger volume "Agricultural Biotechnology and the Poor" which was published in January 2000. That volume reported on the international conference that the CGIAR and the U.S. National Academy of Sciences co-sponsored with many other interested institutions in October 1999.

There is a double shift in the research paradigm: firstly, the need for greater contextualization of research, to be undertaken in the context of the deeper understanding of the sustainable management of the environment and the socioeconomic and gender issues that affect the livelihoods of poor people in rural and urban areas. The second shift is the need to mobilize the new revolution in genetics and biotechnology to improve the productivity of agro-ecological systems and the crops, livestock, fish, trees and other species important to poor people and developing countries.

Without minimizing in any way the vital importance of the first shift, this monograph is devoted to a discussion of the second shift, the challenge of

harnessing the new findings in biotechnology for the benefit of the poor and the environment.

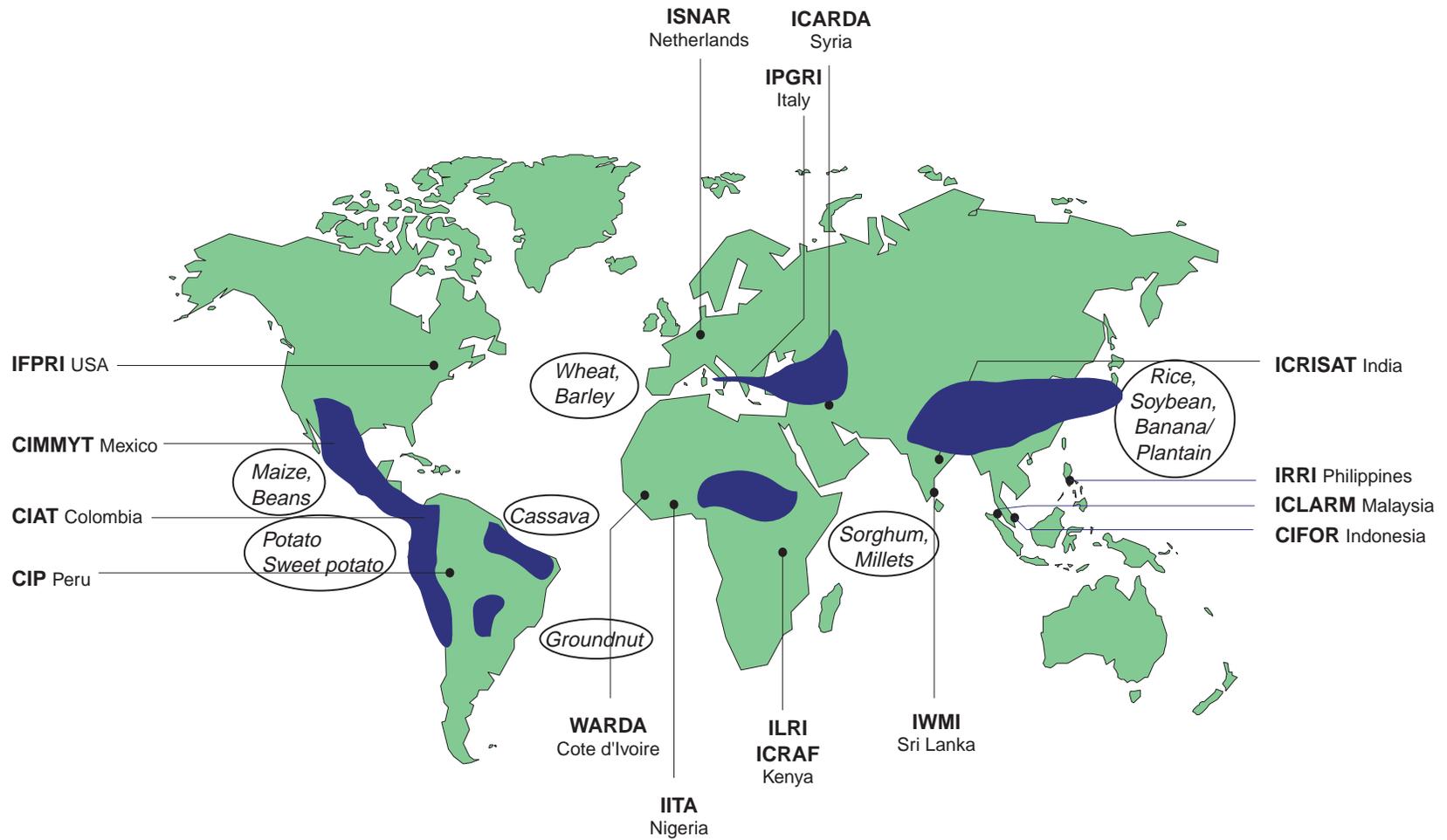
It is here that the newly created Global Forum for Agricultural Research must be seen as an important new vector for bringing about the necessary collaboration amongst farmers, producer and consumer organizations, public and private companies, non-governmental organizations, national agricultural research systems, advanced research organizations and international agriculture research institutes, including the CGIAR centers.

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Schematic illustration of regions of origin of the major food crops and the locations of the research centers of the CGIAR



## Part 1 The Challenge

**T**hroughout history, innovation has driven progress and helped people address the problems of their Age. This progress has not been achieved without pain and controversy. At times, war, famine, and pestilence thwart our best endeavors. Despite setbacks, people the world over continue to strive to understand the natural world, to pursue truth and beauty, and to create a better world for themselves and their children.

Science has a role to play in all these pursuits. However, the very power of the new discoveries in the biological sciences raises fears that these discoveries will not be used wisely. Many believe that they will accelerate the destruction of the natural environment, damage human health, concentrate too much power in the hands of a few global companies, and widen the gap between the rich and the poor, within and between nations.

The task of the Promethean scholars of today is to analyze where modern science can lead to technical innovations and how these can be used wisely to improve agricultural productivity, conserve natural resources, and create wealth especially for poor people in developing countries.

### Global Food Security

*A world of food-secure people is within our reach, if we take the necessary actions.*

The World Food Summit recognized that eradication of poverty is a critical step in improving access to food. Food security covers both the availability of food at the household level as well as access in terms of purchasing power (FAO 1996). *Most people who are undernourished either cannot produce enough food or cannot afford to buy it.* Reduction and elimination of poverty is therefore an integral part of the provision of sustainable global food security.

### Poverty in a Time of Plenty: A Paradox

Although the annual world agricultural growth rate has decreased from 3 percent in the 1960s to 2 percent in the last decade, projections indicate that, given reasonable initial assumptions, world food supply will continue to outpace world population growth, at least to 2020 (Pinstrup-Andersen, Pandya-Lorch, and Rosegrant 1999). Worldwide, per capita availability of food is projected to increase around 7 percent between 1995 and 2020, and for developing countries, by 9 percent (Pinstrup-Andersen, Pandya-Lorch, and Rosegrant 1999).

The paradox is that despite the increasing availability of food, *there are about 840 million people, or 13 percent of the global population, who are food insecure.* These people are among the 4.5 billion inhabitants of the developing countries in Asia (48 percent), Africa (35 percent), and Latin America (17 percent). Of these 840 mil-

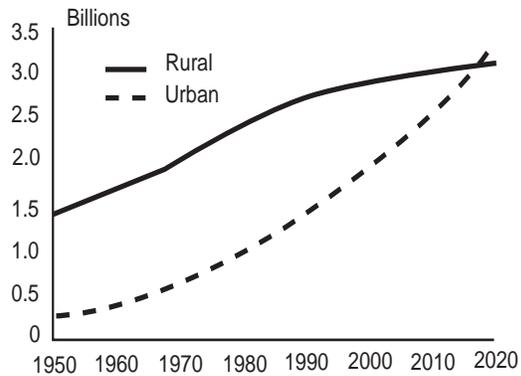
lion, at least 200 million are malnourished children.

It is also paradoxical that food insecurity is so prevalent at a time when global food prices are generally in decline. World cereal production doubled between 1960 and 1990, per capita food production increased 37 percent, calories supplied increased 35 percent, and real food prices fell by almost 50 percent (McCalla 1998).

*The basic cause of the paradox is the intrinsic linkage between poverty and food security. Simply put, people's access to food depends on income.*

Poverty is both a rural and an urban phenomenon. Over 1.3 billion people in developing countries are absolutely poor, with incomes of US\$1 per day or less per person, while another 2 billion people are only marginally better off (World Bank 1997). Malnutrition kills 40,000 people each day. Children and women are most vulnerable to dietary deficiencies, with 125 million children affected by vitamin A deficiency. Many of the poor today live in the low-potential rural areas of the world. With increasing urbanization, a higher proportion of poor people will be living in the cities of the developing countries. The rate of increase of the urban population in the developing countries will be approximately six-fold that of rural areas (Figure 1). Ensuring their access to sufficient nutritious food at affordable prices is also an important component of global food security strategies. *Agricultural research needs to respond to both of these challenges, so as to improve the livelihood of the rural poor and ensure the increased availability of nutritious food at affordable prices for the urban poor.*

**Figure 1 Urban and rural population levels in developing countries, 1950–2020**



Source: United Nations, World Urbanization Prospects: The 1996 Revision (New York: UN, 1996).

### Food Security

Food security is a complex issue that involves:

- Not just *production*, but also *access*
- Not just *output*, but also *process*
- Not just *technology*, but also *policy*
- Not just *global*, but also *national*
- Not just *national*, but also *household*
- Not just *rural*, but also *urban*
- Not just *amount*, but also *content*.

Food production is a necessary but not sufficient condition for food security. Focusing on improving the livelihood of smallholder farmers in developing countries is key to environmental protection, poverty reduction, and food security. The need is to produce differently, not to produce less.

### Global Food Base

Humanity has a narrow food base. Twelve crops account for 95 percent of the plant food base. These are banana/plantain, cassava,

*corn (maize), groundnut, millets, oil crops, potato, rice, sorghum, soybean, sweet potato, and wheat.*

There is also an increasing demand for milk and meat in the developing countries, as dietary preferences change, with increasing urbanization. Indeed, some consider that a “livestock revolution” is taking place in global agriculture that has profound implications for human health, livelihoods, and the environment. Population growth, urbanization, and income growth in developing countries are fueling a massive increase in demand for food of animal origin. These changes in the diets of billions of people could significantly improve the well-being of many rural and urban poor (Delgado and others 1999). Although some of this increase will be met by local rangeland production, some also requires increased production and/or import of feed grains and more intensive livestock production. FAO has nominated 14 priority species in its global strategy on farm animal genetic resources. The most important of these for food production are cattle, sheep, goats, pigs, and chickens. Fish are also an increasingly important component of the diet in developing countries (FAO 1999).

## **World Food Production Challenge**

### ***Production Trends***

Yields of maize, wheat, and rice in developing countries increased from 1.15 to 2.76 tons/hectare between 1961 and 1998. In Africa, they increased from 0.81 to 1.22 tons/hectare over the same period. This presents a significant opportunity to raise cereal production in Africa through yield increases. Globally, meat production in-

creased from 71 million tons in 1961 to 226 million tons in 1999. For developing countries, it increased from 20 million tons to 122 million tons over the same period (Delgado and others 1999).

