Introduction: promoting global health through biotechnology

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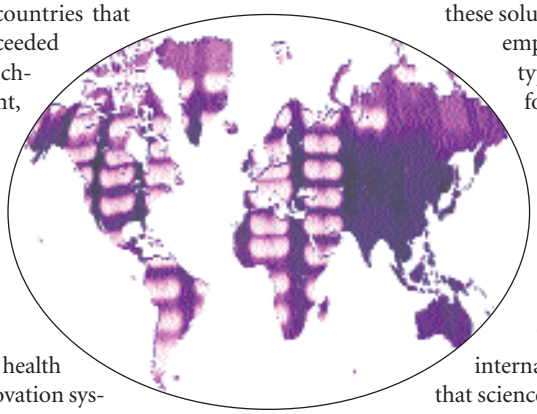
The term 'health biotechnology' evokes images of research-intensive universities such as Stanford University and the Massachusetts Institute of Technology (MIT), as well as initial public offerings on NASDAQ. Typically, we don't think about biotechnology in connection with health solutions for poor people in developing countries. Still, as has been demonstrated in a technology foresight exercise, biotechnology can potentially be applied to a wide spectrum of health problems all over the world[1]. Successful research and development in health biotechnology is taking place in several countries that typically are classified as lower income countries or developing countries. With a view to understanding these successes and reproducing them more widely in the developing world, we have undertaken a detailed study of health biotechnology development in seven countries.

This supplement reports the results of a 3-year study of health biotechnology innovation systems in Brazil, China, Cuba, Egypt, India, South Africa and South Korea. When compared with industrially advanced nations, the seven countries in this study are each at a different stage of economic development, but they can generally be considered 'innovating developing countries' (IDCs)[2]. Our objective was to identify and analyze the conditions encouraging successful development of health biotechnologies in developing countries. Ultimately, we want to identify lessons on how these countries have been able to build up capacity in health biotechnology. These lessons can potentially be put to use in other developing countries that so far have not succeeded in promoting biotechnology development, but may also be of relevance to industrially advanced nations.



This introduction addresses why it is important to study health biotechnology innovation systems in developing countries, who will probably be interested in the findings of the study, the conceptual framework of innovation systems used in the study, the study's methods, the outline of the subsequent papers and the expected outcomes. The crux of the issue is the case studies of seven countries that follow. In a final paper, at the end of the supplement, we highlight our main findings, draw comparisons between the country case studies and outline lessons learned.

Why study innovation systems in developing countries?

There are two interrelated reasons for studying health biotechnology innovation systems in developing countries: to identify potential solutions to health problems of developing countries and to explore how developing countries, through their involvement in health biotechnology innovation, can develop these solutions. A systematic empirical study of this type and magnitude, focusing specifically on developing countries, has never before been attempted.

Improving health in developing countries. There is increasing international recognition that science- and technology-intensive solutions to improve the quality of life are not restricted to richer countries, but are required, and can be developed, also by developing countries around the world. This was one of the central themes in both the United Nations (UN) Development Program's (UNDP; New York, NY, USA) Human Development Report 2001 (ref. 3) and a recent report of the InterAcademy Council (Amsterdam)[4]. It has also been expressed in a recent *Nature* feature on the global imbalance in the scientific impact of various countries[5].

Nowhere is the need for science and technology as a tool for development more relevant than in addressing the health needs of the world's poor. The World Health Organization (Geneva, Switzerland) has highlighted the role of genomics for improving

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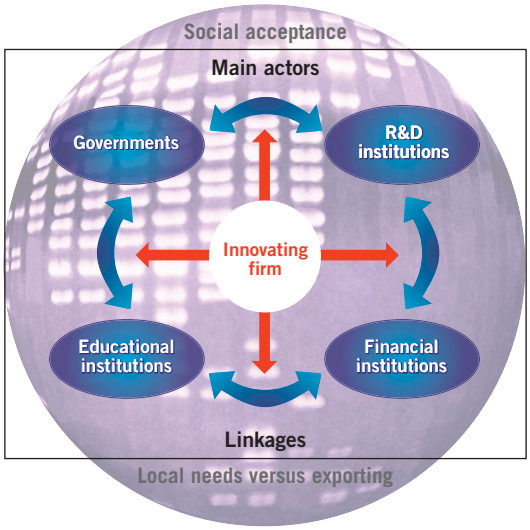

Figure 1 Focus of study on health biotechnology innovation systems in developing countries.

health in developing countries in a recent report[6]. Earlier this year, the UN Millennium Project Task Force on Science, Technology and Innovation outlined approaches for effective application of science, technology and innovation to achieve the Millennium Development Goals[7]. In 2002, an expert panel with intimate knowledge of biotechnology and global health issues identified and prioritized the top ten biotechnologies most likely to improve health in developing countries within 5 to 10 years[1]. In an effort to promote and support these and other scientific and technological innovations for improving health in developing countries, a $200 million research initiative, the Grand Challenges in Global Health[8], was announced in 2003.

