HUMAN GENOME:

Perspectives and Applications

With a Foreword from Lap-Chee Tsui
Past President of the Human Genome Organization (HUGO)

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The Human Genome: Perspectives and Applications

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Foreword

The Human Genome Project is by far the largest international scientific collaboration in biological research in human history. The human genome sequence has already changed the way we study human biology and how we practice in medicine. In fact, the impact of the Project extends well beyond health and disease, into ethical, legal and social issues, crossing cultural and political boundaries.

The unequal distribution of wealth and technological capabilities between developed and developing countries is well acknowledged. The Human Genome Project adds another layer to this asymmetry. Only through international debates and common understandings we will be able to enjoy the true benefit of the Project, for the well being of mankind.

The Human Genome Organisation (HUGO; http://www.hugo-international.org/hugo) is an international organization to promote international discussion and collaboration on scientific issues and topics crucial to the progress of the worldwide human genome initiatives. In addition to the scientific front, HUGO also provides a global forum for addressing the scientific, medical, ethical, legal, social and commercial issues raised by the handling and use of genome knowledge. It has issued statements on patenting of DNA sequences, cloning, benefit sharing, gene therapy, human genomic databases, and, issues on early release of raw sequence data.

Adequate knowledge of the scientific and medical goals, and, the potential applications and implications of the Human Genome Project is crucial to all meaningful public debates and discussions. Education is therefore the key. It has to reach not just the law and policy makers but also the general public. Moreover, the issues related to the human genome are not static. There must be periodic review and revisit of the relevant policies, laws and regulations.

Lap-Chee Tsui
Vice-Chancellor
The University of Hong Kong
Also, past President of HUGO (2000-2002)

Preface

The National Academy of Science and Technology (NAST), in January 2003, invited all institutions doing work in human genetics to respond to a survey conducted by UNESCO on the impact and application of the *"Universal Declaration on the Human Genome and Human Rights"* in the country. The Institute of Human Genetics-National Institutes of Health (IHG-NIH), the University of the Philippines Natural Sciences Research Institute-DNA Analysis Laboratory (UP NSRI), the Philippine Council on Health Research and Development, Department of Science and Technology (PCHRD-DOST) and the National Bureau of Investigation (NBI) responded to the request. While NAST initially set out to produce a unified response to the questionnaire, it was difficult to integrate the varied responses of the institutions with very diverse functions and programs. It became apparent that there was a need to call together and meet with the different groups and agencies involved in the science, whether through research or direct application, in order to collaborate and come up with a unified statement on the human genome and make appropriate recommendations for a future gene policy.

This initiative was timely, even urgent, as various government agencies had previously been called to attend international meetings and present the country's stand on related issues, among them, human cloning. The immense attention given to the Human Genome Project (at the time, the sequencing of the human genome was only just nearing completion) also brought to the fore the need for a better understanding of the science and study of genetics, its many issues — potential benefits and controversies alike, and the current state of its use and practice in the Philippines. At a time when cloning had become a byword and the uproar over certain sensational news reports overshadowed other more useful applications of the science, it seemed imperative for NAST to address possible misinformation and provide a clearer, more realistic perspective on the human genome and its impact on society. Thus, in February of 2003, the NAST Core Group on the Human Genome was born.

Dr Carmencita Padilla, Professor of Pediatrics of University of the Philippines College of Medicine (UPCM) and Director of the Institute of Human Genetics- National Institutes of Health heads the NAST Core Group. The NAST Core Group is composed of experts and specialists in the fields of genetics, science, policy and the law from various institutions. The NAST Core Group members are:

Eva Maria C. Cutiongco MD, Research Faculty of the National Institutes of Health and Associate Professor of Pediatrics, University of the Philippines College of Medicine

Quintin L. Kintanar MD PhD, Academician, National Academy of Science and Technology

Mariluz P. Mojica-Henshaw MD PhD, Associate Professor of Biochemistry, University of the Philippines College of Medicine

Victoria Edna G. Monzon MD, Professor, Department of Medicine and Department of Bioethics, Faculty of Surgery, University of Santo Tomas

Perla D. Santos Ocampo MD, Academician and President, National Academy of Science and Technology and Professor Emeritus, University of the Philippines Manila

Atty. Jose Ma. A. Ochave LLM, Professor, Philippine Judicial Academy

Francisco Supe, Chief, Philippine National Police DNAAnalysis Section, Camp Crame

Celia Aurora T. Torres-Villanueva PhD, Associate Professor, National Institute of Molecular Biology and Biotechnology, University of the Philippines Diliman

Maria Corazon A. de Ungria PhD, Head, DNA Analysis Laboratory, Natural Sciences Research Institute, University of the Philippines Diliman

Five key participating agencies were named: The Department of Science and Technology, the National Academy of Science and Technology, the Philippine Council for Health Research and Development, the Philippine Council for Advanced Science and Technology Research and Development and the Institute of Human Genetics-National Institutes of Health, University of the Philippines Manila.

The first task of the NAST Core Group was to identify the different stakeholders involved in formulating a stand. The NAST Core Group also recognized the need to educate and update not only the general public, but the scientific and academic communities, government agencies and the socio-civic sector as well. A series of Round Table Discussions were planned and the following key issues and topics, each focusing on a different aspect of the human genome and the human genome project were identified: (1) The Human Genome Project, (2) Cloning and Stem Cell Research, (3) DNA Forensics, (4) Genetic Testing and Research and (5) Ethical, Legal and Social Implications of the Human Genome Project. Subcommittees headed by members of the Core Group and composed of invited experts and previously identified stakeholders were each tasked to discuss their respective topics and to prepare a presentation/lecture for the RTDs which would be conducted with various target audiences.

The NAST Core Group was also mandated to draft a NAST Resolution on the Human Genome which would later be presented during the RTDs and at the 70th National Research Council of the Philippines Annual Meeting.

On March 13, 2003, the first Round Table Discussion on "The Human Genome: Promises and Problems" was held at the Traders' Hotel in Manila and attended by representatives from the scientific community, the medical community, the academe, the church and the socio-civic sector. A second RTD, a "Science Legislative Forum on the Human Genome" was held with Congress in attendance at the House of Representatives on May 28, 2003. During each, various reactors, who were likewise experts in fields related to the topics, were invited to give their commentaries on the issues presented.

This NAST Monograph on the " **Human Genome: Perspectives and Applications"** serves as a key output of the NAST Core Group on the Human Genome and as an important documentation of NAST's goal to educate and inform the country's scientists, educators and lawmakers, the church and society. The main portion of the monograph opens with the NAST Resolution on the Human Genome followed by Dr. Kintanar's and Dr. Santos Ocampo's paper on "**Filipino Scientists' Perspectives in Human Genome Research**" which serves as a situationer for the inception of the Resolution and the monograph. The next paper "**The Human Genome Project: The Story Behind the Science**" by Dr. Torres-Villanueva details the purpose, origins and development of the project. It should serve as a very informative, straightforward introduction to the Human Genome Project for the uninitiated, the lay and the general public. For scientists and educators, Dr. Torres-Villanueva's paper provides a concise and sufficiently comprehensive summary of the project.

The paper on "**Cloning and Stem Cell Research**" by Dr. Mojica-Henshaw defines and differentiates between cloning, stem cell research and related concepts which are often lumped together; discusses the various techniques developed so far and presents a realistic perspective on current uses of the technology. It seeks to educate and provide insight beyond the more notorious, highly publicized views and frequently poorly informed perceptions of the field.

In "**DNA Forensics, the Human Genome Project and Human Rights**", Dr. De Ungria presents a brief history and background of DNA forensics, the impact of the Human Genome Project on the field, the current state of its application in the country and various human rights issues involved. Dr. de Ungria also points out the critical role of law and policy in improving the practice of forensics and maximizing its use in the nation's judicial system.

practice of forensics and maximizing its use in the nation's judicial system.

Dr. Cutiongco next writes about "**Genetic Testing and Research**", differentiating between clinical and research testing and discussing the different types of genetic tests including their various uses and benefits. The importance of establishing and implementing guidelines to govern the use of new technologies and genetic information gleaned through such tests is also highlighted.

"**The Ethical, Legal and Social Implications of the Human Genome Project**" by Dr. Victoria Edna G. Monzon recognizes that while the Human Genome Project holds great potential for progress and benefit to humanity, it is also fraught with potential ethical dilemmas. This paper presents a relevant ethical framework outlined in seven basic principles for the Human Genome Project and its applications.

"**The Law and Human Genetics: Opportunities for Legislative Action**" by Atty. Jose Maria A. Ochave is the last article in the Monograph. While it was not in the original list of topics and as such, was not among the lectures given during the first RTD, the NAST Core Group recognized its timeliness and particular relevance for the second RTD's target audience, the legislature. First presented during the "Science Legislative Forum on the Human Genome", the paper identifies three issues for which prompt legislative action would be most critical and valuable: newborn screening, DNA forensics and the judicial system and the protection of privacy of genetic data.