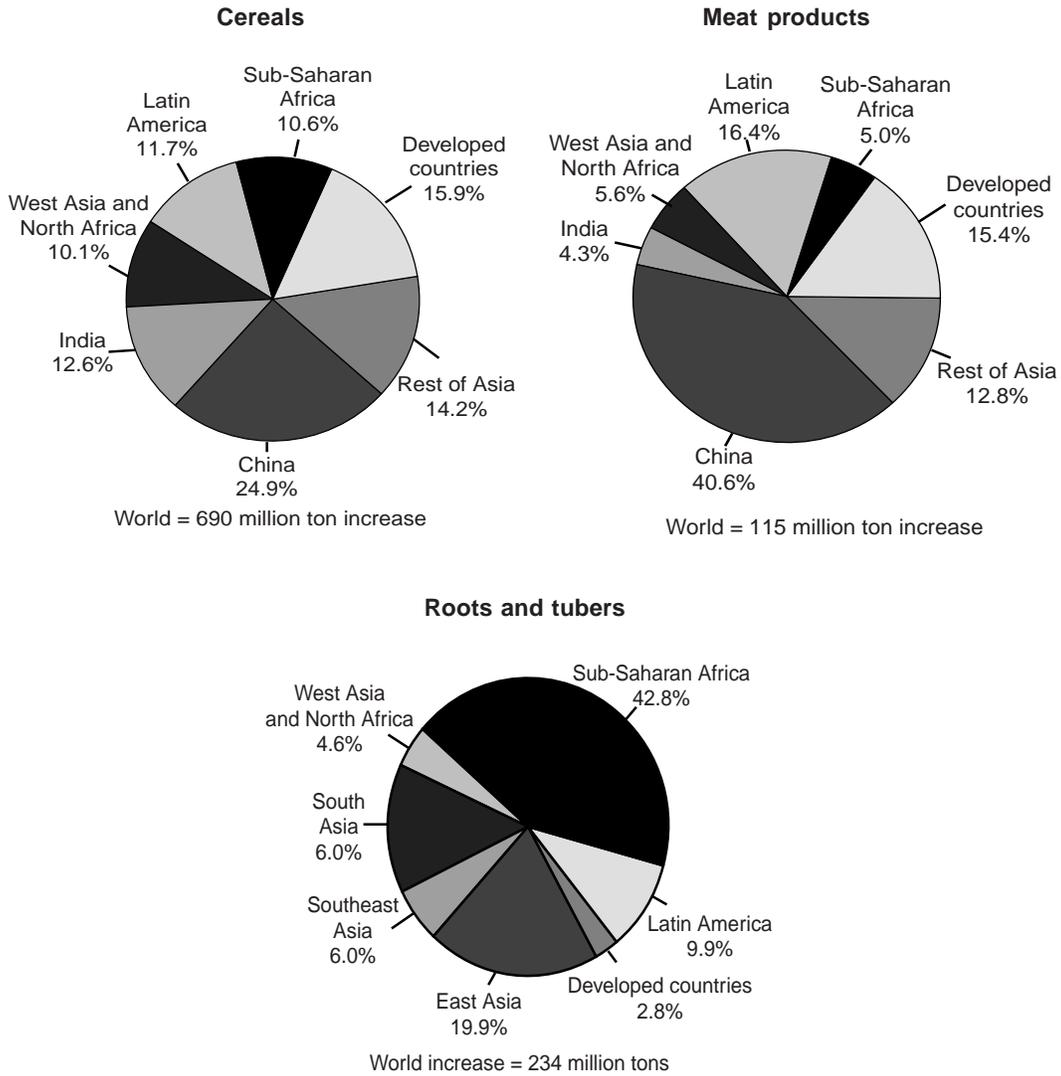
### ***Consumption Patterns***

Demands for food in developing countries are met by both local production and imports. Currently the developing world is a net importer of 88 million tons of cereals/year at a cost of US\$14.5 billion. Since the 1970s the developing countries have become large net importers of milk and meat as demand for livestock products increasingly exceeds supply. Net meat imports by developing countries will increase eight-fold between 1995 and 2020.

Forecasts of future demands for plant and animal products that will drive the production/import requirements of the various regions of the developing world will need to take into account: (a) changes in dietary composition of both food and livestock products; (b) use of cereals as food and feed; and (c) the balance between production and import of plant and animal commodities.

### ***Future Demands***

IFPRI projects that global demand for cereals will increase by 40 percent between 1995 and 2020, with most of the increase in demand coming from developing countries. This will include a doubling in demand for feed grains in the developing world. Net cereal imports by developing countries will almost double by 2020 to meet the gap between production and demand (Pinstrup-Andersen, Pandya-Lorch, and Rosegrant 1999) (see Figures 2 and 3).

**Figure 2 Share of increase in global demand by region, 1995–2020**

Source: IFPRI IMPACT simulations, July 1999.

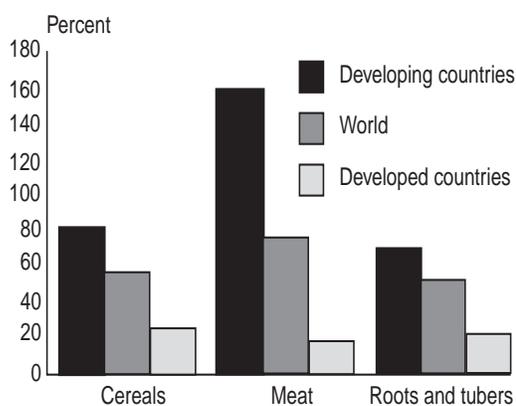
## Beyond the Green Revolution

The food production increases over the past 40 years have been achieved by increasing productivity of cereals, expanding the area of arable land, and massive increases in fertilizer use.

The key element in improving food security during 1960-99 was government policies reflecting a belief that investments

in improving agricultural productivity were a prerequisite to initiating the process of economic development. These policies were supported by both the public and private sectors of the international community. The successful implementation of these policies led to the Green Revolution. Attention was given to the following issues: research and development; technology transfer; human resource development;

**Figure 3 Projected increase in total demand for food, 1990–2020**



appropriate provision of credit; supply and distribution of inputs (seed, water, fertilizer, pesticide); appropriate pricing policies for inputs and outputs; and infrastructure.

The scientific basis for the green revolution stems from joint national and international research programs, which led to the development and distribution of new, high-yielding varieties, primarily of wheat and rice. These varieties gave improved yields, especially when grown in favorable environments with the addition of fertilizer and pesticides.

Plant breeding was carried out with multiple sites worldwide, north and south of the equator. These trials were associated with comprehensive production training programs for scientists and technicians from national agricultural research systems. Informative data on the performance of the genetic materials were provided back to the coordinating center. Local breeding and selection programs were later initiated by the national agricultural research systems, based on the international breeding materials crossed with locally adapted material. This increased the availability of locally adapted varieties for different ecosystems.

The international agricultural research centers also undertook the collection and conservation of the germplasm of their mandate crops, established and maintained large *ex situ* collections of this genetic material, and undertook its partial phenotypic characterization. Some hundreds of thousands of accessions are now held in trust by the CGIAR Centers, under the auspices of the FAO Commission on Plant Genetic Resources.

### Doubly Green Revolution

To meet the food security needs of the world's people in the decades ahead and to create wealth, there is a need to increase agricultural productivity on the presently available land while conserving the natural resource base (Conway 1997). Such a revolution would involve:

- Increasing productivity of the major food crops
- Reducing chemical inputs of fertilizers and pesticides and replacing these with biologically based products
- Integrating soil, water, and nutrient management
- Improving the productivity of livestock.

### Double Shift in the Research Paradigm

*The challenge now is how to use new developments in modern science, communications technology, and new ways of managing knowledge to make complex agricultural systems of smallholder farmers more productive in a sustainable way.*

These issues make for a complex research agenda to improve food security and create wealth. *This new research agenda needs to combine traditional wisdom with modern science.*

There is a double shift in the research paradigm: firstly, the need for greater contextualization of research, to be undertaken in the context of the deeper understanding of the sustainable management of the environment and the socioeconomic and gender issues that affect the livelihoods of poor people in rural and urban areas. This research will need to seek synergies within the farming systems of smallholders, who integrate crop agriculture, livestock, agroforestry, and aquaculture in complex farming systems.

The second shift is the need to mobilize the new revolution in genetics and biotechnology to improve the productivity of agroecological systems and the crops, livestock, fish, trees and other species important to poor people and developing countries.

Without minimizing in any way the vital importance of the first shift, this monograph is devoted to a discussion of the second shift, the challenge of harnessing of the new findings in biotechnology for the benefit of the poor and the environment.

### ***Role of Agricultural Research***

The annual rates of return to investment in agricultural research average 50-80 percent. Thus well directed agricultural research and development programs remain a wise investment of public funds (Alston and others 2000).

There have been several forces that have resulted in the restructuring, downsizing, and refinancing of agricultural and natural resources research systems in industrial and developing countries over the past

decade. They include increasing privatization and competition amongst research providers. These changes are also having a significant impact on donor perceptions, policies, and financial support for national and international agricultural research.

There is a trend toward decreasing public sector investments in research and development. This is partially offset by increasing private sector investments largely aimed at generating new products and processes through biotechnological advances. There is also an increasing use of *participatory processes* involving farmers, civil society, and other stakeholders in the financing, planning, and conduct of research and technology transfer. These approaches seek to enhance successful delivery of useful products and decision-support systems to farmers and consumers.

The coming into force of several international treaties and conventions have also increased the pressure on national governments to meet international obligations.

### ***New Modalities***

New developments in modern biotechnology, information technology, and geographic information systems are revolutionizing global research and development in agriculture and natural resources research. Partnerships between national agencies and international groups may often be the most effective means of developing and delivering new agricultural research technologies of a public goods nature.

These programs need to involve various combinations of national agricultural research systems, nongovernmental organizations, the private sector, farmer groups, advanced research organizations, and the international agricultural research centers.

*This challenge requires the CGIAR to work with more partners, in a wider array of environments, with a broader range of commodities, often grown in mixed systems, and with concern for maintaining the physical and genetic resource base.*

### **The Genetic Imperative**

Rapid progress is being made in understanding the genetic basis of living organisms, and the ability to use that understanding to develop new products and processes useful in human and animal health, food and agriculture, and the environment.

There is now increasing use of modern molecular genetics for genetic mapping and marker-assisted selection as aids to improve crops, livestock, fish, and tree species. Other biotechnology applications such as tissue culture and new diagnostics and animal vaccines are being widely adopted.

Harnessing the full power of the genetic revolution requires going beyond these early applications of modern biotechnology, and recognizing the power of the

new revolution in genomics and associated technologies as aids for genetic improvement. The new technologies will enable greatly increased efficiency of selection for valuable genes, based on knowledge of the biology of the organism, the function of specific genes, and their role in regulating particular traits. This will enable more precise selection of improved strains at the molecular as well as the phenotypic level.

### **Challenge of Biotechnology**

*Biotechnology (see Box 1) offers both promise and perils for the world community.* In human health, it offers new ways to understand the genetic basis of diseases, and to develop improved diagnostics, drugs, and vaccines for their treatment. In agriculture and forestry, it promises new ways to harness and improve the biological potential of crops, livestock, fish, and trees, and improved ways to diagnose and control the pests and pathogens that damage them.

The perils lie in the profound ethical issues surrounding the control and use of

#### **Box 1 Biotechnology defined**

Biotechnology is any technique that uses living organisms or parts thereof to make or modify a product, improve plants or animals, or develop microorganisms for specific uses. All the characteristics of any given organism are encoded within its *genetic material*, which consists of the collection of *deoxyribonucleic acid (DNA)* molecules that exist in each cell of the organism. The complete set of DNA molecules in an organism comprises its *genome*. The genome is divided into a series of functional units, called *genes*. Typical crop plants contain 20,000 to 25,000 such genes.

The genome contains two copies of each gene, one having been received from each parent. The collection of *traits* displayed by any organism (*phenotype*) depends on which genes are present in its genome (*genotype*). The appearance of any specific phenotype trait also will depend on many other factors, including whether the genetic information responsible for the trait (or genes) associated with it is turned on (*expressed*) or off, the specific cells within which the genes are expressed, and how the genes, their expression, and the gene products interact with environmental factors (genotype x environment effects).

these powerful new technologies, and the assessment and management of risks to human health and the environment associated with specific applications. These issues have led to rising public concerns in some countries about various applications of biotechnology. The concerns have been stimulated by an activist campaign against the use of genetically improved organisms in food and agriculture and their release into the environment. *Modern biotechnology raises profound issues, but it also offers enormous promise for dealing with previously intractable problems.*

### **Key Issues**

The key policy issues that will affect the application of new developments in modern biotechnology for the public good are ethics, food and environmental safety, economic concentration, and intellectual property management.

### *Ethics*

A wealth of scientific and popular discussion exists about the benefits and risks of genetic engineering and biotechnology. Confusion surrounds the issue of biotechnology's risks and benefits. What are the social and ethical issues surrounding the use of biotechnology to improve food security and alleviate poverty? Current public debate about the "gene revolution" often does not sufficiently differentiate between risks inherent in a technology and those that transcend it. This differentiation is important in any attempt to reason out the social and ethical implications of biotechnology (Leisinger 2000).

Since the early 1970s, recombinant DNA technology has enabled scientists to genetically modify plants, animals, and microorganisms and introduce a greater

diversity of genes, including genes from distantly related species, into organisms than traditional methods of breeding and selection. Organisms genetically modified in this way are called *living modified organisms*. Concerns exist about the potential risks posed by living modified organisms. The principles and practices required for assessment of technology-inherent risks are well established and draw on the experience of individual countries and regional and international organizations. From an ethical perspective, risks disallowed in industrial countries should not be exported to developing countries. If genetically engineered organisms and biotechnological procedures are used in developing countries, state-of-the-art quality management that takes local ecological conditions into account must be practiced. Such risk assessments allow governments, communities, and business to make informed decisions about the benefits and risks inherent in using a particular technology to solve specific problems.