Although the focus here is on health biotechnology, we recognize that experiences in agricultural biotechnology research and innovation have important lessons for each other. It is now becoming clear that biotechnology solutions for health problems in developing countries are both appropriate and feasible. For example, recombinant vaccines, one of the top-ranking biotechnologies identified from the top ten list for improving health in developing countries, have reduced the incidence of hepatitis B infections around the world[9].

It is important to acknowledge that biotechnology alone will not solve all the health problems in developing countries; however, it is a key part of the solution. To ensure that such countries benefit from the fruits of this new science, it is necessary that they realize these potentials largely through their own efforts and ingenuity. As we document here, some have already started (see **Box 1**).

Involving developing countries in health biotechnology innovation. There have been limited incentives for firms in industrially advanced countries to focus on the small market potentials in developing countries and to produce health products for people in the poorer parts of the world. Médecins Sans Frontières have estimated that from 1975 to 1999, only 15 new drugs were developed for tropical diseases, while 179 new drugs were developed for cardiovascular diseases in the same period[10]. International efforts, such as public-private partnerships, are being initiated to provide remedies for health problems in developing countries. They include the International AIDS Vaccine Initiative, Medicine for Malaria Venture and the Global Alliance for TB Drug Development.

Although it is still too early to assess the success of these public-private collaborations, they probably cannot completely substitute for local efforts. If biotechnology is to deliver health solutions, developing countries themselves have to be fully involved at every level of the innovation process. If developing countries are active innovators in health biotechnology, there is an increased probability that health solutions will be appropriate to the particular health needs of those countries.

Organizations in developing countries are also likely to develop more affordable solutions to local health problems than are organizations based in richer nations. Many conditions of production are cheaper in developing countries than in developed ones, and for a population with limited purchasing power this can be an incentive to develop more affordable innovations. In fact, so-called diseases of poverty can be viewed as market opportunities for firms in developing countries. A further benefit for encouraging developing countries' participation in the field of health biotechnology is the potential economic impact. Biotechnology, if successful, can become a major income-generating sector for the economy of developing countries. An important indirect benefit is that healthier populations can strengthen the economy of developing countries[11].

Who will be interested in this study?

The results of this study will be useful for a wide range of audiences. Stakeholders include local politicians, international bodies, researchers and entrepreneurs.

Government policymakers in developing nations. We anticipate that our study will be of interest to politicians, particularly in countries at levels of development similar to the ones included in our study. They are some of the people best positioned to implement the appropriate lessons we have identified.

Policymakers at international bodies. International donor organizations and bilateral aid agencies can also benefit from our results. Encouraging health biotechnology development is a promising strategy to promote sustainable development.

Box 1 Developing country presence in the BIO conferences

The participation of developing countries in the annual US Biotechnology Industry Organization (BIO) conferences is increasing at a fast pace. BIO 2001 saw only two exhibitors from developing countries with relatively high income levels, Malaysia and Singapore. At the BIO 2004 annual conference, the presence of developing countries increased markedly to 97 exhibitors from seven nations, including China and India.

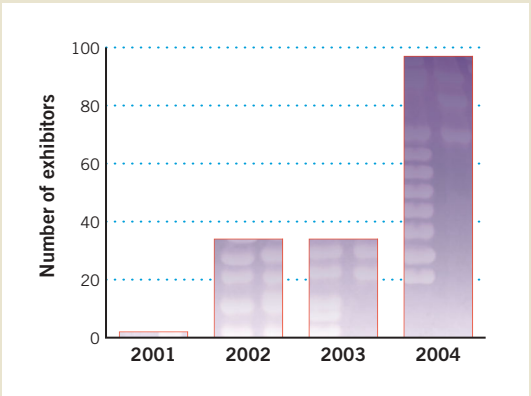

Figure 2 Exhibitors from developing countries at the BIO conferences. Source: Biotechnology Industry Association. http://www.bio.org

Illustrations by R. Henretta

Table 1 Rank of the seven countries studied in the UN Human Development Index

Country	Rank[a]
South Korea	28
Cuba	52
Brazil	72
China	94
South Africa	119
Egypt	120
India	127

[a]Position out of a total of 177 countries. Source: UNDP Human Development Report, 2004.

Researchers. Scientists in both industrially advanced countries and developing countries can realize that many developing countries are active participants in the health biotechnology field. Our study should encourage opportunities for mutually beneficial collaborations.

Entrepreneurs. The results presented here can raise awareness among firms and investors that innovation is possible in developing countries. Entrepreneurs can seize opportunities for strategic alliances and investment opportunities with a range of actors in developing nations. These activities can bring good financial returns, while providing access to much-needed funding and expertise for firms in developing countries.