The NAST Monograph "**Human Genome: Perspectives and Applications**" aims to present an accurate picture of the current state of genetics in the country and the impact of the Human Genome Project on Filipino scientists and various aspects of Philippine life and society — from medicine to law to religion. While it is by no means all-encompassing, this book should serve as an important starting point for future discourses, debates and discussions. It is for scientists, academics, students, teachers, lawmakers, church leaders, the lay, the interested private citizen, our goal being to educate and inform. By laying the groundwork, we hope to stimulate thought and action because indeed, we are on the threshold of *a brave new world.*

The Editors

Resolution on the Human Genome and Human Rights*

Joint Statement of the National Academy of Science & Technology (NAST) and the National Research Council of the Philippines (NRCP)

WHEREAS, the human genome has been sequenced through the International Human Genome Project (HGP), and its applications to Filipino health and national economic development are broad and far-reaching;

WHEREAS, the Universal Declaration on the Human Genome and Human Rights approved by the United Nations General Assembly in 1997 recognizes that research on the human genome and resulting applications open up vast prospects for progress in improving the health of individuals and of human kind as a whole, but emphasizes that such research should fully respect human dignity, freedom and human rights;

WHEREAS, it is the policy of the Republic of the Philippines, as embodied in the 1987 Constitution, to protect and promote the people's right to health and to value the dignity of every human person and guarantee full respect for his or her human rights, including the right to life of the unborn from conception;

WHEREAS, the National Academy of Science and Technology (NAST) and the National Research Council of the Philippines (NRCP) are legally mandated, among others, to serve as reservoirs of scientific and technological manpower and to act as advisory bodies of the President of the Republic of the Philippines and the Cabinet on policies concerning science and technology in the country;

WHEREAS, NAST and NRCP believe in the free exercise of research on the human genome, but with due regard for the principles set out in the United Nations Universal Declaration on the Human Genome and Human Rights and the policies laid down in 1987 Constitution of the Republic of the Philippines;

WHEREAS, the Philippines, being at the early stages of development in genetic research and application, needs to provide guidelines to its scientific community, especially in areas where research activities and applications already exist.

NOW, THEREFORE, the National Academy of Science and Technology and the National Research Council of the Philippines, in assembly, hereby resolve to:

a) Call on the national government to direct all relevant government agencies to develop, promote and support research on the human genome and develop mechanisms so that research results can be accessed and utilized for the benefit of the patients and the general public, while taking into account the principles set forth in the Universal Declaration of the Human Genome and Human Rights and the policies laid down in the 1987 Constitution of the Republic of the Philippines;

b) Create a working group to look into the ethical, legal and social implications of knowledge resulting from the Human Genome Project and to recommend to NAST and NRCP the appropriate policy and procedural guidelines that may be submitted to the national government and research institutions for their consideration and approval. The guidelines should cover, but not be limited to:

   i. genetic testing and research, including the requirement of free and prior informed consent of research subjects; the requirements for packaging, labeling and transport of specimens for validated genetic tests that are only available abroad; and the appropriate standards to ensure that clinical tests offered are of the highest possible quality;

   ii. forensic uses of the DNA for, *inter alia*, human identification, disputed parentage cases, mass disaster cases, and criminal investigations;

   iii. somatic cell nuclear transfer, including the banning of artificial reproductive cloning for the purpose of producing a human being while allowing therapeutic cloning for the purpose of producing stem cells, except if the stem cells are derived from living human embryo; and crafting of policies and regulations on the disposition of excess human embryos; and

   iv. cross-cutting issues such as those relating to privacy and genetic discrimination; intellectual property protection; benefits-sharing mechanisms; and equitable distribution of limited research resources.

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* Prepared by the NAST Core Group on the Human Genome, presented at the National Research Council of the Philippines Annual Meeting on March 15, 2003 and ratified at the NAST Annual Scientific Meeting of the National Academy of Science and Technology on July 10, 2003.

Message

I am very pleased to join you this morning at this Round Table Discussion on "The Human Genome: Promises and Problems". We, in the science community, appreciate this opportunity to discuss this important technological breakthrough with members of the clergy, academe, researchers and other stakeholders. Group discussions such as this provide the venue for us to listen to your concerns and hopefully respond to them.

The dramatic increase in genetic discovery over the past few years owes much to the Human Genome Project, the 15-year, $3 billion effort to map and sequence the entire 3 billion bases of human DNA. With this knowledge will come more spectacular insights into human disease, especially the most common disorders affecting human beings. A drop or two of blood, analyzed by a DNA decoder, will soon yield a genetic profile for every man, woman and child who goes to the doctor for a routine physical. Our genes will soon be an open book, revealing good news (you don't carry a gene for breast cancer or prostate cancer) and bad news (you have a gene that predisposes you to heart disease). Even bad news will be helpful because physicians will be able to replace defective genes with healthy ones or treat people with a diet or drugs that will keep "bad genes" in check.

Direct modification of genes is another major discovery of biomedical research. It is now possible to remove body cells, manipulate them genetically by inserting, with the help of so-called vectors, selected DNA segments from cells into the nucleus. With each new discovery, scientists gain another weapon for an arsenal that may lead to accurate diagnosis and safe and effective genetic therapies.

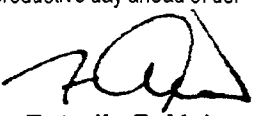
The potential benefits that can be derived from these technologies are indeed enormous, but they also present dangers to human rights which the *"Universal Declaration of the Human Genome and Human Rights"* recognizes. People should be more aware of the ethical dilemmas which research on the genome presents. We should also be vigilant about the potential ill effects of these technologies. The insertion of a gene, for instance, may cause the generation of unexpected harmful substances detrimental to health. There will always exist some possibilities of unforeseen and undesirable results.

The rights stated in the *Declaration* are derived from a unifying concept: the obligation to respect the dignity of each precious individual and to prevent discrimination on genetic grounds; to protect privacy and to ensure that free consent is obtained for the use of the individual's genetic data. The new *Declaration* also expresses the principles which should govern research on the human genome. The most important of these, states, "Practices which are contrary to human dignity such as reproductive cloning of human beings, shall not be permitted."

To encourage people and their governments to become more aware of the ethical issues related to research on the genome, the Department of Science and Technology, through its various agencies and collegial bodies led by the National Academy of Science and Technology (NAST), is partnering with various organizations and institutions in holding this series of activities to formulate our stand on the human genome and initially draft our gene policy. It will be recalled that NAST and the Philippine Council for Health Research and Development (PCHRD) jointly conducted a *"Seminar-Workshop on Cloning and The Human Genome Diversity Project"* in 1997. PCHRD is responsible for establishing ethical standards for health research involving human participants through the creation of the National Ethics Committee (NEC). NEC is tasked to uphold the sanctity of human life and protect the rights of human participants in biomedical research. We at the DOST reaffirm our stand of 1997 on non-support for any research on human reproductive cloning.

In this morning's discussion, we shall assess these new technologies, delineate their potential benefits and perils and confront the ethical, legal, religious and social implications which will impact upon future research and development. We expect that the presentations of our invited scientists will shed more light on some of the critical issues of biomedical research. I have no doubt that this discussion will give all of us an opportunity to learn from them and from one another.

Thank you and may we all have a fruitful and productive day ahead of us.



Hon. Estrella F. Alabastro, PhD
Secretary
Department of Science and Technology

Delivered during the Round Table Discussion on The Human Genome: Promises and Problems on 13 March 2003 at the Diplomat Hall, Traders Hotel, Manila

Message

Recent advances in the field of genetics have brought to light many critical issues with regard to its use and applications. Through developments and innovations in the field of biotechnology, a better understanding of human biology, and consequently, improved medical care, has been achieved.

While the sequencing of the Human Genome through the Human Genome Project (HGP) promises considerable and significant contributions to various fields of science, its applications have profound ethical, legal and social, sociological and logical implications.

In response to the need for a better understanding of these issues and the current state of the use and application of genetics in the Philippines, the National Academy of Science and Technology conducted a Round Table Discussion on "The Human Genome: Promises and Problems" on March 13, 2003 at the Traders Hotel in Manila. Subsequently, a Science Legislative Forum was held in Congress on May 28, 2003 on the same issues. The topics for discussion included: the Human Genome Project, Cloning, Forensics, Genetic Testing and Research and Ethical, Legal and Social Implications. Various experts presented key issues and discussed local experience on each topic. Reactors from a diverse group that included the academe and the church gave their comments and responses to the highlighted issues. The legislative forum was attended by congressmen, their staff, media and consumers.

At the end of the Round Table Discussion, a proposed Resolution on the above issues encompassing the different issues and concerns linked with the field of genetics was formulated. This resolution was presented in plenary during the 70th Annual Meeting of the National Research Council of the Philippines on March 15, 2003. At the 25th Annual Scientific meeting of the National Academy of Science and Technology, this was approved by the general assembly to be pursued as a major thrust in the Academy's action program.

Perla Dizon Santos Ocampo, MD
Academician and President
National Academy of Science and Technology

Delivered during the Round Table Discussion on The Human Genome: Promises and Problems on 13 March 2003 at the Diplomat Hall, Traders Hotel, Manila

Message

As the lead agency for health research in the country as well as the home of the National Ethics Committee, it is our duty to support research and development of appropriate technology in health.

As science and ethics are rapidly evolving, this monograph is a significant step towards reaching a clearer definition and understanding of what we need to achieve.

In examining the areas of concern, we need to pay attention to the following: 1)The appraisal of the levels of genomic science as we use it in pursuit of better understanding of health and disease in the Philippines as well as the extent of scientific investigations we will be able to achieve over time; 2)The policy gaps in defining the limitations we will impose on bio-sample transport and research assigned to our collaborators abroad; 3)The approach in communicating and educating the people on human genomic research and its impact on the individual, communities, society and health care; 4)The assessment of capacities of institutions to handle genomic research as well as their ability to protect human research participants, including the formulation of strategies to strengthen bioethics programs of research institutions; and 5)The importance of establishing regulation, self-regulation and monitoring systems in the use of genomic information, handling of genetic material as well as a system of program development in genomic medicine and research.

We trust that this document will provide the framework of our future discussions, cooperation and commitment towards capacity development and institution of policy safeguards towards the utilization of genomic research –from health to forensics, for a better quality of life for the Filipinos.

