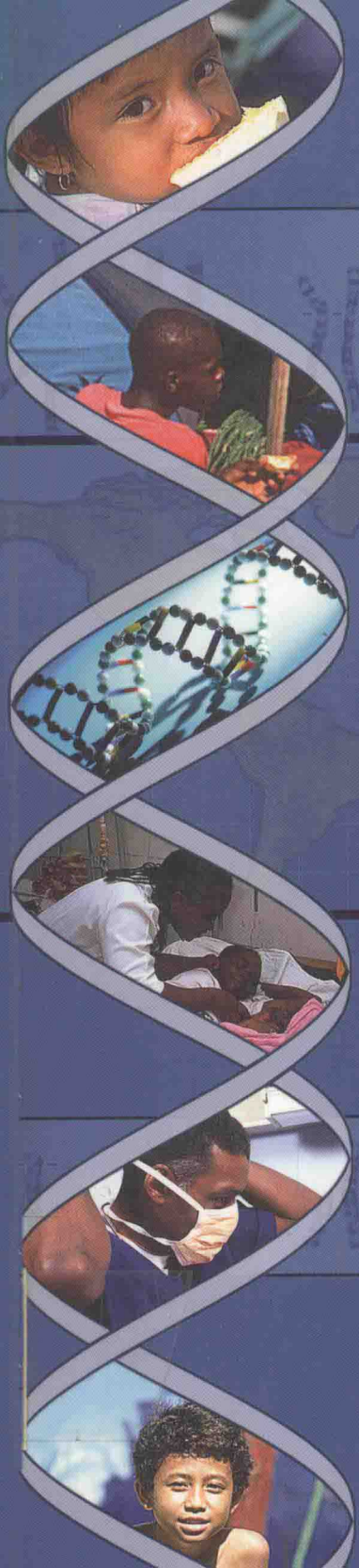

THE ADVISORY COMMITTEE ON HEALTH RESEARCH

Genomics and World Health

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Foreword from the Director General

The announcement of the sequencing of the human genome in 2001 represents an unprecedented milestone in the advancement of our knowledge on the molecular basis of life itself. Together with the advances made in the deciphering of the genomes of many disease-causing microorganisms and their vectors, it is clear that the science of genomics holds tremendous potential for improving health globally.

The information generated by genomics will, over time, provide major benefits for the prevention, diagnosis and management of communicable and genetic diseases as well as other common killers or causes of chronic ill health including cardiovascular diseases, cancer, diabetes, and mental illnesses. It is thus timely and appropriate for WHO to examine the implications of advances in genomics and other critical areas of biotechnology. For this reason, I have asked the Advisory Committee on Health Research (ACHR) to prepare this Report.

The Report focuses on the expectations, concerns and possibilities for the use of new genomic knowledge in improving world health. The specific challenge is how we can harness this knowledge and have it contribute to health equity, especially among developing nations. It is a reality that most genomic and biotechnology research is presently carried out in the industrialized world, and is primarily market-driven. Genomics also needs to be applied to the health problems of the developing world. It is crucial that we actively seek means to involve developing country scientists in innovative biotechnology.

The present Report points out that the genomics revolution has brought with it many complex scientific, economic, social and ethical concerns. These need to be carefully addressed, debated and considered. Recent developments in cloning and stem cell therapy, for example, have raised serious ethical, moral and safety concerns. It follows that societies also need to be better prepared for the era of genomics and its consequences. Public education, understanding and trust on the key issues in genomics is a basic pre-requisite. It is also vital that genomics be considered in the wider context of health and that a relevant balance is maintained in research, development and health care provision between the more conventional and well-tried approaches of clinical research, epi-

demiology and public health and work directed at the medical applications of genomics, both in the context of individual countries and globally.

Strong international leadership is required to achieve these laudable aims. WHO is committed to facilitating this by promoting international partnerships and cooperation strategies to ensure that the fruits of the genomics revolution are equitably shared by all.

Gro Harlem Brundtland, MD, MPH,
Director-General of WHO,
Geneva, Switzerland.

