mans bound in tight social arrangements, such as communes. These include collaborative efforts, but also cheating; aggregate actions, but also personal opportunism; group alliances, but also conflicts; and parliamentary needs often opposed by egoistic tendencies. However, this metaphor neglects the clonal proliferation of elements possible within a genome, and the extensive reassortment of unlinked sequences that accompanies each generation of sexual reproduction. An Israeli kibbutz might be a closer analog of genomic society in this latter regard, because most marriages are outside the collective. It would be even better if a partially randomized clique of kibbutznikim in each generation married a comparable suite from another conclave to initiate each new commune!

Another metaphor might present each genome as a miniature cellular ecosystem with each gene occupying a particular functional niche, yet in which the DNA sequences have evolved elaborate interactions (including parasitism, commensalism, and mutualism) normally associated with species in natural biological communities. However, this metaphor falls short by failing to ascribe to genes the exceptional collaborative responsibilities also entailed in producing a discrete entity (the organism) whose survival and reproduction is key to the evolutionary game.

The hope for any metaphor in science is that it may bring otherwise unfamiliar subjects to life, make connections not otherwise apparent, and stimulate fruitful inquiry. A danger is that a metaphor can restrict rather than expand research horizons. Many genomic metaphors have elements of truth, and each may have its time and place. I doubt, for example, that a depiction of the genome as a molecular ecosystem would have served well in promoting or guiding the human genome project. However, perhaps the time is right for new panoramic images of the genomic landscape that capture proper notions of complexity and evolutionary dynamism. Although no one metaphor is likely to be informative in all respects, some new perspective that views the genome as an interactive community of evolving loci may be especially useful and stimulating at this time.

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VIEWPOINT

Harnessing Genomics and Biotechnology to Improve Global Health Equity

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With decisive and timely action, genome-related biotechnology can be harnessed to improve global health equity. In June 2002 in Kananaskis, Canada, leaders of the G8 industrial nations will develop an action plan to support implementation of the New African Initiative. By extending their discussion of health issues raised in the New African Initiative to include genomics, G8 leaders could signal their intention to increase global health equity by preventing a health genomics divide from developing. There are already some early and growing examples of genome-related biotechnology being applied successfully to health problems in developing countries. But how can genomics be systematically harnessed to benefit health in developing countries? We propose a five-point strategy, including research, capacity strengthening, consensus building, public engagement, and an investment fund.

It is 2010. The World Bank has just released a depressing report on *The Health Genomics Divide*. The report laments that the promise of genome-related biotechnology in the area of health, heralded a decade earlier by the sequencing of the human genome, has been denied those in the developing world. The unfolding revolution resulted in designer pharmacogenomics in rich countries and lost opportunities for advancing the health of those in Africa, Asia, and Latin America (*1*).

However, this future is not inevitable. Imagine what could happen if political leaders seized the opportunity to put this matter on the agenda of the world community. In June 2002 in Kananaskis, Canada, leaders of the G8 industrial nations will develop an action plan to support implementation of the New African Initiative (*2*). By extending their discussion of health issues raised in the New African Initiative to genomics, G8 leaders could signal their intention to prevent a health genomics divide from developing in the first place. This opportunity was lost in information technology (*3*) and agricultural biotechnology (*4*); it must not be lost in the area of human health.

Life expectancy in many developed countries is 80 years and rising; in some sub-Saharan African countries, mainly as a result of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), it is 40 years and falling. These and many other inequities in global health are major ethical challenges in the world today. With decisive and timely action, genome-related biotechnology can be harnessed to improve global health equity.

There are already some early and growing examples of this biotechnology being applied successfully to health problems in developing countries.

1) Diagnosis of leishmaniasis and dengue fever in some Latin American countries has already been improved by the use of polymerase chain reaction techniques. The pioneering work of Eva Harris of the Sustainable Sciences Institute (San Francisco, California) has documented that when appropriately implemented in Nicaragua, Ecuador, and Guatemala, techniques such as PCR and nonradioactive DNA probes are more rapid, sensitive, specific, versatile, safer, and less costly than prevailing methods for detection of pathogenic organisms (*5*, *6*).

2) Despite its embargo against Cuba, the United States has made a specific exemption and is willing to import the only meningitis B vaccine developed by the Carlos J. Finlay Institute in Cuba (*7*), attesting to the potential of biotechnology in developing countries. This vaccine is being tested in the United Kingdom and has been exported and licensed to at least a dozen other countries (*8*). Biotechnology now ranks third, behind only sugar and tourism, among Cuban industries. Cuba holds over 400 biotechnology patents. Brazil, which has its own rapidly evolving genomics and biotechnology industry, has imported several million doses of the Cuban meningitis vaccine.