Gemiliano D. Aligui, MD
Executive Director
Philippine Council for Health Research and Development

Delivered during the Round Table Discussion on The Human Genome: Promises and Problems on 13 March 2003 at the Diplomat Hall, Traders Hotel, Manila

Message

As the country's lead agency in developing R&D capabilities in the field of advanced science and technology, including biotechnology, the Philippine Council for Advanced Science and Technology Research and Development (PCASTRD) has always been proactive in its role of supporting undertakings that adequately and accurately deploy knowledge gained from S&T endeavors.

PCASTRD shares and fully supports the perspective laid down in the NAST Resolution on Human Genome and Human Rights. We believe that the NAST Resolution was prepared and endorsed according to the highest standards of biosafety and ethics.

As early as 1997, PCASTRD issued a press release on behalf of DOST addressing the issue of cloning and why it was not within the DOST's biotechnology research and development priorities. It was the view that advances in human knowledge should be used for more immediate and practical concerns. DOST's stand has not changed.

In the Philippines, biotechnology R&D priorities focus on the improvement of crops and livestock for better agricultural yield, the development of environment-friendly processes in agriculture and industry, and the use of new knowledge to enhance health conditions of living organisms, including crops, livestock, and people.

We trust that this Resolution, along with other declarations advocated by the scientific community, will help our legislators and policy makers in formulating laws and allocating resources for various S&T endeavors. Ultimately, we look forward to our research pursuits being utilized for the greater good.

IDA F. DALMACIO, PhD
Executive Director
Philippine Council for Advanced Science & Technology Research & Development
Department of Science and Technology

Delivered during the Round Table Discussion on The Human Genome: Promises and Problems on 13 March 2003 at the Diplomat Hall, Traders Hotel, Manila

Filipino Scientists' Perspectives in Human Genome Research

Quintin L. Kintanar MD PhD and Perla D. Santos Ocampo MD

INTRODUCTION

Fifty years ago, James D. Watson and Francis H.C. Crick published, in the April 25, 1953 issue of the scientific journal NATURE, their paper proposing the double helix model for the structure of deoxyribonucleic acid or DNA. This structure elegantly explains how genetic information from parents can be passed on to offspring. The DNA structure consists of two strands of the sugar deoxyribose alternating with phosphate wound about each other in the shape of a two-fold spiral. Between the two spirals are nucleotide bases Adenine (A), Thymine (T), Cytosine (C) and Guanine (G) projecting towards the middle like the rungs of a ladder, where A is always paired with T and C with G.

The unique chemical properties of DNA allow it to be replicated accurately when the cell divides into two daughter cells, thus passing the genetic information. A triplet of three consecutive nucleotide bases codes for a specific amino acid (AA). For example, Guanine-Cytosine-Thymine or "GCT" codes for the amino acid alanine, while Adenine-Adenine-Adenine or "AAA" codes for the amino acid lysine. Amino acids are the building blocks of protein. Each of the amino acids, numbering 20 in all, has a unique triplet code of nucleotide bases. A gene consists of a string of triplet codes for the construction of one protein. It varies in size depending on the size of the protein. Human insulin, the hormone lacking in juvenile diabetics, for example, consists of a total of 51 amino acids divided into 21 AA residues in the A chain and 30 AA residues in the B chain.

The molecular mechanism of transmitting information from the nuclear DNA to messenger RNA or mRNA, to transfer RNA or tRNA, and finally to proteins appears to be universally true for all living things from the smallest viruses, to all plants and all animals, including man. The inheritance of characteristics through genes is true for microorganisms, plants, and animals, as it is for humans. The rules for the transmission of dominant and recessive traits (Mendel's Law) were first described in pea hybrids by Gregor Johann Mendel in 1865. Mendel's Law also

applies to the transmission of dominant and recessive traits in man. According to the genetic theory of human nature, all of what makes us what we are—characteristics such as sex or gender, blood type, height, physical appearance, inheritable diseases or susceptibility to diseases—are determined by our genes.

Long before the International Human Genome Project, which was started in 1990, the world had already been benefiting from the application of the science of genetics, now also referred to as genomics. Human insulin, mentioned earlier, was the first important genetically engineered drug produced through recombinant DNA technology. It was approved for clinical use by the US-FDA in 1982. In this instance of recombinant DNA technology, the gene of human insulin taken from the human DNA genome was combined with bacterial DNA of the common intestinal bacteria Escherichia coli. The re-engineered bacteri, now containing the gene for human insulin, were artificially cultured and the human insulin produced was isolated from the culture. In this way, human insulin could be produced not only in large quantities since bacteria multiply very rapidly, but also the final product is exactly the same as human insulin. Before 1982, the only commercial source of insulin was the pancreas of slaughtered cattle. Bovine insulin is slightly different from human insulin, genotypically and phenotypically, but is sufficiently similar to human insulin that it can be a substitute for human insulin in the treatment of diabetes.

The Human Genome Project (HGP) that determined the sequence of some 3 billion nucleotide bases in all of the human genes are contained in about 30,000 genes, which in turn are contained in 23 pairs of chromosomes in the nucleus of every cell, was essentially completed this year. One of the important findings of HGP is that all humans, regardless of race or sex, are 99.9% genotypically the same.

With the completion of HGP, now is the time for all countries, including developing countries like the Philippines, to develop their capacity to take advantage of the many benefits that would surely follow this great scientific achievement. Much has already been achieved, but the potential benefits are even greater. For example, the application of the polymerase chain reaction (PCR)— an ingenius way of rapidly amplifying particular DNA sequences— has already found application in diagnostics, and has enormous potential in microbiology and virology. Increasing knowledge about the human genome has also improved the diagnosis and treatment or management of single-gene disorders such as, inherited hemoglobin disorders, cystic fibrosis and hemophilia.

Understanding the genomics of human pathogens and their vectors holds great potential for the prevention and treatment of infectious diseases, such as leishmaniasis, dengue fever and malaria. Even non-communicable diseases, such as cardiovascular diseases, coronary heart disease, cancer, diabetes, rheumatic diseases, asthma and the major psychosis, including Alzheimers, appear to be related to certain genetic make-up. Better knowledge through the study of genomics and as a result of the complete sequencing of the human genome, can lead to new approaches in the prevention, mitigation and management of these disorders. Indeed, Watson and Crick's seminal work, which has been confirmed and universally accepted by the scientific world, and the Human Genome Project, opened up a whole new world of molecular biology and molecular medicine.

Many scientists and researchers from many countries have been involved in the rapid development of our knowledge about DNA and the related protein enzymes, which uniquely catalyze the many chemical reactions involved in DNA metabolism. The Philippines can be proud that a Filipino scientist—Baldomero Olivera, together with his co-author I. R. Lehman, is recognized both here and abroad, for having first isolated and characterized DNA ligase, an enzyme involved in the joining of polynucleotides in DNA.

METHODOLOGY TO DEVELOP PHILIPPINE POSITION/ RESOLUTION ON HUMAN GENOME RESEARCH

Determining policies on genomics involves both technical scientific expertise and acceptance by the community at large. In this case of genomic policy where technical merit and acceptance of the policy are equally important, the best methodology is for experts to formulate policy in consultation with stakeholders and concerned sectors.

The National Academy of Science and Technology (NAST) serves as a reservoir of competent scientific and technological manpower for the country. It is also charged with the function of advising the President and the Cabinet on policies concerning science and technology. Thus, the development of a national policy on genomic research falls naturally within the purview of NAST and other relevant agencies and institutions under the Department of Science and Technology.

To develop the Philippine Resolution (position) on Human Genome Research, the National Academy of Science and Technology through its President, organized a NAST Core Group on

the Human Genome composed of active Filipino scientists/experts from various scientific institutions and laboratories as follows:

1. Carmencita D. Padilla, M.D.—Head
   Institute of Human Genetics
   National Institutes of Health (NIH)
   University of the Philippines (UP) Manila

2. Eva Maria C. Cutiongco, M.D.—Member
   Institute of Human Genetics
   National Institutes of Health (NIH)
   UP Manila

3. Mariluz P. Mojica-Henshaw, M.D. PhD.—Member
   Department of Biochemistry and Molecular Biology
   UP College of Medicine
   UP Manila

4. Victoria Edna G. Monzon, M.D.—Member
   Department of Bioethics
   University of Santo Tomas, Manila

5. Francisco Supe Jr, M.D.—Member
   Philippine National Police Crime Lab
   DNA Analysis Section
   Camp Crame, Q.C.

6. Maria Corazon A. de Ungria, PhD.—Member
   DNA Analysis Laboratory
   Natural Science Research Institute
   UP Diliman, Q.C.

7. Celia Aurora T. Torres-Villanueva, PhD.—Member
   National Institute of Molecular Biology and Biochemistry
   UP Diliman

8. Atty. Jose Maria A. Ochave, LLM—Member
Judicial Academy of the Supreme Court and
United Laboratories, Inc.

9. Quintin L. Kintanar, M.D. PhD—Member
Academician
National Academy of Science and Technology

10. Perla Dizon Santos Ocampo, M.D. —Member
Academician and President
National Academy of Science and Technology

First, the NAST core group brainstormed on what was to be done. The group identified the need to not only disseminate information about genomics to stakeholders and concerned sectors, but also to involve them in decision making through active consultation. To do this, a series of round table discussions, scientific symposia, and seminars, focusing particularly on the human genome policy, was planned and implemented in 2003.

In these round table discussions, scientific symposia/seminars, those in the NAST core group who were actively involved in basic or applied research work in the field of genomics were tapped to present papers on their respective fields of expertise, namely **Cloning** by Mariluz P. Mojica-Henshaw MD PhD, **Forensic DNA Analysis in the Philippines** by Maria Corazon A. de Ungria PhD, **Genetic Testing and Research** by Eva Maria C. Cutiongco MD, **Ethical, Legal and Social Implications** by Victoria Edna G. Monzon MD, **The Law and Human Genetics: Opportunities for Legislative Action** by Atty. Jose Maria A. Ochave LLM.