Technology-transcending risks emanate from the political and social context in which a technology is used. These risks stem from both the course the global economy takes and country-specific political and social issues. The most critical fears have to do with the potential aggravation of the prosperity gap between industrial and developing countries and growing disparities in the distribution of income and wealth within and between developing countries. The gap in prosperity between industrial and developing countries may grow because of the possible substitution of genetically engineered products for tropical agricultural exports and because the industrial world may not adequately compensate the developing world for exploiting its indigenous genetic resources.

Widespread fear exists that private enterprises and research institutes could gain unremunerated control of the genes of plants native to the developing world and use them to produce superior varieties that would then be sold back to developing countries at high prices. The successful implementation of the Rio Convention on Biological Diversity so that it becomes clear who should compensate whom for what and for how much needs unequivocal regulation. Simple and effective ways need to be found to establish fair compensation.

In assessing the potential impact of biotechnology on food security and poverty alleviation, the interpretation of data is subject to the interests and value judgments of a variety of stakeholders. Identical information can lead some to consider agricultural biotechnologies to be amongst the most powerful and economically promising means of ensuring food security, while others perceive them as a threat to development in poor countries. Differing realities and pluralism of opinion exist. Biotechnology involves a number of economic, social, and ecological risks. But these risks are not a consequence of the technology per se. They arise from particular social settings, transcending the nature of the technology employed within those settings. There are also ethical issues involved in *not* pursuing the use of new technologies that may contribute to improving the productivity and sustainability of agriculture, especially in developing countries (Nuffield Council on Bioethics 1999). All these issues need to be openly debated, and choices made by individuals and nations.

### *Food Safety*

An open, transparent, and inclusive food safety policy and regulatory process is re-

quired, which takes account of public concerns about genetically improved foods. Many consumers in North America, Europe, and China have been eating genetically improved food over the past several years, without any demonstrated adverse effects on human health. The concept and practice of risk assessment, including consistent approaches to the use of substantial equivalence and the precautionary principle, are valuable tools but need to be kept under review.

Food labeling, whether mandatory or voluntary, could be used to provide information about specific products and enable consumers to make informed decisions about their use. The potential long-term impact of genetically improved foods on human health, worker safety, and the environment is unknown, and requires monitoring and research. Methods are available to test allergenicity and toxicity of novel genetically improved foods in humans. Post-market monitoring of such foods may be possible in some markets but impractical in others.

The Organization for Economic Cooperation and Development will report in mid 2000 to the G8 Summit on key issues, including:

- Factual points of departure where there is agreement and disagreement
- Benefits versus risks, which differ for different countries and environments
- Management of genetic modification technologies
- The role of stakeholders
- An international program of activities to inform the public debate and policymaking.

### *Environmental Risks*

When addressing risks posed by the cultivation of plants in the environment, six

safety issues need to be considered (Cook 2000; NRC 2000). These are

- gene transfer to wild relatives
- weediness
- trait effects
- genetic and phenotypic variability
- expression of genetic material from pathogens
- worker safety.

Review of these issues is inherent in the regulatory systems in place today (Doyle and Persley 1996).

The Cartagena Protocol on Biosafety was agreed to by 130 governments in Montreal in January 2000. The Biosafety Protocol is intended to specify obligations for international transfer of living modified organisms that may threaten biodiversity. It sets out means of risk assessment, risk management, advance informed agreement, technology transfer, and capacity building.

Under the Protocol, governments will signal whether they are willing to accept imports of living modified organisms intended for release into the environment, by communicating their decision via a Biosafety Clearing House. Information on living modified organisms that may be contained in shipments of commodities will also be provided to importing countries.

Advanced Informed Agreement procedures will apply to the introduction of seeds, live fish, attenuated vaccines, and other living modified organisms that are to be intentionally introduced into the environment and which may threaten biodiversity. In all these cases, the exporter must provide detailed information to each importing country in advance of the first shipment, and the importer must then au-

thorize the shipment within a one-year period. The Protocol also outlines general procedures for risk assessment. The aim is to ensure that recipient countries have both the opportunity and the capacity to assess any risks to biodiversity involving the products of modern biotechnology. Capacity building is also an important component of the agreement. The Protocol and the World Trade Organization are intended to be mutually supportive. The Protocol is not to affect the rights and obligations of governments under any existing international agreements.

To ensure the safe use of biotechnology in the environment, there is a need for continuing emphasis on:

- Efficient and cost-effective regulatory systems at the institutional and national levels
- Clear guidelines for field tests and commercial releases of living modified organisms
- Informative labeling of novel products for consumers
- Systematic capacity building
- International support mechanisms for early warning of good or bad developments with living modified organisms
- More scientific research on possible short- and long-term effects of living modified organisms on the environment and risks to biodiversity.

### *Economic Concentration*

The trend toward intellectual property protection in biosciences has had several important structural consequences. The private sector life sciences industry has become increasingly centralized. About six companies dominate what was once an industry in which many more small compa-

nies played a major role. The reasons for this are complex. They relate to economic efficiencies in production and marketing, as well as the desire to access specific research and development expertise in smaller companies. Intellectual property protection has contributed significantly to the development of the current biotechnological revolution in agriculture, and to the institutional restructuring that is accompanying that revolution (Barton 1999).

### *Intellectual Property Management*

New scientific discoveries in biotechnology may be protected by plant variety protection, patents, and/or trade secrets. Countries differ in what forms of intellectual property protection may be applied to specific inventions. The 1995 Agreement on Trade-Related Aspects of Intellectual Property Rights requires all members to provide at least a *sui generis* system of protection for plant varieties.

Industrial country moves toward intellectual property protection of the products of biotechnology have led to developing country moves to protect the genetic sources. This culminated in the Convention on Biological Diversity in 1992. This agreement made it clear that nations could enact legislation protecting the export of genetic resources, by arrangements to share the benefits should there be financial return from the exported genetic resources.

Because the private sector holds many of the advanced biotechnologies, the pub-

licly funded agricultural research community must also develop an effective approach to cooperation with the private sector in research and product development. The public sector needs to develop a policy toward intellectual property protection for its own discoveries. In doing so it should set the example in terms of benefit sharing with poor indigenous farmers, and also to consider the possibility for the public sector to obtain intellectual property protection to have bargaining chips to negotiate strategic alliances with multinational companies.

For national governments, it would be desirable to design Trade-Related Aspects of Intellectual Property Rights-compliant legislation in a way that is beneficial to their agriculture, maintaining the possibility for a multilateral regime for germplasm acquisition and transfer. Legislation should be supplemented with improved capabilities in the courts, the law firms, and the law schools, so that the law can be used effectively. There is a real possibility that an antitrust code can be negotiated and this is almost certainly beneficial for developing countries.

Developing countries could also seek ways to use the intellectual property system to encourage research for their needs by giving incentives, such as market protection, to encourage private-sector research on products of benefit to the developing world, in a manner analogous to the Orphan Drug legislation. All such legislation should be the result of substantive public discussion and be adopted in a transparent fashion.

## Part 2 Enabling Technologies

### Evolution of Modern Genetics

Gregor Mendel, the father of modern genetics, published his work on inheritance patterns in pea in 1865, but it took 35 years for others to grasp their significance. Since 1900, there has been steady progress in our understanding of the genetic makeup of all living organisms ranging from microbes to humans. A major step was taken in the 1920s when Muller and Stadler discovered that radiation can induce mutations in animals and plants. In the 1930s and 1940s, several new methods of chromosome and gene manipulation were discovered, commercial exploitation of hybrid vigor in maize commenced, and techniques such as tissue culture and embryo rescue were used

to obtain viable hybrids from distantly related species.

The double helix structure of DNA (deoxyribonucleic acid), the chemical substance of heredity, was discovered in 1953 by James Watson and Francis Crick. This triggered rapid progress in every field of genetics, leading to a rapid transition from Mendelian to molecular genetic applications in agriculture, medicine, and industry (see Box 2).

The most striking differences between the techniques of modern biotechnology and those that have been used for many years in the breeding of new strains of crops and livestock improvement lie in the increased precision with which the new techniques may be used (see Figure 4).

#### Box 2 Recombinant DNA technologies

In the 1970s, a series of complementary advances in the field of molecular biology provided scientists with the ability to identify, clone, and move DNA between close and more distantly related organisms. This *recombinant DNA technology* has reached a stage where a piece of DNA containing one or more specific genes can be taken from nearly any organism, including plants, animals, bacteria, or viruses, and introduced into any other organism. This process is known as *transformation*. The application of recombinant DNA technology has been termed *genetic modification*. An organism that has been improved, or *transformed*, using modern techniques of genetic exchange is commonly referred to as

a *genetically improved organism* or a *living modified organism*. The offspring of any traditional cross between two organisms also are *genetically improved* relative to the genotype of either of the contributing parents. Strains that have been genetically improved using recombinant DNA technology to introduce a gene from either the same or a different species also are known as *transgenic strains* and the specific gene transferred is known as a *transgene*. Not all genetically improved organisms involve the use of cross-species genetic exchange. Recombinant DNA technology also can be used to transfer a gene between different varieties of the same species or to modify the expression of one or more of a given plant's own genes, such as the ability to amplify the expression of a gene for disease resistance (Persley and Siedow 1999).

## Gene Transfer Technologies

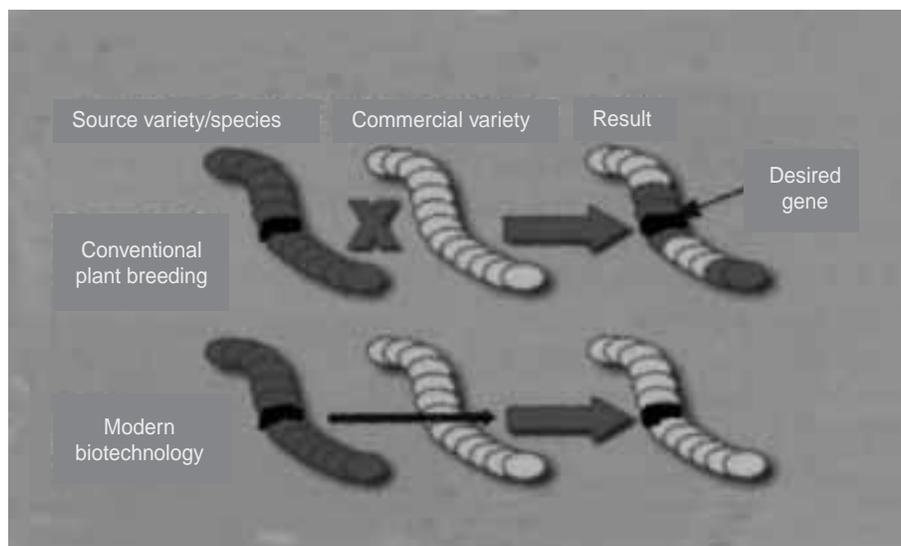
Two primary methods currently exist for introducing new transgenic genetic material into plant genomes in a functional manner. For plants known as dicots (broad-leaved plants such as soybean, tomato, and cotton), transformation is usually brought about by use of the bacterium *Agrobacterium tumefaciens*. *Agrobacterium* naturally infects a wide range of plants by inserting some of its own DNA directly into the DNA of the plant. By taking out the undesirable traits associated with *Agrobacterium* infection and inserting a gene of interest into the *Agrobacterium* DNA that will ultimately be incorporated into the plant's DNA, any desired gene can be transferred into a dicot's DNA following bacterial infection. The cells containing the new gene subsequently can be identified and grown using plant cell culture technology into a whole plant that now contains the new transgene incorporated into its DNA (Persley and Siedow 1999).

Plants known as monocots (grass species such as maize, wheat, and rice) are not readily infected by *Agrobacterium* so the external DNA that is to be transferred into the plant's genome is coated on the surface of small tungsten balls and the balls are physically shot into plant cells. Some of the DNA comes off the balls and is incorporated into the DNA of the recipient plant. Those cells can also be identified and grown via cell culture into a whole plant that contains added DNA.