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3) Clinical trials have begun in Nairobi and Oxford of an AIDS vaccine candidate designed specifically for use in Africa (*9*). The DNA-based vaccine was developed through productive collaboration between the Universities of Nairobi and Oxford and the International AIDS Vaccine Initiative. The vaccine was derived from the observation that some prostitutes in Nairobi develop strong cellular immune responses and do not develop HIV infection despite repeated exposure.

4) Hepatitis B has infected 2 billion people worldwide and is associated with hepatocellular carcinoma, which is among the top three causes of cancer-related death in men in sub-Saharan Africa, most of Asia, and the Pacific. A promising approach for prevention is to produce hepatitis B surface antigen in transgenic plants for oral immunization (*10*). A human trial of a recombinant hepatitis B vaccine that has been incorporated into potatoes has begun (*11*). Similar vaccines are being developed against cholera, measles, and human papilloma virus (associated with cervical cancer, a common malignancy in women in sub-Saharan Africa). Because they do not require refrigeration, plant-based edible vaccines are cheaper than conventional vaccines and could be grown or freeze-dried and shipped anywhere.

5) In a recent collaborative effort between Indian researchers at the International Centre for Genetic Engineering and Biotechnology in Delhi and the Malaria Vaccine Initiative, a candidate vaccine for *Plasmodium vivax*, the main type of malaria in India, has been identified. The research was partly funded by the Gates Foundation through the Program for Appropriate Technology in Health. The vaccine will be developed by Bharat Biotech International of Hyderabad, India (*12*). India is increasingly investing in genomics and biotechnology: The Indian Department of Biotechnology (*13*) recently announced that it would spend $85 million on genomics over the next 5 years, mainly in medical research, and the renowned Indian Institute of Technology has just established a new School of Bioscience and Bioengineering (*14*).

6) Parasite DNA sequencing, bioinformatics, and data mining have already led to the rapid identification of a class of antimalarial drugs (*15*) that have the potential to be effective against multi-drug–resistant parasites, inexpensive, and stable.

7) Pharmacogenetics may save lives and valuable health care resources in developing countries by identifying populations who will respond favorably to therapeutics; there is preliminary evidence for this in relation to certain anti-HIV drugs in West Africa (*16*). If confirmed, this finding could save money and lives through proper drug selection.

We have often encountered people whose first response to discussing health genomics and biotechnology involves questions about genetically modified organisms, especially their release into the environment. But that is only part of the story. Many of the new technologies with potential to improve health care, such as polymerase chain reaction techniques, microarrays, bioinformatics, pharmacogenomics, functional genomics, and proteomics do not involve genetic modification of organisms.

Gro H. Bruntland, the director general of the World Health Organization (WHO), recognized the huge potential of advances in genomics and other critical areas of biotechnology for improving human health in her opening address to the World Health Assembly in May 2001 (*17*). She has asked WHO's highest scientific body, the Advisory Committee on Health Research, to prepare a Special Report on Genomics and World Health by the end of 2001. This report will highlight the importance of genomics for the health of people in developing countries and prepare WHO to be an advocate for improving the health of the disadvantaged and underprivileged.

The WHO report will also address the challenge of managing the risks of genomics. It builds on an earlier WHO report (*18*), which identified draft guiding principles to help manage these risks. The guiding principles are wide-ranging, covering areas such as public debate, benefit sharing, access and control over specimens and genetic information, discrimination, individual versus group interests, intellectual property, academia-industry research relationships, databases, gene therapy, and cloning.

But how can genomics be systematically harnessed to benefit health in developing countries? Progress will require research to identify the most promising technologies and the barriers to their application. We need to understand, for example, why Cuba, China, and India have such strong biotechnology industries whereas neighboring countries do not. The lessons learned can be applied to build successful genomics and biotechnology industries in developing countries and to change the concept of genomics "for" developing countries to one of genomics "by" developing countries. We need to look at past history in the multinational corporate community to understand how to shape business strategies that reward innovation while making technologies available to developing countries.