Executive Summary

Introduction

1. The objective of WHO is the attainment by all peoples of the highest possible level of health. This Report, prepared under the auspices of the Advisory Committee on Health Research (ACHR), is addressed primarily to the 191 WHO Member States, the global and six regional secretariats of WHO, and WHO representatives stationed in 110 countries. It is intended to highlight the relevance of genomics for health care worldwide, with a particular focus on its potential for improving health in developing countries. The stimulus for the Report came from the announcement of the sequencing of the human genome, and the great public interest that this has engendered. Concomitant with the success of the human genome project, the genomes of a number of important pathogens, disease vectors and plants are being characterized; it may be that the knowledge that this work generates will, in the short term, provide greater health gains for the populations of developing countries.

2. This Report should be considered in the context of the primacy of fundamental overarching strategies to improve health, for example through alleviation of poverty, development of health systems, improved education and classical public health approaches to disease control and prevention and health promotion. All Member States must ensure that genome technology is used to reduce rather than exacerbate global inequalities in health status.

Background

3. The application of knowledge gained from the characterization of the genomes of several organisms, including the human genome, holds considerable potential for the development of new health care innovations over the coming decades. It is clear, however, that this new field presents a series of highly complex scientific, economic, social and ethical issues.

4. In order to inform WHO strategy in this crucial area, the Director-General of WHO requested in January 2001 that the ACHR prepare a Report on the likely impact of the genomics revolution on world health, with a primary focus on the implications for developing countries. In order to gather the inputs of key stakeholder groups, three international consultative meetings were held in June and July 2001 in Geneva, Switzerland, Brasilia, Brazil and Bangkok, Thailand. This Report builds upon the evidence presented and consensus points reached at these consultations and was enhanced greatly by discussions with, and feedback from, WHO staff members.

THE SCIENTIFIC BASIS FOR A POTENTIAL REVOLUTION IN HEALTH CARE

5. The characteristics of all living organisms reflect the complex interactions between their genetic make-up, their environment, and the long history of the milieu in which they are raised. It is now recognized that many of the biological functions which result from this interplay will ultimately be explained in terms of biochemical mechanisms which, in turn, reflect the activities of the genes which regulate them. Hence, in recent years there has been a growing emphasis in medical research on the analysis of disease mechanisms at the level of molecules and cells in general, and genes in particular.

6. The sum total of genetic information of an individual, which is encoded in the structure of deoxyribonucleic acid (DNA), is called a genome. The study of the genome is termed "genomics." Recently, the order of most of the chemical building blocks, or bases, which constitute the DNA of the genomes of human beings (estimated to amount to three billion), several other animal species, and a variety of human pathogens and plants has been determined. Over the next few years this remarkable achievement will be completed and augmented by research into functional genomics, which aims to characterize the many different genes that constitute these genomes and their variability of action. Such research will also determine how these genes are regulated and interact with each other and with the environment to control the complex biochemical functions of living organisms, both in health and disease.

7. Work in the field of genomics will also offer completely new insights into the mechanisms of human and animal development and ageing;

and, because our evolutionary history is written in our DNA, it will start to unravel our genetic roots and help us to understand the relationships between and within different species.

THE POTENTIAL OF GENOMICS FOR HEALTH CARE

8. It is now believed that the information generated by genomics will, in the long-term, have major benefits for the prevention, diagnosis and management of many diseases which hitherto have been difficult or impossible to control. These include communicable and genetic diseases, together with other common killers or causes of chronic ill-health, including cardiovascular disease, cancer, diabetes, the major psychoses, dementia, rheumatic disease, asthma, and many others.

9. Research directed at pathogen genomes will enhance our understanding of disease transmission and of virulence mechanisms and how infective agents avoid host defences, information which should enable the development of new classes of diagnostics, vaccines and therapeutic agents. Taken together with the knowledge generated from the characterization of the genomes of vectors that transmit infectious diseases, and of the human genome, the field of genomics may also lead to new approaches for vector control and begin to reveal why there are such wide individual variations in susceptibility to these conditions in human populations.

10. Except for genetic diseases that result from a single defective gene, most common diseases result from environmental factors, together with variations in individual susceptibility, which reflect the action of several genes. Many forms of cancer appear to result from acquired damage to specific sets of genes, oncogenes, usually due to exposure to environmental agents. It is likely that further research into disease-susceptibility genes will help us to understand the mechanisms of these diseases and enable more focused approaches to their prevention and treatment. In particular, it should lead to the discovery of specific molecular targets for therapy, provide information that will allow treatment to be tailored to individual needs, and, in the longer-term, generate a new approach to preventive medicine based on genetic susceptibility to environmental hazards.