## Understanding Plant and Animal Genes

The 1990s have seen dramatic advances in our understanding of how biological organisms function at the molecular level, as well as in our ability to analyze, understand, and manipulate DNA molecules, the biological material from which the genes in all organisms are made. The entire process has been accelerated by the Human

**Figure 4 Differences between conventional breeding and genetic engineering**



Genome Project, which has invested substantial public and private resources into the development of new technologies to work with human genes (Smaglik 2000). The same technologies are directly applicable to all other organisms, including plants, animals, insects, and microbes. Thus, the new scientific discipline of *genomics* has arisen, which has contributed to powerful new approaches to identify the functions of genes and their application in agriculture, medicine, and industry.

Genomics refers to determining the DNA sequence and identifying the location and function of all the genes contained in the *genome* of an organism. The advent of large-scale sequencing of entire genomes of organisms as diverse as bacteria, fungi, plants, and animals, is leading to the identification of the complete complement of genes found in many different organisms.

This is dramatically enhancing the rate at which an understanding of the function of different genes is being achieved. This new knowledge will radically change the future of breeding for improved strains of crops, livestock, fish, and tree species (Box 3).

The present major technical limitation on the applications of recombinant DNA technology to improving agriculture is insufficient understanding of exactly which genes control agriculturally important traits and how they act to do so. This is why new developments in understanding gene function and linking this new information with breeding and genetic resources conservation programs is so important.

Research in plant genome projects, for example, is showing that many traits are *conserved* (that is, shared) within and even between species. The same gene(s) (DNA sequences) may confer the same trait in dif-

### Box 3 New technology developments in genomics

- Rapid developments in DNA sequencing technology have made the acquisition of whole genome sequences a reality. Such data, when interpreted using new analytical tools, give a complete listing of all the genes present in an organism, thus providing a genetic blueprint of it.
- Several technologies are being developed for genome analysis that allow rapid genotyping and gene expression studies. It should become possible to scan rapidly the genomes of different organisms and to develop a systematic approach for mapping genetic traits, both complex (controlled by multiple genes) and single gene traits.
- Advances in bioinformatics may allow the prediction of gene function from gene sequence data. Given a listing of the genes of an organism, it may become possible to build a theoretical framework of the biology of that organism.
- The comparison of physical and genetic maps and DNA sequences across different organisms will reduce significantly the time frame for the identification and selection of potentially useful genes. Thus the gene discovery process becomes shorter through comparative genomics, because many genes are conserved (i.e. the same) between different organisms.
- The new genomics and new technological developments will accelerate the acquisition of fundamental knowledge about biological systems. Genomes will change the approaches used to solve biological problems, which will result in novel uses of biotechnology to develop and improve agricultural productivity.
- Marker-assisted selection will link with more efficient gene-assisted selection, and will greatly facilitate and accelerate the characterization of crop and livestock genetic resources, so they can be more effectively deployed in different ecosystems.

ferent species. Thus, a gene for salt tolerance in fish may confer salt tolerance if it is transferred and expressed in rice. A gene for drought tolerance in millet may also confer drought tolerance if transferred to maize. These advances in genomics should lead to a rapid increase in the identification of useful traits that will be available to enhance crop plants and livestock in the future. In other areas such as animal health, knowledge of the genome of a parasite such as *Theileria parva* should assist in the identification of essential proteins of the parasite against which an immune response can be targeted and hence may accelerate effective vaccine development when combined with the necessary biology and immunology (see Box 4).

### **Platform Technologies**

Rapid advances are occurring in three major areas: DNA sequencing, genome analysis, and computational biology (bioinformatics). First, developments in DNA sequencing have made the acquisition of whole genome sequences possible. These data, when interpreted with bioinformatics, can provide a complete listing of all the genes present in an organism, the so-called genetic blueprint of an organism. Rapid progress is being made in the Human Genome Project, by both public and private laboratories. The first genome sequence of an organism more complex than a virus was published in 1996. Already 23 genome sequences are available, and some 60 or more genome sequencing projects of a wide variety of organisms, including plants, animals, parasites, and microbes, are under way (see The Institute for Genomic Research web site at <http://www.tigr.org/>).

Second, different types of technologies have been developed for genome analysis, which speed up the process. With the immense increase in the amount of DNA sequence data available, it is possible to scan whole genomes rapidly and to develop a systems approach for mapping genetic traits.

It is also possible to use the new developments in bioinformatics to understand the complex genetic interactions involved in growth, development, and environmental interactions. Developments in bioinformatics are allowing the prediction of gene function from gene sequence. Thus from genome sequences of DNA it is possible to build a theoretical framework of the biology of an organism. This forms a powerful base for further experimentation. In addition, as the numbers of physical and genetic maps of different species increase, it becomes possible to compare these across different organisms (comparative genomics), be they microbes, plants or animals, and to significantly reduce the time required to identify important genes. These technologies allow novel approaches to addressing biological problems, which are just beginning to be understood.

### **Functional Genomics for Trait Discovery**

Much of the discussion about molecular biology today is focused on the opportunity and risks associated with gene transfer through transformation and the risks to human health and the environment associated with the use of such living modified organisms. The same science brings new tools to assist plant and animal breeders to identify and transfer genes through

#### Box 4 Fighting East Coast Fever

Parasitic diseases of livestock caused by *Theileria* species lead to annual losses estimated at US\$1 billion worldwide. The most important of this group of parasites in Africa is *Theileria parva*. This parasite causes East Coast Fever in cattle, which occurs in 11 countries of sub-Saharan Africa and kills about 1 million animals annually. Farmers who own only a few cattle are disproportionately affected, because of the high percentage mortality in affected herds. Also, they are less likely either to be able to afford or have access to present control methods of chemical dips for stock, or the presently available infection/treatment vaccine, which costs approximately US\$25 per dose.

A robust and affordable vaccine to protect cattle against East Coast Fever in Africa would be of great benefit to small-scale livestock producers. Integrating the new findings in genetics, immunology, molecular biology, and genomics offer promising new strategies for vaccine development.

East Coast Fever has a two-stage infective process. One prospective candidate antigen (p67) has been identified by International Livestock Research Institute scientists through molecular biology and immunology approaches. It is active at the first transient stage of infection and gives partial but not sufficient protection to infected animals. It seems likely that an effective East Coast Fever vaccine will need to be effective against both stages of the disease.

In the second stage of the infective process, the parasites invade the host cells and cause infected cells to behave like cancer cells. The parasites induce host cells to proliferate. The parasites attach to the cellular division apparatus and so divide in synchrony with host cells, resulting in huge increases in parasite numbers. New methods

of disease intervention may arise from studying this phenomenon and the molecules that mediate the process. This research may also contribute to human medicine, particularly in leukemia research, by contributing to a greater understanding of the molecular mechanisms of some human cancers.

The major mechanism of immunity against *T. parva* infection is known to be the action cytotoxic T cells. Each T cell recognizes a small fragment of a parasite antigen, a peptide fragment about 9 amino acid residues long, that is displayed on the surface of the infected cells in association with major histocompatibility antigens. Identifying these peptide antigens directly is technically very demanding.

As part of its strategy for East Coast Fever vaccine development, the International Livestock Research Institute is now collaborating with The Institute for Genomic Research to determine the DNA sequence of *Theileria parva*. It is estimated that the genome is about 10Mb and contains 5000-6000 genes (Nene and others 2000).

From the genome sequence of the parasite, all the genes encoded within the genome may be able to be identified using bioinformatics. From these data and the available knowledge about the types of desirable protein antigens it should be possible to identify additional candidate vaccine antigens. Using in vitro screens, it should then also be possible to identify which ones to take further in terms of animal experiments.

The two collaborating institutes intend to place the genome sequence data for *T. parva* in the public domain, as it becomes available. In this way, it will be accessible to other research institutes concerned with developing new vaccines for more effective control of *T. parva* and related parasites, such as *T. annulata*, *Babesia*, *Eimeria*, *Plasmodium*, and *Toxoplasma*, that cause disease in livestock and humans.

conventional approaches. In many environments, future gains in productivity will depend to a large extent upon manipulation of complex traits, such as drought or heat tolerance. These are often difficult to identify and utilize in a conventional breeding program without the additional help of modern science. For future crop improvement, plant genomic projects will be the engine to drive trait discovery and help solve intractable problems in crop production and protection.

A completely sequenced plant genome such as rice, for example, will provide an enormous pool of genetic markers and genes for rice improvement through marker-assisted selection in conventional breeding, and/or the introduction of specific genes through transformation (see Box 5).

To fully exploit the wealth of molecular data it is necessary to understand the specific biological functions encoded by DNA sequence through detailed genetic and phenotypic analyses. Thus unlike genome sequencing per se, functional genomics requires diversity of scientific expertise as well as genetic resources for evaluation. In many important food crops national and international public sector research has a large investment in genetic resources and breeding materials, and a long history of understanding biological function and genotype x environment interactions. These scientific and biological resources will become increasingly important in gaining knowledge about the function of genes and in developing

molecular markers to assist the breeding process.

Previously, the genetic resources were provided largely by developing countries, and bred in publicly funded crop and livestock breeding programs, the outputs of which were publicly available. Now, the advent of private investments in research and development and strong intellectual property protection has radically changed this relationship. A new compact is required to address the current imbalance.

The gathering and provision of so much sophisticated genetic information in computerized databases, by both the private and public sectors, and the patenting of genes and enabling technologies require a new paradigm for using new biotechnologies to improve crops and livestock, especially in developing countries where food needs are most urgent. This paradigm requires public and private partnerships amongst farmers, consumers, genomics specialists, breeders, and scientists knowledgeable about the species and the environments upon which the world depends for food.

*These new technologies and the associated explosion of information have major implications for the future research and investment strategy of the CGIAR system, and its role in harnessing modern science to increase sustainable productivity of agriculture in the developing world.*

## Part 3 Putting Technologies to Work

### **Crop Improvement**

The applications of modern biotechnology to crops are in:

- Improved diagnosis of pests and diseases
- Tissue culture/micropropagation techniques
- The construction of transgenic plants with improved yields, disease, pest, and stress resistance, and/or nutritional quality
- The use of genetic markers, maps, and genomic information in marker-assisted and gene-assisted selection and breeding.

### **Diagnosics**

The use of monoclonal antibodies and nucleic acid technologies has improved the specificity, sensitivity, and ease of diagnosis of plant pests and pathogens. These new diagnostics have also greatly assisted in the study of the ecology of pests and diseases, their more rapid identification in quarantine, and in the propagation of disease-free planting material.

### **Micropropagation Techniques**

Tissue culture and other in vitro micropropagation technologies provide a practical means of providing disease-free plantlets of current varieties with significantly improved yield gains by the removal of pests and pathogens. Micropropagation,

when linked with new diagnostics, has been especially useful in vegetatively propagated crops such as sweet potato and banana and for the rapid propagation of tree species. Tissue culture is also a critical step in the construction of transgenic plants by enabling the regeneration of transformed cells containing a novel gene.

### **Modern Plant Breeding**

The application of biotechnology to agriculturally important crop species has traditionally involved the use of *selective breeding* to bring about an exchange of genetic material between two parent plants to produce offspring having desired traits such as increased yields, disease resistance, and/or enhanced product quality. The exchange of genetic material through conventional breeding requires that the two plants being crossed be of the same, or closely related, species. Such active plant breeding has led to the development of superior plant varieties far more rapidly than would have occurred in the wild due to random mating.

Traditional methods of gene exchange, however, are limited to crosses between the same or closely related species. It can take considerable time to achieve desired results, and frequently, genes conveying desirable traits do not exist in any closely related species. Modern biotechnology, when applied to plant breeding, vastly increases the precision and reduces the time with which these changes in plant characteristics can be made, and greatly increases

the potential sources from which desirable traits can be obtained.

The application of recombinant DNA technology to facilitate genetic exchange in crops by transformation techniques has several features that complement traditional breeding methods. The exchange is far more precise because only a single specific gene that has been identified as providing a useful trait is being transferred to the recipient plant. There is no inclusion of ancillary, unwanted traits that need to be eliminated in subsequent generations, as often happens with traditional plant breeding. There has been some debate over the transfer of antibiotic marker genes with the single trait gene, and considerable research has now gone into eliminating the antibiotic marker genes from the final products prior to commercial use. Better still is to use markers that do not require antibiotics, such as new sugar-based markers.

The technical ability to transfer genes from any other plant or other organism into a chosen recipient means that the entire span of genetic capabilities available among all biological organisms has the potential to be genetically transferred or used in any other organism. This markedly expands the range of useful traits that ultimately can be applied to the development of new crop varieties.

The use of genetic markers, maps, and genomic information will improve both the accuracy and time to commercial use of single and polygenic traits in plant breeding (for example, the use of marker-aided selection in breeding for disease resistance in rice is illustrated in Box 5).