Celia Torres Villanueva PhD presented the status and general information about the international **Human Genome Project** to open each of the scientific fora on the human genome and Dr. Carmencita D. Padilla served as convener and chairperson. In all of these fora, appropriate reactors representing various stakeholders and interested groups were invited to participate. The audience was also given the opportunity to participate by way of questions or comments that were answered by the resource speakers or other scientists present.

So far, three such symposia/ seminars/ consultative conferences or round table discussions

have been conducted, as listed below:

1. Round Table Discussion on the Human Genome—Promises and Problems, March 13, 2003, Traders Hotel, Manila

2. National Research Council of the Philippines Annual Meeting—Advancing the Frontier of Knowledge for National Development and Welfare, March 15, 2003, Manila Hotel, Manila

3. Scientific Legislative Forum—The Human Genome, June 3, 2003, House of Representatives, Quezon City

The NAST core group also helped prepare the Philippines' answers to the UNESCO Survey on various activities of member countries in the field of genomic research and services. The UNESCO Survey asked questions related to how well each member country adhered to the principles of the Universal Declaration on the Human Genome and Human Rights, which was adopted by the UN General Assembly in 1998.

This Philippine Monograph on the Human Genome contains an introductory paper by two NAST academicians, and six scientific papers prepared by the members of the core group presented in the series of scientific fora on the Human Genome. The monograph also contains excerpts from the questions and answers portion of the scientific fora held. Finally, the full document of the approved Philippine Resolution on the Human Genome and Human Rights is reproduced.

PHILIPPINE RESOLUTION ON HUMAN GENOME & HUMAN RIGHTS

The NAST Resolution on Human Genome Research and Human Rights was prepared by the NAST Scientific Core Group on Human Genome Research and further refined through a wide-ranging consultative process involving the scientific community, educators, legislators, representatives of religious groups and civil society. The resolution calls on government to develop, promote and support research on the Human Genome, taking into account the constitutional policy on equal protection of the mother and the unborn from the moment of conception. The resolution was ratified by the annual general meeting of the NAST on July 10, 2003 and endorsed by the National Research Council of the Philippines and the Philippine Council for Health Research and Development.

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The Human Genome Project: The Story Behind the Science

Celia Aurora T. Torres-Villanueva PhD

INTRODUCTION

"We've discovered the secret of life."

Francis Crick
28 February 1953

On April 14, 2003, the International Human Genome Sequencing Consortium announced that the Human Genome Sequence had been completed. This date has special meaning, for the structure of the DNA was first described in a paper by James Watson and Francis Crick on April 25, 1953, almost exactly 50 years earlier. This year's announcement may be considered to have formally closed the Genomics Era, and to officially have opened the Post-Genomics Era, as scientists refer to this age in human history following the announcement of the completion of the working draft of the Human Genome in the year 2000.

The Human Genome Project is a story of big science and big business; of molecular biology and Ethical, Legal and Social Issues (ELSI); of far-reaching benefits and serious concerns. This paper gives a concise and inevitably incomplete version of this rich and complex story. May it be the beginning of the reader's heightened awareness of this momentous scientific discovery that will surely shape human history, hopefully for the better.

DNA, GENES AND THE GENOME

"We've called the human genome the blueprint, the Holy Grail, all sorts of things. It's a parts list. If I gave you the parts list for the Boeing 777 and it has 100,000 parts, I don't think you could screw it together, and you certainly wouldn't understand why it flew."

Eric Lander, Millennium Evening at the White House
14 October 1999

First of all, let us begin by defining some terms that are indispensable in the narration of this scientific and highly technical story. Those who are comfortable with molecular biology may opt to pass over this part and proceed to the next section of this paper.

By the term "genome", we mean the totality of genetic information in a human being. In molecular terms, this refers to all the genes (to be defined later) and other information contained in the deoxyribonucleic acid, or DNA, of most of our cells.[1] This DNA can be found in a compartment within most of our cells called the nucleus. Inside this nucleus are 23 pairs of chromosomes (Figure 1).[2] One of the pairs of chromosomes are the sex chromosomes (XX for females, XY for males). The totality of genetic information in all these chromosomes is referred to as the genome.

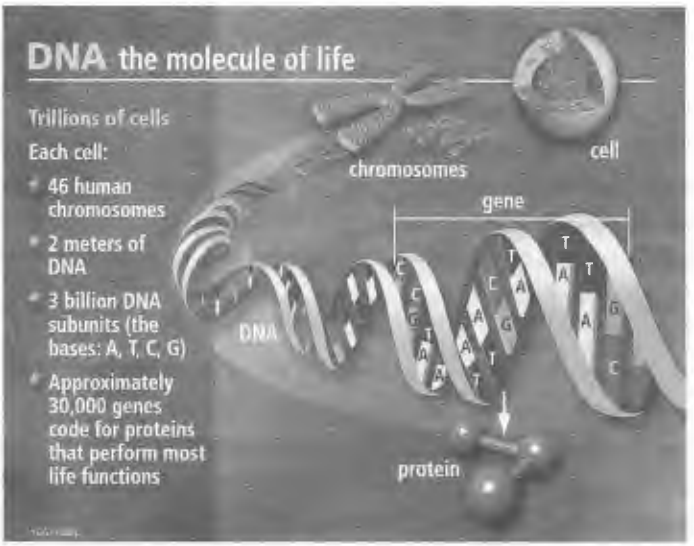

Figure 1. From DNA to Life. Source: www.ornl.gov/hgmis

[1] DNA can be found in cells that have a nucleus, called nucleated cells. Some cells, such as the red blood cell, have no nucleus, and therefore do not contain genomic DNA. Our cells contain another kind of DNA found in another cellular compartment called the mitochondrion. The DNA herein is known as mitochondrial DNA and is technically not part of genomic DNA.

[2] Most of our cells are called somatic cells, and have diploid content, meaning they have 46 chromosomes. The exceptions are our gametes or germinal cells (eggs in females, sperm in males) that have haploid content of DNA, meaning they only have 23 chromosomes.

Genes are parts or sequences of the genome that encode for specific molecules. These molecules are mostly proteins, but some genes code for ribonucleic acid, or RNA. However, as you know, our cells and bodies are made up of more than just proteins and RNA. We are also made up of fats and carbohydrates. These fats and carbohydrates are taken up from the foods we eat, and are formed into the various materials that make up our cells through the function of various proteins. Hence, our genes need *to encode for*, or, in molecular biology terminology, *to express*, only proteins (and a few RNA molecules) to produce the rest of the materials that form our cells and ultimately, our bodies.

How much DNA do humans have? As shown in Figure 1 above, we have DNA that is about 3 billion *bases* long. Bases refer to the nitrogen bases, which are molecules that make up our DNA. There are four bases in DNA. These are adenine, thymine, cytosine and guanine. In genetic shorthand, we refer to these bases by their letter-symbols, A, T, C and G, respectively. The secret of the structure of DNA, revealed to James Watson and Francis Crick exactly 50 years ago as a double helix, is that these bases can pair with each other in specific combinations. That is, A pairs with T, and C pairs with G. These are the complementary base pairs. Therefore, as Watson and Crick realized intuitively, the sequence of one strand of DNA dictates the sequence of the other strand, known as the complementary strand.

These As, Ts, Gs and Cs are arranged in linear sequences on our DNA. Using the analogy of the human genome as a "book of life", the As, Ts, Gs and Cs spell the words and sentences in our genome. Our genes are the sentences, and words in that sentence are made up of three letters each. Three-letter words (or *codons*) code for specific amino acids, which are the molecules that comprise proteins. Some 3-letter words signal the end of a sentence (acting like the period punctuation mark), or the gene, and are called *stop codons*.

How does the cell "read" the sequence in the DNA and convert that information into proteins?[3] I like to use the following analogy. Think of the DNA sequence as an architectural blueprint (fittingly, DNA is often referred to as a genetic blueprint, although in some ways, this term is misleading). This blueprint (gene) contains the information for the construction of a building (protein). However, the blueprint is confined in the reserve section (nucleus) of the public library (cell), and therefore cannot be taken out. So how can the construction workers

[3]For simplicity, we will confine our discussion to genes that code for proteins.

use the blueprint as a guide for their construction of the building, which will be built outside the library (in the cytoplasm, or area outside the nucleus, of the cell)? Simple. The blueprint is first photocopied (*transcribed*) into messenger RNA, or mRNA. This copy of the gene is then transported outside the nucleus into the cytoplasm. In the cytoplasm, the mRNA is *translated* by ribosomes (the construction workers) and the information from the mRNA is converted into a string of amino acids (or polypeptide) that will then make up the protein. Figure 2 diagrammatically shows these processes (transcription and translation).

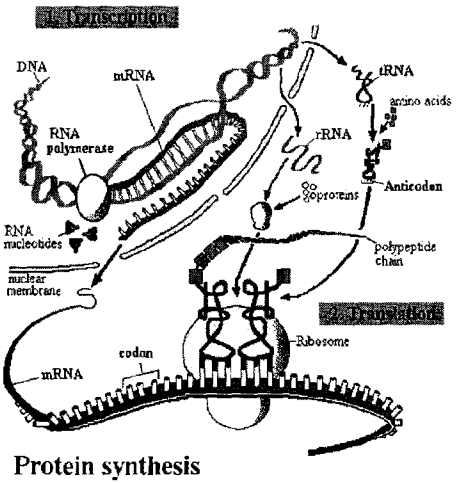

Figure 2. From Gene to Protein. *Source: www.excessexcellence.org*

These proteins then perform a myriad of functions in the cells and in our bodies, including the formation of the very structure of our cells and bodies.