11. Some of the claims for the medical benefits of genomics have undoubtedly been exaggerated, particularly with respect to the timescales required for them to come to fruition. Because of these uncertainties, it is vital that genomics research is not pursued to the detriment of the well-established methods of clinical practice, and clinical and epidemiological research. Indeed, for its full exploitation it will need to be integrated into clinical research involving patients and into epidemiological studies in the community. It is crucially important that a balance is maintained in medical practice and research between genomics and these more conventional and well-tried approaches.

12. Although this Report focuses on human and pathogen genomics, the consequences of research into plant genomics and the genetic modification of crops has great potential for improving human health through nutritional gains and the production and delivery of vaccines and therapeutic agents.

TECHNOLOGICAL RISKS AND ETHICAL, SOCIAL AND ECONOMIC IMPLICATIONS OF GENOMICS

13. Because many of the medical benefits of genomics research may, at least at first, be very expensive, there is a danger that these new developments will increase the disparity in health care within and between countries. There are particular concerns that inequalities in health care will be accentuated by the current trends in the management of intellectual property, particularly the patenting of basic genomic information.

14. The lack of biotechnology and information technology development in many developing countries is also of concern. While there are major international research programmes focused on HIV/AIDS, tuberculosis and malaria, the control of many important infections will undoubtedly fall to individual countries or regions. The lack of market incentives for the global pharmaceutical industry to pursue genomics-based research and development towards neglected diseases of the world's poor countries means that, unless their biotechnology capacity is developed or mechanisms can be fostered to facili-

tate greater investment from public and private institutions in both developed and developing countries, the potential of genomics to combat these diseases will be not be realized and existing inequalities in health will be exacerbated.

15. In genomics research and its medical application, familiar ethical issues such as informed consent, confidentiality, and avoiding discrimination and stigmatization take on different forms because of both the nature of genetic information and the specific social and economic contexts of individual countries. These questions need to be debated widely so that countries can establish their own ethical framework and regulatory structures based on principles which have been agreed internationally.

16. There are many aspects of recombinant DNA technology, particularly those which involve the manipulation of human or animal genomes, which require regulation on matters of public safety, the health of research workers, risks to the environment and the potential for social and political misuse. In addition, the use of genetically modified plants will necessitate the development of more effective mechanisms to minimize the risks to consumers, and to biodiversity and the rights of traditional farmers. In many countries, particularly those which are introducing recombinant DNA technology for the first time, adequate regulatory frameworks do not exist to safeguard against these risks and hazards. The establishment of these structures represents a crucial priority.

17. Societies need to be better prepared for the era of genomics and its consequences. Genomics research is complex and an understanding of its medical potential and the ethical issues involved requires a basic understanding of the principles of genetics. This will only be achieved by a major effort to increase the quality of education in this field at all levels, with particular emphasis on improving science teaching and the introduction of the principles of ethics to schoolchildren. The development of mechanisms to communicate these concepts effectively and engage the general public in an informed dialogue regarding these issues is equally important.

RECOMMENDATIONS

18. The following recommendations are set against a background of current and anticipated future requirements of WHO Member States. Member States will need to make their own assessments of these requirements and their relative priorities. Member States should, with the encouragement of WHO, explore opportunities for regional collaboration, collaboration between developed and developing countries and between developing countries. To support its Member States, WHO will need to:
    - enhance its capacity for responding to requests for technical cooperation from Member States;
    - exercise its normative function for setting standards and guidelines and harmonization of procedures;
    - fulfil its advocacy role to ensure that the benefits of these scientific advances are shared by all countries, rich or poor.

Technical cooperation between WHO and its Member States

19. Given the remarkable speed of progress in genomics research, the coming decades are likely to see an enormous expansion of this field, with important potential for its clinical application to benefit health care globally. Member States need to be prepared for this completely new approach to medical research and practice. Furthermore, the capacity for genomics research and downstream biotechnology research and development varies enormously between countries, and, if uncorrected, this situation will undoubtedly exacerbate existing inequalities in health. Member States should consider undertaking analyses of their existing biotechnological capacity as a basis upon which to develop their strategic priorities in this field.

    To assist its Member States, WHO should develop the capacity to evaluate advances in genomics, to anticipate their potential for research and clinical application in the many different environments of the Member States and to assess their effectiveness and cost in comparison with current practice. Where appropriate, WHO may respond to requests from Member States to enhance their capacity in this research field.