The present major technical limitation on the application of recombinant DNA technology to improving plants is insufficient understanding of exactly which genes control agriculturally important traits and

how they act to do so. This is the constraint that can be addressed through studies of plant genomes, as an aid to crop improvement.

The rapid progress being made in genomics should greatly assist conventional plant breeding, as more functions of genes are identified and able to be manipulated. This may enable more successful breeding for complex traits such as drought and salt tolerance. This would be of great benefit to those farming in marginal lands worldwide. Breeding for such complex traits has had limited success with conventional breeding in the major staple food crops.

Another important trait of great potential benefit to smallholder farmers would be apomixis. This is the ability to propagate plants asexually through seed. This would confer the benefits of hybrid vigor without the need to purchase new seed each season. Research is underway by scientists at CIMMYT, Mexico, working with other collaborators in France and the USA, to identify the genes conferring this trait.

### ***Commercial Applications of Genetically Improved Crops***

Substantial commercial cultivation of the first generation of new genetically improved plant varieties commenced in the mid-1990s. In 1999, approximately 40 million hectares of land were planted worldwide with transgenic varieties of over 20 plant species, the most commercially important being cotton, corn, soybean, and rapeseed (James 1999). These new crop varieties are planted in Argentina, Australia, Canada, China, France, Mexico, South Africa, Spain, and, predominantly, the United States. Approximately 15 percent of

### **Box 5 Molecular breeding: biotechnology at work for rice**

Marker-assisted selection is the application of molecular landmarks—usually DNA markers near target genes—to assist the accumulation of desirable genes in plant varieties. There are many reasons why molecular markers are useful in plant breeding. Improved disease resistance in rice is a good example.

Bacterial blight is a widespread disease in irrigated rice-growing areas and can cause widespread yield loss. The incorporation of host-plant resistance through conventional breeding has been the most economical means of control, and has eliminated the need for pesticides. There are now over 20 genes available for use in rice improvement, but not all of these genes are equally effective in different environments. The pathogen eventually overcomes the resistant gene. Using conventional approaches the plant breeder must be continually adding and changing genes just to maintain the same level of resistance. Breeding effort spent in “maintenance” is a potential loss to gains in other traits.

A more sustainable system can be developed by deploying more than one resistance gene at a time. The challenge is to find the right combination of genes and put them into varieties most suitable for local production. When two or more genes are incorporated into a variety it is called “gene pyramiding.” Up to four genes for bacterial resistance have been pyramided in rice, and there is evidence that collectively they are more effective than would be ascribed to their additive effects. Because each gene may mask the presence of another gene, it is difficult to pyramid more than two genes by conventional breeding and selection; but it can be done with molecular markers.

Over the past several years, scientists at the International Rice Research Institute and its national partners in the Asian Rice Biotechnology Network have applied DNA marker technology to address the bacterial

blight problem. First, DNA markers are used to tag nearly all the bacterial blight resistance genes in available genetic stocks. Second, DNA markers are used to describe the composition of pathogen populations unique to each region. This parallel analysis of the host and the pathogen has enabled scientists to determine the right combination of genes to use in each locality.

In Asia, a number of resistance genes (Xa4, xa5, Xa7, xa13, Xa21), all with molecular tags, have been introduced in various combinations into locally adapted varieties.

The Asian Rice Biotechnology Network is promoting sharing of these elite lines and gene pyramids from different countries with other countries in Asia. This will allow the useful marker-assisted selection products to be rapidly disseminated through collaborative field testing across the region.

Marker-assisted selection has delivered some of the promises of biotechnology, and there are other examples of use in rice. The impact of new selection techniques will continue to be significant, particularly in an increasingly intellectual property-conscious environment. Marker technology is based on knowledge of endogenous DNA sequences; this has important practical implications, as the rice genome will be completely sequenced by an international effort, led by the Rice Genome Research Program of Tsukuba, Japan. As long as there is a public commitment to maintain all rice sequences in the public domain, useful genes for marker-assisted selection should be readily accessible to national and international rice breeding programs. Thus, because of their relative simplicity, easy integration into conventional breeding, and minimal background intellectual property, DNA marker technology and marker-assisted selection are expected to be strong driving forces in crop improvement in the future.

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the area is in emerging economies. The value of the global market in transgenic crops grew from US\$75 million in 1995 to US\$1.64 billion in 1998.

The traits these new varieties contain are most commonly insect resistance (cotton, maize), herbicide tolerance (soybean), delayed fruit ripening (tomato) and virus resistance (potato). The main benefits of these initial varieties are better weed and insect control, higher productivity, and more flexible crop management. These benefits accrue primarily to farmers and agribusinesses. There are also economic benefits accruing to consumers in terms of maintaining food production at low prices. Benefits also accrue to the environment through reduced use of pesticides, and the reduction in carcinogenic mycotoxins caused by fungal contamination in food crops.

Other crop/input trait combinations presently being field-tested include virus-resistant melon, papaya, potato, squash, tomato, and sweet pepper; insect-resistant rice, soybean, and tomato; disease-resistant potato; and delayed ripening chili pepper. Research is aimed at modifying the oil content (rape-seed), increasing the amount and quality of protein (maize), or increasing vitamin content (rice) (James and Krattiger 1999).

Much greater emphasis is now being given to improving the nutritional value of foods. There also is work in progress to use plants such as corn, potato, and banana as bio-factories for the production of vaccines and biodegradable plastics.

### **Characterizing Biodiversity**

Genes and gene combinations selected in the past in nature and by humans will re-

main a vital source for germplasm improvement. They need to be conserved in seed banks, and in situ where possible and desirable. Genomics can play a key role in the characterization and conservation of genetic resources. It can be used to determine which genes and chromosome segments are duplicated, which are unique, and how easy it will be to recreate the various combinations of chromosome segments in modern plant breeding programs (Flavell 1998).

Comparative genetics can enhance exploitation of genebank collections. The CGIAR has an opportunity to become an important player in the field, by exploiting its own comparative advantages of germplasm management and enhancement and its international network of research centers and collaborators. The location of the Centers and their international network of collaborators coincide well with the centers of origin of the world's major food crops (see Map). Jointly, the CGIAR, national programs, and advanced laboratories now have an historic opportunity to work together to make optimal use of new developments in science, for the molecular characterization of agriculturally important species and their wild relatives amongst plant, livestock, and microbial genetic resources to achieve their goals.

The application of comparative studies to enhance the use and management of plant germplasm collections was the focus of an international workshop in The Hague in August 1999. It was co-organized by the International Rice Research Institute and the International Service for National Agricultural Research through the System-Wide Genetic Resources Program.

*The major finding was that the CGIAR centers must take advantage now of the latest technologies in genomics research to apply comparative genetics to the germplasm collections that they hold in trust (System-Wide Genetic Resources Program 1999).*

The principal conclusions from the workshop were that:

- Comparative genetics can provide the most precise, unambiguous and comprehensive tool for germplasm characterization
  - Cross-species comparisons will allow identification of the germplasm sources of superior, potentially optimal genetic sources for specific traits. Comparative genetics will provide a multilateral flow of knowledge between major and minor crops
  - CGIAR centers need to take the initiative to develop comparative genetics research for several crops, including cereals, roots/tubers, and legumes
  - Use of comparative genetics will help reposition CGIAR genebanks for the future and enhance use of germplasm in crop improvement programs
  - The strong comparative advantage of CGIAR centers to conserve, phenotype, and use germplasm should be linked with expertise in comparative genetics existing in many laboratories worldwide. This will require innovative investment and institutional arrangements
  - Additional investment by the CGIAR in comparative genetics and bioinformatics will ensure that the results and benefits are available as international public goods.
- The initial potential of comparative genetics may best be demonstrated with traits where gene action is simple and well understood, such as resistance to some pests and diseases, submergence tolerance, starch accumulation, nutritional qualities, phosphate uptake, resistance to soil toxicity, weed competitiveness, and flowering response. Comparative studies may facilitate:
    - The systematic search for useful genes that contain these traits in germplasm accessions without having to discover the genes for each crop
    - Identification of genetic resources containing useful genetic combinations
    - Understanding of the genetics underlying important traits
    - Better understanding of the structure of biodiversity that will enhance management of germplasm collections.

Comparative genetics provides the potential for trait extrapolation from a species where the genetic control is well understood, and for which there are molecular markers, to a species that has a limited amount of information. Rice, for example, is regarded as a model for cereal genomics because of its small genome. The similarity of cereal genomes means that the genetic and physical maps of rice can be used as reference points for the exploration of the much larger and more difficult genomes of the other major cereal crops, and be applied to the minor cereals. Conversely, decades of breeding work and molecular analysis of maize, wheat, and barley can now find direct application in rice improvement. These studies are much more advanced for cereals than for roots/tubers, and legumes. This reflects the large public

and private sector investments in the rice genome project, coordinated by Japan. This has recently been strengthened by the decision of Monsanto to donate its knowledge on the rice genome to the public sector effort. Other investments on the maize and wheat genomes in Europe and North America are making rapid progress.

The opportunities to apply comparative genetics now are furthest advanced in the cereals in which considerable research investment has already been made.

Investment in other agriculturally important species, especially for tropical crops such as cassava, banana, and food legumes, is limited. Without significant investment in the immediate future, the research gap between the CGIAR centers, national research institutes, and advanced laboratories already heavily involved in comparative genetics will widen. Collaboration with advanced laboratories is essential to exploit fully the potential of comparative genetics on all the agriculturally important species.

## **Bioinformatics**

The CGIAR centers have gathered a huge resource of phenotypic data through the germplasm collections and the crop improvement and international testing programs conducted over the past 30 years. Research in molecular biology, genome sequencing, functional genomics, and comparative genetics are producing large amounts of new genomic data. Bioinformatics is essential for the management, integration, and analysis of phenotypic and genomic data if the promise of molecular biology for genetic improvement is to be realized.

New discoveries in comparative genetics indicate a high degree of conservation of genetic material across the genomes of many species. This applies in terms of gene order and gene structure and has important implications for the ability to translate findings in molecular biology in one species to others. This process will not be possible unless the bioinformatics tools are also compatible across species.

Numerous research projects worldwide are collecting genomic data. These are often made available for bioinformatic analysis in public databases. The task of linking these data resources, integrating the CGIAR's own contributions, and analyzing the products is too great for any one CGIAR center to handle. People with skill and experience in this new and rapidly changing field are rare and dispersed.

The CGIAR centers have a unique role to play in the design and deployment of a bioinformatics system for use by the international centers and their collaborators. CGIAR centers need to work together and with advanced research institutes and NARS partners to develop, deploy, and extend an integrated bioinformatics system for the major food crops. This will require new investments, new skills, and innovative organizational arrangements that cut across traditional commodity, discipline, and Center responsibilities.

## **Livestock Improvement**

### ***Constraints to Livestock Productivity***

Three groups of technical constraints need to be overcome to improve livestock productivity in the developing world. These relate to improvements in genetic potential,

health, and management practices, including nutrition. In some cases these constraints are specific to tropical and subtropical environments, such as specific diseases and stresses. In others, the constraints are shared by industrial and developing countries.

Infectious diseases of livestock not present in the industrial countries, and for which there are as yet no sustainable means of control, present a formidable barrier to increasing the efficiency of livestock productivity in developing countries.

*Disease is one of the major factors contributing to poor productivity of livestock in developing countries. In sub-Saharan Africa, animal losses due to disease are estimated to be US\$4 billion annually, approximately a quarter of the total value of livestock production.*

Tsetse fly-transmitted trypanosomosis and tick-borne diseases are the most important disease problems in developing countries. Therapeutic agents are available for some of these diseases, but problems remain. Chemotherapy, based on the use of trypanocides, has problems due to toxicity, residues in milk and meat, and the excretion of large quantities in feces that are then applied to crops. Some of the trypanocides are potential carcinogens and would not be licensed for use in industrial countries. Intensive application is creating drug-resistant organisms.

Current drugs have been in use for over 30 years. The problem of drug resistance is becoming acute in some regions, and the likelihood that new drugs will be developed is low due to development costs and lack of return on investment. Vaccination offers a potentially more effective and sus-

tainable method of disease control (Morrison 1999), but technical challenges remain to be resolved.