At this point, it is important to stress that the Nature vs. Nurture debate on the roles of genes and the environment in the formation of human beings is essentially over. Molecular biologists now understand that both nature AND nurture are involved in making us what we are. Therefore, we are truly greater than the sum of our parts (genes). We cannot discount the effects of nutrition, upbringing, environment and education in our formation into the sentient, feeling and intelligent individuals that we all are.

BIG DREAMS, BIG DOUBTS, BIG SCIENCE

"I'm surprised that consenting adults have been caught in public talking about it (sequencing the genome)...It makes no sense."

Robert Weinberg, New Scientist
5 March 1987

"The total human sequence is the grail of human genetics."

Walter Gilbert, Science
27 June 1986

The Human Genome Project is now touted as the "Crown Jewel of 20th Century Biology". Yet at its inception, it was criticized by some as "absurd", "dangerous" and even "impossible".

One of the very first "genome dreamers" was Robert Sinsheimer, then chancellor of the University of California (UC) at Santa Cruz. Inspired by UC astronomers who were planning to build the world's biggest telescope, Shinsheimer wanted to do something "big" in his own field of biology. In 1985, he assembled brilliant scientists in the field of genome analysis to brainstorm over a proposal, but the resulting proposal was not feasible and died a natural death. Nevertheless, it had captured the interest of Walter Gilbert of Harvard University, who along with Allan Maxam had developed a method for sequencing DNA. Gilbert then convinced James Watson and Charles DeLisi.

DeLisi is a cancer biologist who was then at the Office of Health and Environmental Research at the Department of Energy (DOE). DeLisi felt that sequencing the human genome was imperative in order that DOE could fulfill its mandate to study the effects of radiation on human health. To study these effects, they would have to study the effects on human DNA, and what changes (or mutations), if any, result from radiation. But how can "changes" be detected when you don't know the "original" unmutated state of the DNA? The DOE felt that the human genome must be sequenced. But others were skeptical. The basic questions regarding the project then were: Should the human genome be sequenced? If yes, can it actually be done?

It is interesting to note that during the heated and intense debates regarding the feasibility and exigency of the Human Genome Project, the National Institutes of Health (NIH) stayed discreetly on the sidelines, and DOE was left to lobby for the project. That the DOE and not

the NIH was promoting the project fueled one of the critics' main concerns, as articulated by David Botstein of the Massachusetts Institute of Technology (MIT), "The fear is not big science so much as bad science." Botstein dismissed the project as "a scheme for unemployed bomb-makers."

Specific objections to the project could be summarized into three main objections: (1) that such a big project would siphon money away from small, hypothesis-driven science; (2) that most of the human genome was comprised of "junk DNA" that did not code for genes, and sequencing such junk would be a waste of time and money;[4] and (3) that sequencing the entire human genome was technologically impossible.

Despite the harsh criticisms and the unwavering skepticism among some of the most respected scientists in the world, the National Laboratories of the DOE began producing libraries of the human chromosomes.[5] Finally, in 1988, the NIH wrested control of the project from the DOE and created a special office for genome research. This drastic change in the enthusiasm of the NIH to go ahead with the project was perhaps prompted by the project having gained congressional funding and having achieved respectability in the scientific community. The National Research Council had bestowed its official seal of approval on the project. Also in 1988, the DOE and NIH signed a memorandum of understanding wherein they outlined their cooperative effort in genome research. The Human Genome Organization (HUGO) of genome scientists was also founded in the same year.

The science of the human genome was not the only concern of HUGO and the Human Genome Project. The scientists were well aware that the sequencing of the human genome entailed various ethical, legal and social issues (ELSI). In 1990, the DOE and NIH established a working group to study these issues. Finally, in 1990, the DOE and NIH presented a 5-year plan to Congress. This marked the beginning of the project, which was initially conceived to be a 15-year project, to be completed in 2005.

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[4] It turns out that this so-called "junk" DNA in fact contains valuable sequences that tell a gene when it should be turned on or off, as well as other biologically important sequences.

[5] The technologies utilized in the sequencing of the human genome will no longer be described here, in the interest of simplicity. "Libraries" here are used to refer to the collections of fragmented chromosomal DNA that are "cut and pasted" (or cloned) into artificial chromosomes. These artificial chromosomes are then used to sequence the parts of the genome that they contain. The separate, fragmented, overlapping parts are then pieced together like a jigsaw puzzle (albeit a puzzle with one dimension, since the sequence is linear).

THE PROJECT GOALS

"Know then thyself, presume not God to scan,
The proper study of Mankind is Man."

Alexander Pope, Know Then Thyself

At the inception of the project, its goals were the following:

1. To identify all the genes in the human genome;
2. To complete the sequence of 3 billion bases of the human genome;
3. To store the human genome information in databases;
4. To develop tools for the analysis of data;
5. To transfer technologies to the private sector;
6. To address the ELSI that may arise from the project.

BIG SCIENCE VERSUS BIG BUSINESS

"The information is so important that it cannot be proprietary."

C. Thomas Caskey, Science
24 July 1987

"The idea of the company is to be a service to the biotech and pharmaceutical industries and to the research community... (the sequence data) would be made available to everyone —for a price."

Walter Gilbert, Science
24 July 1987

"The scientific community thinks this is just a business project, and the business community thinks it's just a science project."

J. Craig Venter, Science
18 June 1999

The 15-year estimate for the project turned out to be an overestimate. By the year 2000, ten years after the plan was presented to Congress, a working draft of the genome had been completed. The single factor that catalyzed the hastening of the completion of the project was the involvement of big business in the project.

Craig Venter, who was originally involved in the project with the NIH, had left the public consortium and teamed up with a private corporation, Perkin-Elmer (which had developed an automated sequencing machine). Venter then immodestly announced that his new company, now called Celera Genomics, would single-handedly sequence the entire human genome in only 3 years, and for only 300 million dollars.[6] Venter's bold challenge spurred a historic race between his company and other private companies sequencing the genome on one hand, and the public consortium on the other. This race was important not only in terms of who would get the credit or the glory; more practically, the race had profound implications on intellectual property rights governing the human genome sequence. The private companies understandably expected a return of investment to come partly in the form of patents on the DNA sequences themselves. The public consortium wanted the genetic information to be within the public domain and freely accessible to everyone. Hence, the race was not so much about glory (although concededly it partly was), but also about economics.

In the end, the two groups finished a working draft at roughly the same time. To show a unified front and avoid a monopoly on the credit and glory for one of the most significant scientific breakthroughs of all time, it was important that the drafts be announced by the groups jointly. With Aristides Patrinos of the DOE acting as intermediary, the NIH group, headed by Francis Collins, and Celera Genomics under Venter agreed to make a joint announcement of the completion of the working draft of the human genome, thus "sharing the glory, but not the credit". This announcement was made in June 2000. However, due to disputes over submission of sequences to the public database GenBank (with Celera refusing to do so), the two groups published the sequence separately but simultaneously, in the journals *Science* (Celera) and *Nature* (public consortium) in February 2001.

WHOSE GENOME IS IT, ANYWAY?

"We ignore the intimate relatedness of all humans when we look for and amplify the minutest distinctions among us, until we find ourselves surrounded by what looks more like our natural enemies than members of our own close-knit species."

Erich Hart, Dawn of a Millennium

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[6] The publicly funded Human Genome Project, on the other hand, was conceived to require about US$200 million a year.

[7] DNA can be recovered from fossils and mummified remains, and hopefully will lead to answers to these questions.

Although this paper will no longer delve into *how* the genome was sequenced, let's see whose genome was actually sequenced. The sequence was derived from a composite genome from several different people. The sequence generated was taken from 10 to 20 primary samples taken from many anonymous donors of diverse ethnic and racial backgrounds. This was done to ensure that the composite genome would be more or less reflective of humanity throughout the world.

WHAT WE KNOW SO FAR

"What is your substance, whereof are you made,
That millions of strange shadows on you tend?"
William Shakespeare, What is Your Substance

The work leading to the completion of the human genome sequence has been accompanied by many revolutionary breakthroughs in genetics and the biological sciences. These will no longer be covered in this paper. The basic information, however, derived from the sequence are the following:

1. The size of the entire human genome is 3.1647 billion base pairs.
2. There are in fact only about 30,000 genes in the genome. Originally, it was believed there would be about 100,000 genes.
3. These genes vary in length and can cover thousands of bases.
4. Less than 2% of the genome actually codes for proteins.
5. "Junk DNA" make up at least 50% of the genome, maybe as much as >90%.
6. Almost all (99.9%) bases are exactly the same in all people.

WHAT WE DON'T KNOW

"A little learning is a dang'rous thing,
Drink deep, or taste not the Pierian Spring"

Alexander Pope, A Little Learning

Like any scientific discovery, the answers come with more (sometimes many, many more) questions than answers. Some questions that come to mind include, if we are only 99.99% different from each other genetically, why are we so apparently different? We are

also only 99% different from our primate cousins, the chimpanzee, yet the leap in intelligence between us is incredible. What is so extraordinary about that 1% difference that underlies our profound differences as a species?

What is the implication of our having so few genes, only two to three times more than the lowly, minute fruit fly? Does it then take only two to three times more kinds of proteins to make a human being than it does to make a fruit fly?

Where is the seat of the human soul, or human consciousness? Can a clone genetically identical to us generated from our own body cells somehow share our memories?

WHAT GENES DON'T TELL US

"I have said that the soul is not more than the body,
And I have said that the body is not more than the soul."