Innovation systems

Experts who have studied technology innovation and development know it involves a complex set of influences[12]. The typical assumption that basic research is the first stage in the innovation process to produce useful input for technology is a simplification of a much more interactive and dynamic process. It has become clear that a systemic approach is needed to understand these complex influences—and conditions shaping innovation, leading to the development of an innovation systems framework over the past 15 years[13–15]. Innovation systems are made up of institutions that contribute to the creation, diffusion and use of new, economically useful knowledge. They are held together by a web of linkages and synergies. Knowledge creation, diffusion and use are at the core of innovation systems, but the process involves nonlinear, multidirectional knowledge flows among the various actors. The behavior of an innovating agent is influenced by a range of influences and institutions that provide constraints and incentives, including laws, health regulations, cultural norms, social rules and technical standards.

Figure 1 represents a schematic model of the focus of our study. To understand health biotechnology innovation, we have focused on identifying the roles of the main institutions in the innovation process. At the core of these systems are innovative firms, most of them in the private sector. They need to integrate various types of knowledge to be able to develop new health products or innovative processes. We looked at the roles that firms in developing countries play in their health biotechnology sectors, the characteristics of these firms and the main strategies they use. In addition, we have studied the contribution of governments, including their roles in setting up institutions, developing policies that support health biotechnology innovation and providing legal-regulatory frameworks (and intellectual property regulations) that can have considerable influence on sector development. Health biotechnology development is very science intensive, so local research and educational institutions tend to play important roles. Finally, health biotechnology development requires long-term funding, so we have examined the financing of health biotechnology development in the seven countries studied.

> We chose to study seven developing countries that have demonstrated some success in the health biotechnology sector. They are a diverse group, representing various parts of the world, with differences in income levels and size.

We have also analyzed the extent and patterns of linkages among all the actors in the health biotechnology sector. This analysis is extended beyond national boundaries, in that information is collected on the role of international linkages in the development of health biotechnologies in the countries under study. As the debate on agricultural biotechnology has demonstrated, the development of science- and technology-intensive fields is highly dependent on public attitudes, so we have sought information on the social and cultural acceptability of health biotechnology in the relevant countries. We have also sought information on the role of health biotechnology innovation systems in meeting local needs versus developing products for export.

Study methodology

We sought to select a representative set of countries that could provide useful pointers and lessons in developing a health biotechnology sector to other countries in the developing world. Information was gathered from interviews with individuals who were located in, or had particular expertise on, a particular country.

Table 2 Number of interviews for each case country

Country	Number of interviews
Brazil	33
China	22
Cuba	32
Egypt	25
India	38
South Africa	28
South Korea	29
Total	**207**

Choice of countries. We chose to study seven developing countries that have demonstrated some success in the health biotechnology sector. Thus, as a group they can be considered IDCs. They are a diverse group, representing various parts of the world, with differences in income levels and size. One of our choices, South Korea, no longer fits the typical image of a developing country. We included it to show how, in a few decades, a country can go from a development level similar to that of low-income nations to being comparable to wealthier nations of the Organization for Economic Cooperation and Development (OECD, Paris).

Table 1 shows how each of the seven countries selected ranked according to the UNDP's Human Development Index, which measures achievements in three basic dimensions of human development: life expectancy, educational attainment and standard of living. Two of the countries we studied, South Korea and Cuba, fall within the 'high human development' category. The five other countries fall within the 'medium human development' category. Life expectancy at birth in our seven countries ranged from 48.8 years for South Africa to 76.7 years for Cuba. South Africa and India have lower life expectancy than the global average of 64.6 years for developing countries[16].

Study design. We used a case study approach involving formal collaborations with researchers who lived in the subject country or who had intimate knowledge of the country. The Canadian Program on Genomics and Global Health (CPGGH) at the University of Toronto Joint Centre for Bioethics coordinated the project. The research was approved by the Ethics Review

Box 2 Format for presentations of case studies

Each of the seven case studies presented in this supplement addresses four aspects of a country's biotechnology sector. These can be summarized as follows:

- The success of the country's health biotechnology sector
- The main features of the country's health biotechnology sector
- Main challenges for the health biotechnology sector
- Reasons for the success of the health biotechnology sector and lessons learned

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We have broadly defined biotechnology as "the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services."[17] We have limited our study to biotechnologies for human health and did not include those for such fields as agriculture, the environment and industry. For the purpose of this study, we have also included genome-related technologies and tools (for example, bioinformatics and proteomics), as well as the study of and development of products from indigenous plants.

Data collection. The case studies relied on multiple sources, including background documents, interviews, scientometric data and patent information.