There has been limited success in exploiting the genetic potential of indigenous livestock breeds to resist disease and environmental stresses and to better utilize the available natural feed resources. Further improvements in livestock genotypes now need to relate more to the quality of the final product and the efficiency of its production rather than simple increases in quantity. Improvements in animal health are moving from interventions at the level of the individual animal to interventions at the herd and flock health level, with a focus on prevention rather than treatment and subclinical rather than clinical disease. Vaccines play an important role in disease management by developing herd immunity to target diseases

### **Applications**

The main applications of new biotechnologies to livestock are in the areas of genetic improvement, reproductive technologies, and animal health. These new technologies speed up the reproductive process in animals and enable the more efficient selection of breeds with improved productivity. Animal genome projects are also shortening the gene discovery process and demonstrating many potential applications where the manipulation of the genome may be useful in livestock improvement.

The fundamental differences in reproduction between plants and animals are reflected in the significant differences in the costs and efficiency of effecting production increases through breeding programs. These differences favor investments in crop rather than livestock breeding and

for short-term rather than long-term returns.

Phenotypes of commercial livestock breeds that are highly productive in temperate climates and intensive production systems do not realize their production potential in subtropical/tropical production systems. This is due to a number of factors including dietary constraints, adaptability to local environmental conditions, and susceptibility to disease.

National structures in developing countries, whether public or private, have often been unsuccessful in commercially exploiting the production capacities of indigenous livestock, which are adapted to the local environment and diseases, by selective breeding or some form of cross-breeding with exotic genotypes. This has been due to the need for long-term investment in such breed improvement programs and their complexity of management, especially when only small numbers of livestock are present on individual farms. Performance recording schemes are difficult to initiate and maintain, making breeding, selection, and expansion of improved livestock an expensive and inefficient process (Doyle 1993).

### ***Molecular Breeding***

Advances have been made in overcoming the genotypic constraints to increased production efficiency. Improvements have been made both in genetic characterization at the molecular level, and in technology to expand rapidly the available numbers of improved genotypes. In molecular characterization, linkage maps of sufficient resolution for use in breeding improvement schemes based on marker-assisted selection are now available for cattle, pigs, poultry, and fish. These maps are being refined, and the process of identi-

fying molecular markers with desirable biological and commercial traits is under way. The applications of these technologies to fish are illustrated in Box 6.

Another example of the use of molecular markers has been in tracing the origins of different cattle breeds. Genomes contain the history of the origin and evolution of the different cattle breeds and modern molecular techniques have been used to rapidly decipher their story (Bradley and others 1996; Hanotte and others 2000).

The physical location of individual genes on chromosome maps is also well advanced. The rapid development of both linkage and physical maps of the genomes of domestic livestock is a clear example of how the large investment in basic biology (the construction of genetic maps of mouse and humans) can effectively and economically be captured to the benefit of domestic livestock improvement.

The International Livestock Research Institute (and previously the International Laboratory for Research on Animal Diseases) has been involved for the past decade in a worldwide collaborative effort to create and improve the genetic maps of the bovine genome and to identify markers associated with genetic resistance to trypanosomiasis. The use of such maps will significantly reduce the generation time for developing improved breeds, as compared to conventional breeding procedures based solely on phenotype selection. The determination of genetic distances, together with genetic maps, also will increase the effectiveness of measures for conservation of endangered livestock species by allowing characterization at the genetic rather than phenotypic level.

The application of comparative genomics between breeds and species may mean that such selection strategies in one

### **Box 6 Applications of biotechnology in fisheries and aquaculture**

There is growing importance of molecular markers for biodiversity research, genome mapping, and trait selection in fish and other aquatic organisms. International groups are already collaborating on developing genetic maps of tilapia, common carp, salmonids, catfish, zebrafish, and pufferfish. Maps for commercially important invertebrate species including shrimp and oysters are being initiated.

The feasibility of developing and using transgenic species of fish is being explored by several research institutes and companies in the fisheries and aquaculture sectors on various species including tilapia and salmon. It is anticipated that there will be an increase in the number of species and strains into which genes are introgressed, and the number of gene constructs available for transgenesis (governing biological functions in addition to growth) will also be increased. Transgenesis may become a cost-effective means of enhancing indigenous species important to one or a few countries and not covered by international breeding efforts.

Sex manipulation (for example the production of all male populations of fish, especially tilapia) is also an active area of research, designed to avoid the detrimental production effects of early maturation and cessation of growth. In carp species, however, all-female populations are required. It is also anticipated that sex reversal will be used more widely in breeding programs to increase the speed of production of inbred lines. Haploid fish will be important for similar reasons.

A wide range of new molecular diagnostic techniques is being developed for applications such as disease diagnosis, sexing of juvenile fish, and for assessing progeny relationships in large populations of fish raised together to reduce environment-specific variations in production. Other techniques include tissue culture, or other manipulations of embryos or embryonic cells, for the isolation of viruses, bacteria, and fungi pathogenic to fish.

*Source:* International Center for Living Aquatic Resources Management.

species/breed may be more easily adapted to that of other species/breeds, when looking for similar traits. However, because of the high cost, genomics technology is presently being applied more to the lucrative markets, breeds, species, and production environments of the industrial world than to the needs of livestock improvement in the developing countries.

*The concerted application of modern breeding strategies for livestock of relevance to smallholder production in developing countries is unlikely to occur in the absence of major public sector initiatives.*

This is because of present lack of funding, the low commercial value of the breeds, lack of effective conventional breeding programs in developing countries, and the requirements to conduct selection in the relevant production environments due to high genotype x environment effects in animal breeding.

The applications of biotechnology to fisheries and aquaculture offer the prospect of increasing the efficiency of protein production, and the speed of conversion of feed to protein. They may also enable economically efficient protein production in enclosed aquaculture, and reduce problems of effluent disposal (see Box 6 for applications).

### ***Transgenic Livestock***

Technology exists for the creation of transgenic livestock including mammals, birds, and fish. Practical applications of the technology are presently restricted to production of human biological pharmaceuticals in the milk of sheep. Small herds of transgenic animals are likely to be able to produce sufficient quantities of high-value biological products, such as pharmaceuticals, in the immediate future. There has also been work on the creation of transgenic lines of virus-resistant poultry, which contain a modified virus gene that confers disease resistance. A similar strategy has proved useful to introduce virus resistance in plants.

In the future, transgenic pigs may be used as a source of tissue and organ transplants to humans, provided safety and ethical concerns are met. The major health issue for review and research at present is the possible trans-species movement of viruses from pig tissue to humans.

The impact of transgenic animals on animal breeding and production is presently limited by the dearth of single gene traits in livestock, and the fact that the propagation process of a transgene in an animal population is relatively slow (Cunningham 1999). There is also a risk that the desired gene may not be inherited by subsequent generations or may be turned off in the offspring from a transgenic animal.

If desired genes controlling a trait can be identified and transferred, their expression physiologically controlled and the trait is heritable, then a quantum leap in improvements in livestock productivity can be envisaged.

### ***Livestock Genetic Resources***

There is potential to find genes for disease tolerance and other adaptive traits such as heat tolerance in wildlife and transferring these to domestic livestock. In disease resistance, for example, this would have greater impact in developing than in industrial countries.

There are possible opportunities for the developing countries, through the analysis of the genomes of their unique animal genetic resources, to identify genes encoding traits that may be of benefit to both developing and industrial countries. Although the animal genetic resources in developing countries are plentiful, they have not been tapped to any great extent. The characterization of these genetic resources may offer opportunities for developing countries to benefit from their appropriate use and agreed benefit sharing (FAO 1999).

### ***Diagnostics and Therapeutics***

Molecular technologies are also applicable to the study of livestock parasites and other pathogens. They provide effective means for identifying, isolating, characterizing, and producing molecules that can be used to induce protective responses against the parasite (Morrison 1999). The new technologies can also be used to generate products and gene sequences, which can form the basis of improved diagnostics. They also provide effective means of elucidating the metabolic pathways of pathogens that confer drug resistance or drug sensitivity on these organisms. Genetic markers are increasingly being used to identify with

greater precision the species, subspecies, and types of pathogenic agents. Recombinant or genetically modified pathogens also offer new approaches to vaccine delivery, as does direct injection of DNA into animals.

Disease, however, is the result of the interactions of two genomes - the pathogen and the host. To exploit the new technologies, particularly for the development of vaccines and for the exploitation of disease resistance traits, it is important to understand the biology of the pathogen as well as the host.

### ***Vaccine Development***

The use of vaccines in disease control has the advantage of using an already existing domestic animal gene pool. From a management/breeding point of view this is logistically easier to consider as a disease control strategy than using marker- or gene-assisted selection to breed disease-resistant strains of improved domestic animals. Vaccines developed using traditional approaches have had a major impact on the control of the epidemic viral diseases of livestock, such as foot-and-mouth disease and rinderpest. There are many other important diseases, notably parasitic diseases, for which vaccines have not been developed successfully.

Rapid advances in biotechnology and immunology over the last two decades have created new opportunities to develop vaccines for parasitic diseases. Initial optimism in the early 1980s that vaccine products would quickly emerge from applications of recombinant DNA technology has not been fully realized. Subsequent experience has demonstrated that, unlike traditional approaches to vaccine development, effective

exploitation of recombinant DNA technology requires knowledge of the target pathogens and the immune responses they induce, as well as an understanding of how those immune responses can be manipulated. Such information was lacking in the early 1980s. There has been a series of fundamental discoveries in immunology that have led to a detailed understanding of how the immune system processes and recognizes pathogenic organisms, and the different ways that infections are controlled by immune responses. This new knowledge is directly relevant to all stages of vaccine development, from identification of the genes or proteins that need to be incorporated into a vaccine, to the design of a vaccine delivery system that will induce a particular type of immune response. These advances, coupled with further developments in the application of DNA technology, now provide a strong conceptual framework for the rational development of new vaccines (Morrison 1999).

Two main approaches are being pursued to develop vaccines using recombinant DNA technology. The first of these involves the deletion of genes that are known to determine virulence of the pathogen, thus producing attenuated organisms (nonpathogens) that can be used as a live vaccine. This strategy is presently more appropriate for viral and bacterial diseases than for protozoan parasites. Attenuated live vaccines have been developed for the herpes viruses that cause pseudorabies in pigs and infectious bovine rhinotracheitis in cattle.

The second strategy is to identify protein subunits of pathogens that can stimulate immunity. This is the preferred approach to many of the more complex pathogens. It requires knowledge of the

immune responses that mediate immunity, which helps identify the relevant target proteins. The strategy can be illustrated by the approach taken by the International Livestock Research Institute to develop a vaccine against *Theileria parva*, the parasite that causes East Coast Fever of cattle in sub-Saharan Africa. Studies of immune responses to the parasite have revealed antibody responses to the tick-derived infective stage of the parasite, as well as cell-mediated immune responses against the parasite stages that reside within cattle cells. A parasite protein recognized by the antibody response and the corresponding parasite gene (p67) have been identified. Protein expressed from this gene, when used to vaccinate cattle under experimental conditions, has been shown to protect a proportion of animals against the disease. Identification of the parasite proteins recognized by the cell-mediated immune responses presents a greater challenge, but a number of recently developed methodologies for this purpose are now being applied to the problem (McKeever and Morrison 1998). As part of its strategy for the development of a vaccine against East Coast Fever, the International Livestock Research Institute is collaborating with The Institute for Genomic Research to map the genome of *T. parva* (Nene and others 2000) (see Box 4).

### ***New Vaccine Delivery Systems***

Live attenuated vaccines stimulate immune responses similar to those induced by the parent pathogen, and usually provide long-lasting immunity. Vaccines using killed organisms require incorporation of adjuvants (agents that enhance immunity-giving characteristics), and the immune

responses they induce are usually more limited and of shorter duration than with live vaccines. Advances in biotechnology have provided a number of alternative vaccine delivery systems for subunit proteins that overcome these shortcomings and offer some of the advantages provided by live vaccines. Two of the most promising approaches are the use of attenuated organisms as live vectors and vaccination with DNA (Morrison 1999).

Live-vectored vaccines involve the incorporation of a gene encoding a subunit protein into the genome of an attenuated organism, which itself may be in use as an attenuated vaccine. The protein is then produced when the organism replicates in the animal.

*A vaccine containing a rabies virus gene has been used to protect foxes against rabies and its use has resulted in the eradication of rabies from northern continental Europe.*

The use of DNA for vaccination is based on the discovery that injection of genes in the form of plasmid DNA can stimulate immune responses to the respective gene products. This occurs as a result of the genes being taken up and expressed by cells in the animal following injection. Stimulation of immune responses and partial protection have been reported for a number of pathogen genes in livestock species, but none of these has yet led to a fully effective vaccine. The live vector and DNA vaccination systems are amenable to further manipulation to enhance the immunity-conferring characteristics of the gene products. Experimental studies have demonstrated that these systems have enor-

mous potential for development of vaccines that induce appropriate and enduring immune responses.