Walt Whitman, A Hub for the Universe

It is also important to stress that while our genetic information is powerfully predictive, able to tell us about our predispositions to disease, and possibly, eventually, our abilities and talents, it does not by itself determine our fates. Genes interact with the environment. A healthy life style can lead to a longer life for an individual with cancer-causing genes, than for another individual who smokes, drinks and leads a stressful life. A good education and loving home environment can mold intelligent and balanced individuals better than numerous genes for IQ.

Finally, knowing all the parts that make us human does not automatically lead to a better understanding of our humanity. Whether "the soul is not more than the body", or "the body is not more than the soul" are questions certainly beyond the realm of science. But even biologically speaking, we are truly greater than the sum of our (genetic) parts.

GOALS FOR THE FUTURE

"If there is anything worth doing twice, it's the human genome."

David Haussler, interview with E. Pennisi
July 2000

"The prevailing view is that the genome is going to revolutionize biology, but in some ways it's overhyped. In the end, the real insights are coming from individuals studying one gene at a time in real depth."

Gerald Rubin, interview with E. Pennisi
May 2000

Upon completion of the working draft and recently, the complete sequence, the goals as envisioned by Francis Collins are:

1. To identify the function of the human genome;
2. To understand how and why genes can cause and/or prevent disease;
3. To speed up the use of genetic information in biomedical research and put it to work.

The above goals are relevant to biomedical applications in particular. The following goals are also recommended by this author with respect to developing countries like ours:

1. To harness the information for its maximal beneficial applications;
2. To promote research that will gather more information from the sequence (data mining);
3. To improve and ensure access to the information and to the benefits to be derived therefrom;
4. To actively address the ethical, legal and social implications (ELSI) that surround the human genome sequence.

BIG SCIENCE, GREAT BENEFITS

"The sequence of the human genome would be perhaps the most powerful tool ever developed to explore the mysteries of human development and disease."

Leroy Hood, Issues in Science and Technology
Spring 1987

There are hundreds to thousands of possible benefits that can be derived from the human genome sequence. These benefits can be summarized under 5 main applications: (1)

medical benefits; (2) microbial genome research; (3) DNA forensics; (4) studies of evolution and human migration; and (5) risk assessment.

MEDICAL APPLICATIONS

With the complete human genome sequence now available, it is foreseen that there will be improved diagnosis of disease, particularly those that are genetic. In addition, the predisposition of an individual to certain diseases can now be detected earlier, given their genetic sequence.

With a greater understanding of disease, it may also be expected that drug design will now be "rational", rather than through trial and error, or through discoveries of effect, without understanding the mechanism of action of the drug. Drugs can now be designed to target the specific genes or gene products that may be responsible for the disease or for control of the disease.

In addition to rational drug design, we are now at the threshold of customized or "personalized drugs", through the development of the field of pharmacogenomics. Knowing what genes or gene products should be targeted and knowing the genetic make-up of the individual who will receive treatment, will allow personalized drug design and delivery.

In the same way, gene therapy can now be efficiently applied, with the knowledge of which genes should be replaced or substituted in a particular individual suffering from a particular disease.

MICROBIAL GENOME RESEARCH

The Human Genome Project has led to the development of many computational and laboratory tools that are applicable to genome research on other organisms, including microbes. Microbial genome research would cover studies into the application of microbes to environmental uses. Microbes, for example, can be used to monitor changes and pollutants in the environment. In addition, they can aid in developing tools or function as the tools themselves, for safe and efficient toxic waste cleanup.

Knowledge of microbial genomes can also lead to the development of methods by which we can protect ourselves from biological warfare and naturally occurring diseases.

DNA FORENSICS

DNA forensics, or the ability to distinguish individuals through their DNA make-up as applied to crime and law, can benefit a lot from the human genome sequence. DNA forensics thus empowered can then lead to the identification of potential suspects at the crime scene and the identification of crime and catastrophe victims when such victims are rendered otherwise unrecognizable by the crime or catastrophe.

In civil cases, DNA forensics can be successfully applied to resolve paternity cases, as well as elucidate other family relations under question.

Finally, the same information from DNA forensics can also be used in medicine to successfully match organ donors with recipients in transplant programs, thus obviating the problem of incompatibility leading to organ rejection.

STUDY OF EVOLUTION AND HUMAN MIGRATION

Now, the genomes of disparate and genetically, culturally, ethnologically diverse people can be sequenced and compared. How are we different from or similar to each other? What about the people who live on the other side of the mountain, on distant shores, on distant continents? And finally, how are we different from, and similar to, the other animals in the animal kingdom, past and present? And to the various humanoid species that came before us?

RISK ASSESSMENT

Finally, in fulfillment of the hopes of the DOE that the knowledge of the human genome sequence can aid them in their mandate to study the effects of radiation on human health, risk assessment is one field greatly empowered by the completion of the project. It is foreseen that the assessment of health damage and risks due to exposure to mutagens, radiation and cancer-causing toxins may be aided by the knowledge of the "normal" sequence. This can then lead to measures aimed at the reduction of the likelihood of heritable mutations.

GREAT BENEFITS AMIDST SERIOUS CONCERNS

"The bravest are surely those who have the clearest vision of what is before them, glory and danger alike, and yet notwithstanding, go out to meet it."

Thucydides, quoted by Francis Collins, Princeton
26 February 1999

With information as powerful as the human genome sequence, we can expect that it can also be used to do harm rather than good. There are serious concerns, all lumped together as ELSI, surrounding the human genome. Initially, these concerns were confined (though already broad and multifarious) to the following: (1) privacy issues and fair use of genetic information; (2) the integration of genetic technologies into the clinical setting; (3) issues surrounding research ethics; (4) the education of the public and of professionals alike.

Later, upon realization of the intricacy of the implications of the human genome, these concerns were expanded to include the following: (5) the impact of knowing the complete human genome sequence on society; (6) the interpretation of genetic variations among individuals; (7) the integration of genetic technologies not only into clinical settings but into non-clinical settings as well; (8) religious, philosophical, ethical and socioeconomic concerns.

Politically, the United States has wrangled with and confronted some political issues arising from the above concerns. Specifically, they have debated and addressed the concerns on genetic discrimination with regard to insurance, employment, legislation and genetic testing in the reproductive sciences (i.e. abortion of fetuses shown to have a serious genetic defect).

Lest we forget that nuclear energy brought us nuclear weapons and pesticides brought us environmental ruin, let us also take some time to reflect upon the many concerns related to the human genome. Though we may bravely go forth to where no one has gone before, let us take care that such bravery is not foolhardy. The benefits of the human genome sequence are upon us. Let us exploit them with the appropriate dose of caution.

TO BE CONCLUDED...

" It's like a book in a foreign language that you can't understand. That's the first job, working the language out."

Frederick Sanger, Science
16 February 2001

The story of the Human Genome Project may be said to have drawn to a close... in some ways. We know that the story of the human genome sequence is really just beginning. Now that we have the complete parts list of the human genome, we need to figure out what each part does, and how each part interacts with the other parts and the whole. To use the analogy of a dictionary, just knowing the genome sequence is like having a dictionary with just a list of words. We don't know yet what each word in that book means. The work required to come up with a completely meaningful "book of life" is more daunting and formidable than the sequencing of the genome itself. This work will entail collaboration amongst geneticists, molecular biologists, biophysicists, clinical physicians, computer scientists, and many, many more experts in various fields. The various areas of study related to the elucidation of this book of life come in many new names never before seen in English dictionaries. Genomics, proteomics, metabolomics, transcriptomics, pharmacogenomics, bioinformatics and immunoinformatics, are just some of the many terms now being bandied about in what is perhaps the next wave of science and technology. It is exciting, if not downright exhilarating, to imagine the world in decades to come, profoundly changed by all these new sciences.

And so, this story for now is at its end. But the real story of the human genome is only beginning.

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Excerpts from the Open Forum

Cynthia P. Saloma PhD, Associate Professor, National Institute of Molecular Biology & Biotechnology, University of the Philippines Diliman

... Health benefits encompasses the areas of therapeutics, diagnostics, disease monitoring, health prevention and related matters. We should look at genetics in the context of all of these areas of human health. Genetics is only one of these areas. There are others. In fact, we are already in the post-genomics era. The science has branched out and diversified into functional genomics, proteomics, and so on. We should not think that genetics will hold all the promises and answer all our questions and solve all our problems. Because if you think about it, the uniqueness of the individual resides in the genotype of the individual. And the phenotype of the individual is determined, not solely by genes but by the way the genes are regulated and expressed as proteins and other molecules in the body. When we look at human health, we should look at it in a more comprehensive context. Therefore, we should not forget to pursue areas of research other than genetics. For example, we should be looking at what would benefit Filipinos the most, the most being our goal. Then, perhaps we should attend to other tests for disease including protein-based tests like immunodiagnostics which would probably be more affordable for many Filipinos.

CLONING & STEM CELL RESEARCH

Mariluz P. Mojica-Henshaw MD PhD

INTRODUCTION

Cloning, in general, is defined as the production of genetically identical organisms. Scientists have used the term cloning to describe a number of different processes by which identical copies of biological material are produced. These processes include asexual reproduction, mitotic division, cloning as a result of recombinant DNA techniques, embryo splitting and somatic cell nuclear transfer. Cloning can thus refer to DNA molecules, cells, or whole plants and animals that are genetically identical.

There are three ways to clone mammals: 1) twinning; 2) the Roslin technique (technique used to create Dolly); and 3) the Honolulu Technique. Twinning, involves the splitting off of cells from an early developing embryo to give rise to two or more embryos. This process occurs normally in nature, with embryo splitting resulting in identical twins in about one out of 75 human pregnancies. These embryos are genetically identical and are therefore clones of each other. In a similar manner, if an 8-cell stage embryo were vigorously shaken causing the cells to separate, each of these cells when implanted into the uterus of 8 separate mothers has the capacity to grow into a complete organism. This technique has been used in the breeding of cattle.