The documents we analyzed included a variety of published papers and books on different aspects of the health biotechnology sector, governmental reports and other government documentation (for example, policy briefs and descriptions of the legal and regulatory arrangements), as well as websites of institutions and firms. We developed a template for collecting information from background documents to ensure that similar information would be collected for each country. We collected as much statistical data as possible on various aspects of health biotechnology development but found that several of the countries studied have limited statistics available on technological development. This is common for developing countries.

Interviews with key sources were a central part of the data collection. An interview guide was developed and used in semi-structured face-to-face interviews in all seven countries studied. The key interviewees were current or former employees of the major institutions involved in or supporting health biotechnologies in the countries under study. Interview subjects were chosen on the basis of their expertise in health biotechnology in the subject countries. They came from such organizations as government departments, public and private research institutes, educational institutions, private-sector enterprises, regulatory agencies, intellectual property institutions and nongovernmental organizations (NGOs). They were identified by examining not only background documents describing the health biotechnologies innovation systems in the countries under study, but also information on websites from subject institutions. Recommendations were also sought from people knowledgeable in this field. The first set of participants helped identify additional informants, a technique sometimes called 'snowball' sampling. In **Table 2**, we present the number of interviews carried out in each country.

Information on scientific publications provided additional quantitative data. The firm Science-Metrix (Montréal, PQ, Canada) was contracted to measure the scientific activities in genomics and health biotechnology of the seven countries by examining the publication patterns of scientists from these countries for the period from 1991 to 2002. The analysis is based on the use of the Thomson ISI Science Citation Index Expanded database (SCI Expanded), which includes papers from more than 6,000 journals[18]. The SCI Expanded database probably does not include all the papers published by researchers in the seven countries, because local journals are in many cases not included in the database. The journals covered in the SCI Expanded database are considered the most important peer-reviewed journals in health biotechnology and genomics, and are the most widely cited journals in the world. The scientometric analysis therefore provides analysis of the most influential health biotechnology contributions from the seven countries.

The study also gathered patent data. Using the United States Patent and Trademark Office (Washington, DC, USA) database, we studied the extent of patenting in health biotechnology by inventor in the United States by nationals from the seven case countries. This does not cover all the patenting of the nationals in the countries we have examined, but because of the dominant role of the United States in the field of health biotechnology, these data probably represent these individuals' most significant inventions. By focusing on US patenting, we have also more comparability between the countries than we would have if we had analyzed national patenting in the countries under study.

Data analysis. Using multiple sources of evidence, we mapped the presence and level of activity of the main actors in the innovation systems under study. We triangulated data from different sources to maximize comprehensiveness and diversity. The analysis combined the in-depth qualitative analysis of the interviews with descriptive quantitative indicators gleaned from the documents and from the scientometric and patenting data.

We have validated the findings in three ways. First, we carried out member checks, which entailed approval and verification of the case studies with participants from the interviews.

Second, the research findings were presented at the CPGGH's Genomic Policy Executive Courses[19], including meetings held for the Eastern Mediterranean, Latin America, Caribbean and Indian regions. These courses bring key actors in the science, business, policymaking and NGO communities of a country or region together to exchange diverse views on various topics related to genomics and health. Feedback was sought from the participants.

And finally, the CPGGH held a 2-day workshop from May 31 to June 1, 2004, with the collaborators, researchers and invited external experts to discuss and exchange ideas on the case studies. The external discussants have extensive expertise on this subject, and come from organizations such as the International Development Research Centre (Ottawa, ON, Canada), the UN Conference on Trade and Development (Geneva, Switzerland), the International Development Centre of the Open University (Milton Keynes, UK) and the Program on Globalization and Regional Innovation Systems (Toronto).

Presentation of results

The results for all the country case studies are presented here using a standardized format (see **Box 2**). At the beginning of each paper, we provide an example of a health biotechnology initiative that highlights the innovation potential of each country. We identify the main successes in the health biotechnology sector, describe the main features of their respective health biotechnology sectors and discuss some of the main challenges they face.

Finally, we describe the main lessons learned for each country.

In the last article of the supplement, we draw comparisons among the country case studies and analyze the generally applicable lessons learned. We highlight the lessons that can be applied in developing countries and in some cases they may also be of use for industrially advanced countries.

Expected outcomes

Our intention with this supplement is to encourage both increased dialogue and initiatives that will expand health biotechnology innovation in developing countries, especially those that address the health needs of poor people. This study shows that successes will depend on the commitment from developing countries themselves to promote their health biotechnology innovation systems. There is no single model for health biotechnology development, and not all the lessons identified in one country can be automatically implemented in other countries. Many of the developments we observe in the innovating developing countries are context-specific and not easily replicated. Nevertheless, our study will fill a gap in knowledge on how developing countries may be able to embark on harnessing biotechnology to address health needs and to spur economic development. With increased knowledge, more developing countries have the opportunity to apply their efforts and ingenuity to benefit from the new developments of health biotechnology.

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