New vaccines are likely to be produced against some or all of the major animal diseases, given the necessary scientific and financial resources. The complexity of the problems that are being addressed should not be underestimated. The opportunities presented by advances in biotechnology can only be exploited effectively if there is a thorough understanding of the biology of the target pathogens and the diseases they produce. The new technologies allow detailed studies on the two interacting genomes, the pathogen and the host, the

identification of genes essential for causing infection and disease and thus the identification of targets for vaccine development.

Vaccine development for domestic livestock could benefit from technology spillovers from vaccine development for humans because the same research concepts and approaches can be applied, albeit to different pathogens. Public-private sector cooperation emerging in the eradication of polio, and in the search for a malaria vaccine, may yield innovative research cooperation models and knowledge that could be applied to vaccine development and delivery for the benefit of smallholder livestock producers in the developing world.

## Part 4 The Way Ahead

The Human Genome Project is providing a major impetus to understanding the genetic basis of life. It is, for example, resulting in the early identification of predisposition to genetic diseases, such as cystic fibrosis and breast cancer, leading to earlier detection and better treatments. The applications of modern science are strongest in health care where they offer new hope to patients with AIDS, genetically inherited diseases, diabetes, influenza, and some forms of cancer. Biotechnology-based processes are now used routinely in the production of many new medicines, diagnostics, and medical therapies.

These new developments are underpinning important new international health initiatives, such as the the children's vaccine initiative. This will be the basis of further international health initiatives as new order vaccines and therapeutics are developed. The important initiatives in the health sector, such as the "Roll Back Malaria Campaign," are being sponsored by the World Health Organization, the World Bank, and private foundations. These initiatives are mobilizing expertise and financial resources of governments, international agencies, private foundations, and the pharmaceutical industry. They are expected to lead to major improvements in human health over the next decades.

Modern science offers the potential for similar major contributions to improving food security and nutrition of the poor. However, the large private sector investments in modern bioscience are directed

at traits of interest to producers and consumers in industrial countries. The current debate over the value of these new products is also largely dominated by the perspectives of civil society in industrial countries. The potential value of modern science in producing food for the poor will not be realized without major additional efforts involving all stakeholders, including civil society, small-scale farmers, urban consumers, and governments in developing countries.

*The need to produce sufficient food for the world's population is urgent, compelling, and complementary to improving human health.*

About 73 million people will be added to the world's population every year from now until 2020. Much of this population growth will occur in the cities of the developing world. Meeting world food needs requires increases in production and productivity, and matching these to dietary changes, including the rapidly increasing demands for livestock and fish as sources of protein. Demand for meat in the developing world is projected to double between 1995 and 2020.

World grain production will need to increase by 40 percent by 2020, while the increases in crop yields have been plateauing. Neither meat nor cereals production in the developing world is keeping pace with demand, and imports are increasing (Pinstrup-Andersen, Pandya-Lorch, and Rosegrant 1999).

Under this scenario, food insecurity and malnutrition will persist to 2020 and beyond. The International Food Policy Research Institute predicts that, without significant new developments in increasing productivity, 135 million children under 5 years of age will be malnourished in 2020, a decrease of only 15 percent on 1995. Approximately 77 percent of these children will live in Africa and South Asia.

The most promising approaches to increasing productivity on small-scale farms are agro-ecological approaches, albeit recognizing the potential role of modern biotechnology, and the use of modern information technology and precision farming. It will require the successful integration of these three approaches to achieve the full potential of modern science and ensure the necessary increases in production while conserving the natural resource base.

The initial applications of modern biotechnology to commercial agriculture have resulted in new genetically improved varieties of maize, cotton, rapeseed, soybean, and potato. These were grown on 40 million hectares worldwide in 1999, increasing from 1.5 million hectares in 1996. Fifteen percent of the area is in emerging economies of Argentina, China, Mexico and South Africa. There are also applications to livestock and fish, largely related to the production of more productive strains of commercially important species and the development of useful diagnostics and vaccines.

Several emerging economies are making major investments of human and financial resources in biotechnology with the aim of using these new developments in science to improve food security and reduce poverty. They include Argentina, Brazil, Mexico, China, India, Thailand,

Kenya, and South Africa, amongst others (Persley and Lantin 2000).

However, the major research and development efforts of the private sector in biotechnology have been directed at opportunities for introducing traits useful to producers and consumers in the markets in industrial countries. This is where bioscience companies hope to recoup their investments. Initial research and development has concentrated on production traits such as insect resistance. More recent emphasis is on products with improved nutritional qualities.

It is the responsibility of civil society and governments, at the national and international level, to ensure that developing countries consider the benefits and risks of the use of modern science. All stakeholders need to assess the potential benefits and risks of new technologies to reduce food insecurity and poverty. This will require communicating about the role of science in development. It will require also mobilizing the expertise and resources of both the public and private sector nationally and internationally to address the specific problems that damage human health, constrain agricultural productivity and threaten the environment. New approaches that mobilize both public and private resources and involve nongovernmental bodies are needed if poor people are not to be bypassed by the revolutions in science and information technology.

This strategy of using modern science as a component of the overall policy to foster sustainable economic development, reduce inequities, and improve the livelihoods and well being of the poor, will require good governance and political skills and leadership of a high order, and new policies and actions by governments (Persley 1999; [www.ifpri.org](http://www.ifpri.org)).

## Food for the Poor

To achieve the required productivity increases in crop and livestock production to keep pace with population growth, there is a need for a major global effort on *Food for the Poor*. Its purpose would be:

*To mobilize the new developments in science and technology to increase the productivity of the world's twelve major food crops, five species of livestock, and fish, that provide 95 percent of the food in the developing world.*

Several actions are urgently required to accomplish this, the most important of which are:

1. *Plant and Animal Genomes*: Ensure that the descriptions of genomes of the agriculturally important species are mapped and that this information is put in the public domain, able to be used by scientists worldwide to generate improved crop varieties and livestock breeds adapted to local ecosystems, and useful biological products. The species are: banana, cassava, maize (corn), groundnut, millets, oil crops, potato, rice, sorghum, soybean, sweet potato, wheat; cattle, sheep, goats, pigs, chickens; and fish species.

2. *Identify Traits for the Poor*: Identify the genes conferring traits that are important to poor producers in marginal environments. It is likely that research will show that some of these are governed by genes that are conserved (shared) across species (for example drought tolerance in cereals). This knowledge would greatly accelerate breeding for these difficult traits,

increase the productivity of major food crops and livestock in the tropics, and enhance their ability to be more productive in difficult environments.

3. *Conserve and Characterize Genetic Resources*: Maintain and characterize the farm animal and plant genetic resources of the world's major agricultural species. The largest in vitro collections of plant genetic resources are held in trust for the international community by the CGIAR centers. A recent review commissioned by the CGIAR Technical Advisory Committee suggests that it will require US\$70 million to upgrade the present plant collections, and thereafter US\$8 million per year to maintain them. Additional investments are required to collect, characterize, and conserve farm animal genetic resources (see FAO 1999). The in vitro and in vivo collections of plant and animal genetic resources, and the biological information pertaining to them, are a vast but underutilized resource for genetic studies and the identification of useful traits.

4. *Access Enabling Technologies*: Obtaining access to key enabling technologies in agricultural biotechnology, many of which are proprietary technologies held by the private sector, is key to the successful applications of biotechnology in the developing world. It will enable the characterization and application of useful genetic information for crop and livestock improvement and the control of the pests, parasites, and pathogens that affect them. The economic concentration of agricultural biotechnology is a real issue that affects the potential beneficial use of new biotechnologies on the problems of poor farmers and consumers in developing countries.

5. *Establish Alliances of the Caring:* A concerted international effort is needed to establish a new compact between the public and private sectors of the industrial and developing countries, so that the new developments in genetics and biotechnology are able to be used more effectively to increase agricultural productivity in a sustainable way. This could, for example, involve a Food for the Poor initiative, whereby a trust fund is created with public and private donations, to conserve and characterize phenotypically and genetically the genetic resources of the world's major agriculture species in perpetuity.

New and nontraditional partnerships amongst public and private sector organizations are needed to make best use of all available resources involving farmers' associations, nongovernmental organizations, governments, and private sector organizations. Some alliances could be formalized into specific research consortia that address specific constraints and are financed to achieve agreed outputs.

6. *Increase Investments in Agriculture:* Significant additional investments by the public and the private sectors are required if agricultural productivity is to increase in the developing world in an environmentally sustainable way.

7. *Provide Incentives for Private Sector Participation:* Incentives are needed to encourage the national and international private sector to address the problems of agriculture in developing countries. These incentives may include improving the enabling environment for agribusiness in developing countries, providing financial incentives for research and development on orphan commodities, and incentives for entrepreneurs to establish bio-based

businesses in developing countries, as a source of technology, job creation, and wealth.

8. *Mobilize the Global Scientific Community to Address the Problems of Food for the Poor:* The CGIAR centers presently spend about US\$25–35 million each year on agricultural biotechnology, out of a total budget for all the CGIAR centers of US\$340 million. These investments are impressive but insufficient by themselves. The CGIAR centers are also the custodians of the world's largest in vitro collections of plant genetic resources. The CGIAR centers and the national agricultural research systems are the repository of a vast array of knowledge of the biology of the world's major food crops, livestock, fish, and tree species, and their associated pests and pathogens. The CGIAR centers operate long-standing crop improvement programs and international testing programs, located throughout the world's major ecosystems. In combination, these scientific, biological, and financial resources are a powerful platform. However, the agricultural research efforts in the developing world now need to be mobilized with the global scientific community in new and imaginative ways, if a quantum leap is to be made in producing food for the poor by 2020.

It is here that the newly created Global Forum for Agricultural Research must be seen as an important new vector for bringing about the necessary collaboration amongst farmers, producer and consumer organizations, public and private companies, nongovernmental organizations, national agricultural research systems, advanced research organizations and international agricultural research institutes, including the CGIAR centers.

9. *Identify Desired Outputs:* Innovations that will be required to contribute to improved food security and to create wealth in the poorer regions of the world include:

- Improved genotypes and better agricultural practices to ensure sustainable increases in productivity of the world's agriculturally important commodities.
- New biological products, such as vaccines, biocontrol agents, and diagnostics, for the control of major endemic diseases of crops and livestock. Illustrative priority species, constraints, and targets on which additional research is urgently needed are shown in Box 7.

Development of these outputs will require marshalling and directing financial and scientific resources in new ways, both nationally and internationally. This will have profound implications for the CGIAR if it is to recognize and respond to these challenges with the appropriate strategy and tactics. Note, however, that whatever research and development work is being advocated on the genetic side must be seen, along with other crop, livestock and fish productivity work, within the context of improved agroecological, socioeconomic and gender-sensitive approaches.

10. *Challenge to the CGIAR:* The CGIAR has a challenge to invest in and mobilize the necessary human, financial, and bio-

**Box 7 Illustrative examples of some priority constraints able to be addressed through biotechnology**

| <i>Commodity</i> | <i>Constraint</i>          | <i>Regions</i>    |
|------------------|----------------------------|-------------------|
| <b>Crops</b>     |                            |                   |
| Banana/plantain  | Black Sigatoka disease     | Global            |
| Cassava          | Cassava mosaic virus       | Africa            |
| Maize            | Apomixis (all cereals)     | Global            |
|                  | Quality protein maize      |                   |
|                  | Drought                    | 1                 |
| Millets          | Blast resistance           | Africa/South Asia |
|                  | Photoperiod response       | Global            |
| Sorghum          | Drought, heat tolerance    | Africa/South Asia |
| Rice             | Blast, submergence         | Global            |
|                  | Vitamin A content          |                   |
|                  | Yield potential            |                   |
| Wheat            | Heat tolerance             | Africa/Asia       |
|                  | Drought/salinity tolerance |                   |
| <b>Livestock</b> |                            |                   |
| Cattle           | Trypanosomosis             | Global            |
|                  | East coast fever           | Africa            |
| Sheep            | Heat tolerance, helminths  | Global            |
| Goats            | Helminths                  | Global            |
| Chicken          | Newcastle virus            | Global            |
| Pigs             | Viral diseases             | Global            |

logical resources to address the production and sustainability problems of agriculture in new and exciting ways. This will require the CGIAR to:

- Invest more, and with a greater sense of urgency, in science to solve problems, marshalling the new in-depth understanding of the agroecological issues with the new opportunities of modern genetics and biotechnology
- Build on traditional strengths in breeding, biology, and genetic resources
- Analyze, interpret, and make more accessible its wealth of biological data, using new tools in biotechnology and information technology
- Access new skills in the global scientific community to achieve new goals
- Form new strategic (in addition to project-specific) alliances to achieve common objectives
- Create more flexible and innovative institutional arrangements that cut across traditional Center boundaries
- Provide financial incentives for innovation and reward success.