The Roslin technique was developed by Ian Wilmut and Keith Campbell at the Roslin Institute in Edinburg, Scotland. The team began the cloning of Megan and Morag from embryo derived cells in 1995 and the cloning of Dolly from adult mammary gland cells in 1996. Dolly was the first organism ever cloned from an adult cell and sparked public interest in cloning. Her birth proved that cloning of adult animals from adult cells could be done. It also raised the possibility of creating clones of humans.

The technique used to create Dolly is referred to as somatic cell nuclear transfer (SCNT). In this technique (shown in Figure 1), the nucleus from an adult cell is transferred to or fused with an unfertilized egg cell which has been enucleated. In Dolly's case, the source of the donor

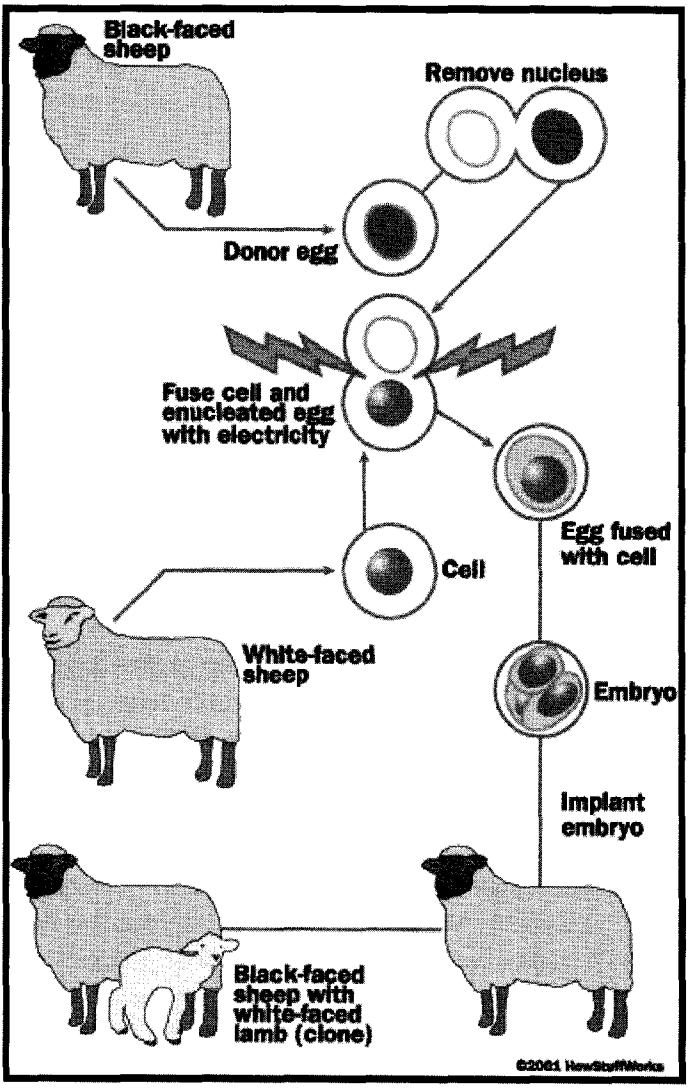

Figure 1a. The Roslin Technique. This method of somatic cell nuclear transfer was used in the creation the Dolly, the first animal to be cloned from an adult cell. (Source of figure: http://www.howstuffworks.com)

aside from the cancer and arthritis, she was apparently normal. Dolly also had full reproductive functions having given birth to 6 sheep produced the normal way.

The third method of cloning mammals is a technique developed by Teruhiko Wakayama and Ryuzo Yanagimachi at the University of Hawaii in Honolulu, Hawaii. They announced in July 1998 that they had produced 3 generations of genetically identical mice. Wakayama also made clones of clones and allowed the original clones to give birth normally to prove that they had full reproductive functions. At the time he released his results, Wakayama had created fifty clones. Wakayama's technique also involved somatic cell nuclear transfer but had a number of modifications from that of the Roslin Technique because of inherent differences in the fertilization process between sheep and mice. With Wakayama's modifications, he had a higher success rate with 2-3 live mice born for every 100 blastocysts transferred. This is more efficient than the Roslin Technique although it is still relatively inefficient. This technique is more reliable and is expected to be employed in the creation of transgenic cattle.

COMMERCIAL APPLICATIONS OF ANIMAL CLONING

There are a number of commercial applications of animal cloning. These include the use of animal cloning as a means of producing superior livestock. This is currently being used in cattle breeding. Another application is in the creation of animals which have been genetically altered to produce human proteins which are medically important (hormones, drugs, and vaccines), in their milk. An example of this is the production of alpha-1-antitrypsin for the treatment of cystic fibrosis and emphysema. This is probably the most beneficial application of animal cloning.

Yet another commercial application of animal cloning is in the area of organ transplantation. There is a current shortage in the availability of organs that are suitable for transplantation. Xenotransplantation, which is the transplanting of organs from one species to another, provides a solution to organ shortage. Animals (pigs in particular) can be genetically modified, through recombinant DNA technology, to express human proteins in their cell surfaces thereby making their organs less likely to be rejected during organ transplantation in humans (Figure 2). Pigs are an ideal alternative source of organs (heart, liver or kidneys) for transplant to humans since the pig's organs are about the same size as that of humans.

To date, at least six mammalian species — sheep, mice, cattle, goats, pigs, and cats have

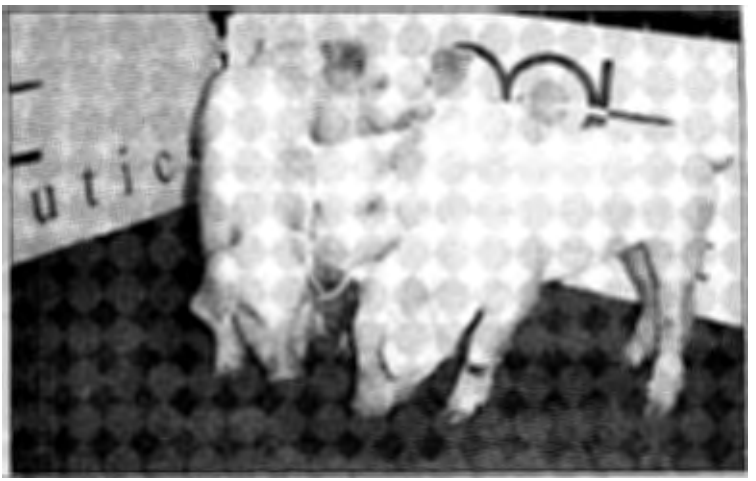

Figure 2. Transgenic pigs developed by PPL Therapeutics in Scotland are genetically modified such that their organs can be transplanted into humans since they do not have both copies of genes that causes rejection. Source of photo: http://www.bbcnews.com

been successfully cloned from adult or fetal cells and one of the questions that have been asked is the possibility of generating genetically identical humans. Human cloning, as used in this paper, refers to all methods of cloning involving human genes and encompasses both human reproductive cloning and human therapeutic cloning.

The National Academies (USA) define human reproductive cloning as "assisted reproductive technology that would be carried out with the goal of creating a newborn genetically identical to another human being". Human therapeutic cloning, on the other hand, encompasses methods involving stem cell research, where stem cells are removed from an embryo, cord blood, bone marrow and peripheral blood in order to produce healthy tissue or organs for transplant into a sick person (Nussbaum, et al Genetics in Medicine, 2001).

As early as December 1997, Richard Seed, a physicist from Illinois, announced that he planned to clone a human being. More recently, there have been at least 3 other groups of researchers and private individuals who have verbalized their intent to clone human beings. These include Severino Antinori, a fertility doctor in Rome; Panayiotis Zavos, of the Andrology Institute in Lexington, Kentucky; and Clonaid, a biotechnology company founded by a religious sect (the Raelians) specifically to produce genetically identical human beings.

In April 2002, at a conference in the United Arab Emirates, Dr. Severino Antinori announced that he had successfully initiated a pregnancy through human reproductive cloning. More recently, in December 2002 and January 2003, Dr. Brigitte Boisselier, the managing director of Clonaid, announced the births of the first human clones. (As of this writing [June 2003], their website claims that there have been 5 successful births of human clones.) Although these claims have yet to be scientifically substantiated and are for the most part regarded with much skepticism, the fact remains that the technology (somatic cell nuclear transfer) that enables the creation of genetically identical human beings has been developed. The three groups of researchers have maintained that at least 10 more such pregnancies are scheduled by the end of 2003.

The manner in which human reproductive cloning will most likely be carried out is through somatic cell nuclear transfer (Figure 3). The principles of the process are very similar to those used in the creation of the sheep Dolly. In this case, donor eggs are enucleated and then fused with the nucleus from an adult cell of the person who wants to be cloned. This fused egg cell will be induced to divide and form an embryo which will then be implanted into the uterus of a surrogate mother.

HUMAN CLONING AND HUMAN EMBRYONIC STEM CELLS

At the present time, most people agree that engaging in human reproductive cloning is unethical and should not be done for whatever purpose. There is a five-year moratorium on human reproductive cloning and a call for a worldwide ban. In the Philippines, we support this ban on human reproductive cloning.

There are, however, two aspects to human cloning. One is human reproductive cloning and the other is human therapeutic cloning. Nussbaum et al. (2001) defines human therapeutic cloning as encompassing methods involving stem cell research, where stem cells are removed from an embryo, cord blood, bone marrow and peripheral blood in order to produce healthy tissue or organs for transplant into a sick person. This is the broader definition of the term.