Developing countries need to generate their own expertise in addressing the scientific, ethical, legal, social, and policy aspects of genomics and biotechnology (*19*). The formation of science advice capacity in the U.S. Department of State exemplifies the importance that governments are giving science and technology in international diplomacy, provides opportunities for capacity-building regarding science diplomacy in African countries, and offers prospects for improved dialogue between the United States and Africa (*20*). Leadership development programs are needed to create a constituency on genomics policy in developing countries and strengthen the capacity to participate in international negotiations; for example, on trade-related intellectual property rights. Individuals such as those trained through the bioethics program established by the Fogarty International Center of the U.S. National Institutes of Health will be needed to address ethical aspects of genomics research. Building scientific and policy capacity also involves forming productive and mutually enhancing partnerships with centers of excellence wherever these may be; existing centers should be identified and supported and

Fig. 1. Participants at the First Roundtable on Africa, Science, and Technology in the Age of Globalization. The authors are in the back row third from left (Daar) and second from right (Singer), and John Mugabe is in the middle row on the extreme right.

new centers established (*21*).

Building consensus among the public, international organizations, academics, industry, governments, nongovernmental organizations, and the media will be difficult but essential to address different value orientations and develop wise public policy. It is possible that a commission on genomics and global health could serve as a platform to raise awareness, mobilize resources, and bring stakeholders together to focus on their common interest in the health of people in developing countries and close gaps in health equity. Commissions can occasionally be effective. The Commission on Health Research for Development (the Evans Commission) galvanized the health research community (*22*) with the concept of the "10/90 gap": that 90% of research expenditure is dedicated to the health problems of 10% of the world's population. An early consensus-building effort is now underway on a regional basis. On 8 August 2001 in Nairobi, Kenya, the First Roundtable on Africa, Science, and Technology in the Age of Globalization (Fig. 1) resolved to establish a regional process to develop science and technology strategies aimed at closing the digital and genome-related biotechnology gaps with the rest of the world. The Roundtable appointed John Mugabe, Director of the African Centre for Technology Studies, as interim secretary. Participants included 38 leading policy-makers and scientists, including permanent secretaries and directors of science and technology policy bodies, from 11 African countries. This process provides an opportunity to pursue biotechnological advances in the context of the New African Initiative, which is on the G8 agenda next year.

The voices of those in developing countries must be heard as the health biotechnology revolution unfolds. Those protesting in Genoa are not the ones who are sick in Africa. We need to develop a mechanism to tap the views of opinion leaders in developing countries on important policy questions and in real time.

Finally, it will be necessary to create innovative financing mechanisms to channel large investments into promising scientific ideas targeted on health problems of developing countries. One major project established this year by the United Nations, the Global Health Fund, set a goal of raising $7 billion to $10 billion, but only about $1.4 billion had been pledged by early August 2001 (*23*). The fund is an important development, but this result may indicate fatigue on the part of developed-country governments for donations. A possible investment model is the one developed by Globalegacy (*24*), a United Kingdom–based organization working to create long-term social and economic growth through commercial ventures with deprived urban communities. An investment fund based on similar principles but focusing on health genomics and biotechnology in developing countries could channel needed investment to undercapitalized scientific ideas. The business model would optimize health improvement in developing countries but would also provide economic return on investment. If one or more developed-country government invested just 10% of the 0.7% of gross domestic product target for official development assistance to such a fund for only 1 year, and this investment was matched by the private sector, the fund would have sufficient capital to pursue its work.

We will know that these efforts are successful when the G8 take up this challenge in Kananaskis, when we see more examples like the Cuban meningitis vaccine, and when we ultimately see decreased inequities in life expectancy and other indicators of global health equity. Perhaps the best indicator of success will be if there is no World Bank report in 2010 on the health genomics divide!

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VIEWPOINT

Global Efforts in Structural Genomics

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A worldwide initiative in structural genomics aims to capitalize on the recent successes of the genome projects. Substantial new investments in structural genomics in the past 2 years indicate the high level of support for these international efforts. Already, enormous progress has been made on high-throughput methodologies and technologies that will speed up macromolecular structure determinations. Recent international meetings have resulted in the formation of an International Structural Genomics Organization to formulate policy and foster cooperation between the public and private efforts.

A major international structural genomics effort is now in progress, with the goal of obtaining three-dimensional (3D) protein structures on an equivalent scale to the genome sequencing projects. During the past 2 years alone, more than half a billion dollars of additional public and private funds have been invested worldwide in structural genomics projects. Most of this effort is focused on protein structure determinations that will finally delineate the total repertoire of protein folds and provide representative structures for each of the individual protein families (*1*).

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