## Epilogue

Prometheus changed the world forever when he unleashed the forces of innovation and creativity. The Promethean scholars of today seek to use the new discoveries in molecular biology and genetics to understand and protect the natural world and to improve the productivity of agricultural systems. These developments are being driven by the scientific and industrial wealth of the industrial world. It is here

that the early benefits of biotechnology are accruing. It is also where the debate as to the wisdom of using modern biotechnology at all is fiercest.

Modern biotechnology offers promise to increase the productivity of the agriculturally important species in developing countries. However this is unlikely to happen in time if present trends continue. The development of relevant and appropriately fine-tuned applications in developing countries will be hampered by a lack of access to the necessary scientific and financial resources. This means that the potential of the human and natural resources of the developing countries will not be fully realized and the world will be a poorer place.

The present economic concentration of investment, science, and infrastructure in industrial countries and the lack of access to the resulting technologies are major impediments to the successful applications of modern biotechnology to the global problems of the Age, namely the need to guarantee food security to all people and to create wealth for the presently poor people and countries.

Creativity in finding solutions to these policy and institutional impediments to innovation are as important and challenging as new scientific discoveries, if the promises of Promethean science are to be realized. Even more, the ability to link the findings and techniques of the new biological and genetic sciences within a framework that respects the agro-ecology of smallholder farming systems, and integrating all of that with the wisdom of the farmers themselves is the key to where a better future for all lies.

# Glossary of Terms

*Apomixis*: reproduction (e.g. parthenogenesis) involving specialized generative tissues but not dependent on fertilization.

*Bioinformatics*: the assembly of data from genomic analysis into accessible forms. It involves the application of information technology to analyze and manage large data sets resulting from gene sequencing or related techniques.

*Diagnostics*: more accurate and quicker identification of pathogens using new diagnostics based on molecular characterization of the pathogens.

*Functional genomics* is the knowledge that converts the molecular information represented by DNA into an understanding of gene functions and effects: how and why genes behave in certain species and under specific conditions. To address gene function and expression specifically, the recovery and identification of mutant and over-expressed phenotypes can be employed. Functional genomics also entails research on the protein function (proteomics) or, even more broadly, the whole metabolism (metabolomics) of an organism.

*Gene chips* (also called DNA chips) or microarrays. Identified expressed gene sequences of an organism can, as expressed sequence tags or synthesized oligonucleotides, be placed on a ma-

trix. This matrix can be a solid support such as glass. If a sample containing DNA or RNA is added, those molecules that are complementary in sequence will hybridize. By making the added molecules fluorescent, it is possible to detect whether the sample contains DNA or RNA of the respective genetic sequence initially mounted on the matrix.

*Genomics*: the molecular characterization of all the genes in a species.

*High throughput* (HTP) screening makes use of techniques that allow for a fast and simple test on the presence or absence of a desirable structure, such as a specific DNA sequence and the expression patterns of genes in response to different stimuli. HTP screening often uses DNA chips or microarrays and automated data processing for large-scale screening, for example to identify new targets for drug development.

*Insertion mutants* are mutants of genes that are obtained by inserting DNA, for instance through mobile DNA sequences, transposons. In plant research, the capacity of the bacterium *Agrobacterium* to introduce DNA into the plant genome is employed to induce mutants. In both cases, mutations lead to lacking or changing gene functions that are revealed by aberrant phenotypes. In-

sersion mutant isolation, and subsequent identification and analysis are employed in model plants such as *Arabidopsis* and in crop plants such as maize and rice.

*Molecular breeding*: identification and evaluation of useful traits using marker-assisted selection.

*Parthenogenesis*: reproduction by development of an unfertilized (usually female) gamete that occurs especially among lower plants and invertebrate animals.

*Shotgun genome sequencing* is a sequencing strategy for which parts of DNA are randomly sequenced. The sequences obtained have a considerable overlap and by using appropriate computer software it is possible to compare sequences and align them to build larger units of genetic information. This sequencing strategy can be automated

and leads to rapid sequencing information, but it is less precise than a systematic sequencing approach.

*Single nucleotide polymorphisms* (SNPs) are the most common type of genetic variation. SNPs are stable mutations consisting of a change at a single base in a DNA molecule. SNPs can be detected by HTP analyses, for instance with DNA chips, and they are then mapped by DNA sequencing.

*Transformation*: introduction of single genes conferring potentially useful traits.

*Vaccine technology*: using modern immunology to develop recombinant DNA vaccines for improved control of animal and fish disease.

(Source: *Biotechnology and Development Monitor 1999*)

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*We cannot prevent this being a world  
In which children suffer,  
But we can reduce the number  
Of suffering children.*

*If we do not do this,  
Who else in the world will do it!*

*Albert Camus*



## **Background Brief**

# **PROMETHEAN SCIENCE AGRICULTURAL BIOTECHNOLOGY, THE ENVIRONMENT, AND THE POOR**

**P**rometheus, according to Greek mythology, was a Titan, responsible for introducing fire to humans, a remarkable innovation in its time, but having benefits and risks, depending on its use. Promethean has since come to mean *daringly original and creative*.

Today, the Human Genome Project is providing a major impetus to understanding the genetic basis of life. Biotechnology-based processes are now used routinely in the production of most new medicines, diagnostics, and medical therapies that offer hope to people with AIDS, genetically inherited diseases, diabetes, influenza, and cancer. They also underpin new international health efforts, such as the children's vaccine initiative, that are mobilizing expertise and financial resources of governments, several international agencies, private foundations, and the pharmaceutical industry. These are expected to lead to future major improvements in human health worldwide. Modern science offers the potential for similar major contributions to improving food security and nutrition of the poor.

*The need to produce and improve access to sufficient food for the world's population over the next 20 years is as urgent, compelling, and complementary to improving human health.*

About 73 million people will be added to the world's population every year from now until 2020. Meeting the food needs of this growing and increasingly urbanized population requires increases in production and productivity and matching these to dietary changes, including the increasing demand for livestock and fish. World grain production alone will need to increase by 40 percent by 2020. Without new developments in increasing productivity, food insecurity, and malnutrition will persist to 2020 and beyond. There are likely to be 135 million malnourished children in 2020, 77 percent of whom will be living in Africa and South Asia.

The most promising approaches to increasing productivity on small-scale farms are agro-ecological approaches, albeit recognizing the potential role of modern biotechnology, and the use of new information technology and precision farming. It will require the successful integration of all three approaches to achieve the full potential of modern science and ensure the necessary increases in production while conserving the natural resource base.

Large private sector investments in agricultural biotechnology are directed at traits of interest to producers and

consumers in industrial countries. The current debate over the value and safety of these new products is also dominated by the perspectives of civil society in industrial countries. The potential value of modern science to agriculture and the environment in developing countries will not be realised without major additional efforts involving all stakeholders, including civil society, producers, consumers, and governments.

Several emerging economies (including Argentina, Brazil, China, India, Thailand, Kenya, and South Africa, amongst others) are making major investments of human and financial resources in biotechnology with the aim of using these new developments in science to improve food security and reduce poverty.

There is a need for major additional global efforts *to mobilize the new developments in science and technology that, along with better policies, are needed to increase sustainable productivity and improve access to food.*

In terms of the world's agriculturally important species, twelve crops (banana/plantain, cassava, maize, groundnut, oil crops, millets, potato, rice, sorghum, sweet potato, soybean, wheat), five species of livestock (cattle, goats, sheep, pigs, and chickens), and fish species provide approximately 95 percent of the food in the developing world.

### **Several actions are urgently required:**

1. *Plant and Animal Genomes*: Ensure that the descriptions of genomes of the world's agriculturally important species are genetically mapped and that this information is put in the public domain, able to be used widely to generate improved varieties and breeds adapted to local ecosystems, and useful biological products.

2. *Identify Priority Traits*: Identify the genes conferring traits that are important to poor producers in marginal environments. Some, such as drought tolerance in cereals, appear likely to be shared across species. This knowledge would greatly accelerate breeding for these difficult traits and enhance the ability of the target crops to be more productive in difficult environments.

3. *Conserve and Characterize Genetic Resources*: Maintain and characterize the farm animal and plant genetic resources of the world's major agricultural species. A recent

review of the CGIAR's in vitro collections suggests that it will require US\$70 million to upgrade the present plant collections, and thereafter US\$8 million per year to maintain them. According to FAO studies, additional investments are required to collect, characterize, and conserve farm animal genetic resources. The collections of plant and animal genetic resources, and the biological information pertaining to them, are a vast resource for genetic improvement and the identification of useful traits. There is an urgent need to ensure that these collections are financed in a more sustainable way so as to ensure that the genetic resources of the world's major agriculture species are conserved, characterized, and accessible for use, in perpetuity.

4. *Access Enabling Technologies*: Obtaining access to proprietary technologies is key to the successful applications of biotechnology to agriculture in the developing world. This will enable the characterization and application of useful genetic information for crop and livestock improvement and the integrated control of pests, parasites, and pathogens.

5. *Establish Strategic Alliances*: A concerted international effort is needed to establish a new compact between the public and private sectors of the industrial and developing countries, so that the new developments in modern science are able to be used more effectively.

6. *Increase Investments in Agriculture*: Significant additional investments by the public and the private sectors are required if agricultural productivity is to increase in the developing world in an environmentally sustainable way.

7. *Provide Incentives for Private Sector Participation and Partnerships*: Incentives are needed to encourage the private sector to address the problems of agriculture and the environment in developing countries, for mutual benefit.

8. *Mobilize the Global Scientific Community to Address the Problems of Food for the Poor*: The CGIAR centers presently invest US\$25-35m each year on agricultural biotechnology, out of a total CGIAR budget of US\$340 million. The CGIAR centers and the national agricultural research systems are also the repository of a vast array of knowledge of the biology of the world's major food crops, livestock, fish, and tree species and their associated pests and pathogens. International crop improvement programs are located throughout the world's major ecosystems. These scientific, biological, and financial resources are a powerful platform. They now need to be mobilized with the global scientific community in new and imaginative ways, if a quantum leap is to be made in improving agricultural productivity, food access, and livelihoods by 2020. The Global Forum for Agricultural Research may play an important role here.

9. *Identify Desired Outputs*: Innovations that are required to contribute to improved food security and to create wealth

in the poorer regions of the world include: Improved genotypes and better agricultural practices to ensure sustainable increases in productivity; new biological products, such as vaccines, biocontrol agents, and diagnostics for the control of major endemic diseases of crops and livestock.

Achieving these outcomes will require marshalling and directing public and private financial and scientific resources in new ways, both nationally and internationally. Also, R&D advocated in the area of genetic and other productivity improvements must be seen in the context of improved agro-ecological, socio-economic and gender-sensitive approaches.

10. *Challenges to the CGIAR*: The CGIAR must seek to invest in and mobilize the necessary human, financial, and biological resources to address the production, policy, and sustainability challenges. This will require the CGIAR to:

- Identify the researchable constraints
- Invest more and with a greater sense of urgency in science to solve problems, integrating the new understanding of agroecological issues with the new opportunities in genetics and biotechnology
- Build on traditional strengths in breeding, biology, genetic resources, and information management
- Analyze, interpret, and make more accessible the wealth of biological data
- Access new skills to achieve new goals
- Form purposeful strategic and project-specific alliances
- Create more flexible and innovative implementation arrangements that cut across traditional Center and institutional boundaries
- Provide financial incentives for innovation and reward success.

## Epilogue

Prometheus changed the world forever when he unleashed the forces of innovation and creativity. In considering the applications of new developments in science, the challenge is to find ways to maximize the benefits, while also seeking to understand and minimize the risks.

The economic concentration of investment, science, and infrastructure in industrial countries and the lack of access to the resulting technologies are major impediments to the successful applications of modern biotechnology to the needs of global food security and to create wealth for the presently poor people and countries. Creativity in finding solutions to these policy and institutional impediments to innovation are as important and challenging as new scientific discoveries, if the promises of Promethean science are to be realized.