The term "human therapeutic cloning" has also been used in a more specific sense to refer to the generation of human embryos by somatic cell nuclear transfer and growing these embryos in culture in the laboratory instead of being transferred and implanted in the uterus of a surrogate mother. The main purpose of creating these cloned human embryos is to generate a limitless

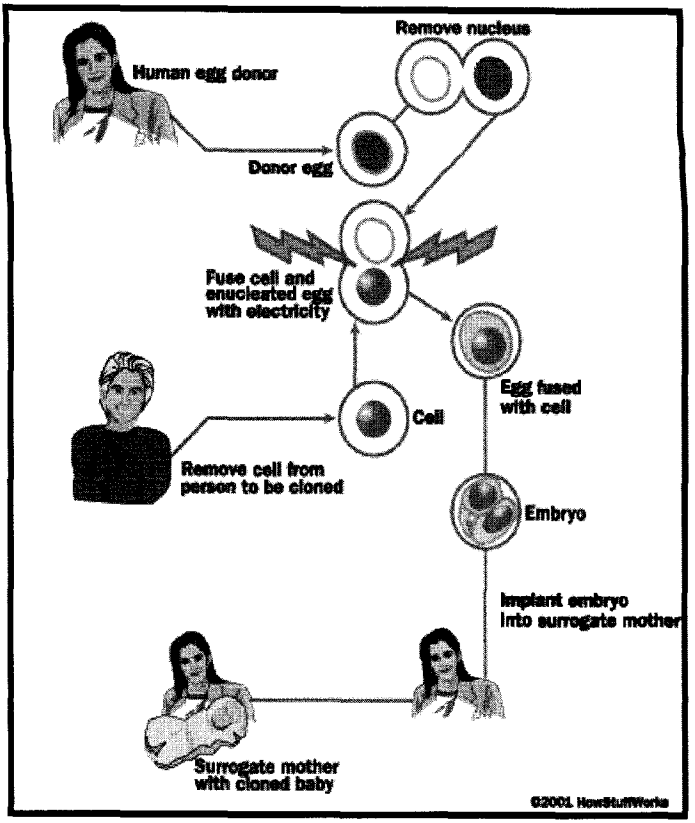

Figure 3. Human reproductive cloning using somatic cell nuclear transfer. (Source of figure: http://www.howstuffworks.com)

source of cells in culture which can be transplanted back to the donor of the nuclei to cure a specific disease without fear of rejection. The cover of the February 2002 Scientific American showed the first cloned embryo in the 6-cell stage (Figure 4) created by researchers at Advanced Cell Technologies, a biotechnology company in Worcester, Massachusetts.

To generate human embryonic stem cells (HESCs), human embryos are grown in culture for 5-7 days until they develop into the blastocyst stage (Figure 5). The blastocyst has an inner cell mass consisting of a cluster of about 150 cells. The inner cell mass is harvested and grown in culture for about 25 days, at which time distinct colonies of identical embryonic stem cells can

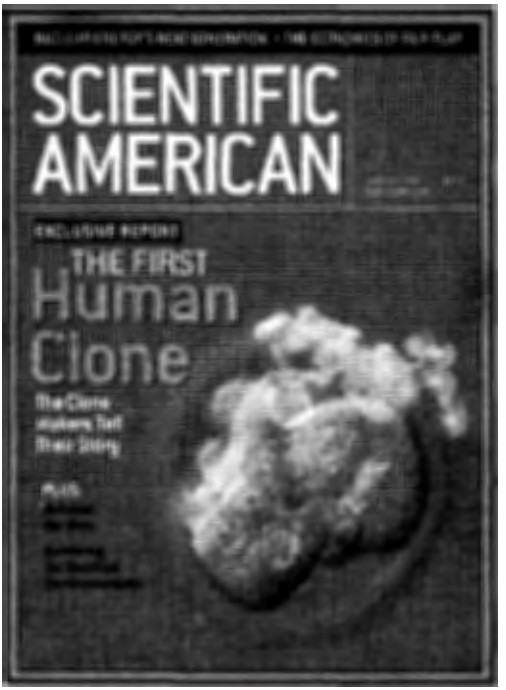

Figure 4. The February 2002 cover of *Scientific American* showing a cloned human embryo in the 6-cell stage. Source of photo: http://www.sciam.com

be derived (each of these colonies is referred to as HESC lines). These HESCs, at the early stages of development, are totipotent, that is, they have the potential to develop into more than 200 different cell types needed for all tissues and organs in the body. Being stem cells, these cells have the capacity to divide and prcliferate and self-renew. At the same time, they can be potentially directed to differentiate into specific mature cell types given the right growth conditions in culture (Figure 6). Thus, it is possible to direct these stem cells to differentiate into liver cells, heart muscle cells, nerve cells, pancreatic islet cells, bone cells and blood cells. This means that stem cells can be used to generate cells that can be used to repair organs and tissues; and diseases like diabetes, spinal cord injuries, Alzheimer's, Parkinson's Disease, heart failure may have potential cures. At present, no cure exists for these diseases.

The main source of human embryos for the derivation of HESCs has been spare or excess pre-implantation embryos created by in vitro fertilization. Aside from being a source of

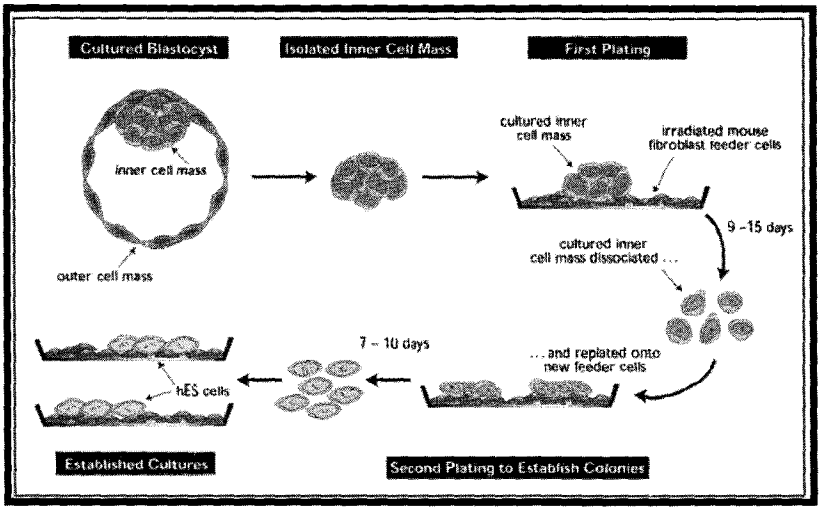

Figure 5. Derivation of human embryonic stem cell lines. Source of image: http://www.biology.iupui.edu

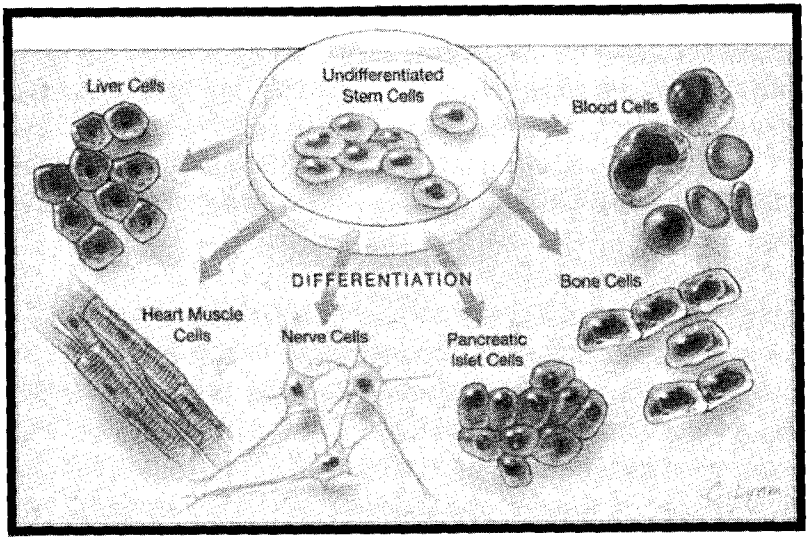

Figure 6. Human embryonic stem cells can have the potential to differentiate into all of the different specialized cell types in the body. Source of figure: Vastag B (2001) Suddenly 64 Stem Cell Lines. JAMA 286:1163.

cells to repair organs or tissues, cultured embryonic stem cells can also be used for drug development and toxicity tests and experiments to study development and gene control. The results of these researches may help explain congenital birth defects, identify genetic/ molecular/ cellular events, and determine methods for preventing these defects. Use of HESCs in drug development and toxicity testing may provide a safer and cheaper model, compared to animal models that are currently in use, since the source of the cells would be human and the screening tests would better mimic the in vivo response.

There are a number of benefits of cloning. These include rejuvenation; the possibility that infertile couples could have children through cloning; the possibility of gene therapy to alleviate suffering resulting from defective genes; the potential to produce organs or tissues to repair or replace damaged ones; and the potential to reduce immunoreactivity of transplants.

ETHICAL CONCERNS

Although there are many potential advantages to using human embryonic stem cells, one of its disadvantages is its being ethically controversial. There are 3 main issues that come to mind: 1) Is it ethical to engage in "human reproductive cloning"?; 2) Is it ethical to engage in "human therapeutic cloning"? and 3) Is it ethical to produce and/or use living human embryos for the preparation of ES cells?

The consensus at present is that human reproductive cloning is unethical and should not be done. The Philippines supports the effort of the worldwide initiative to ban human reproductive cloning.

With regard to human therapeutic cloning, stem cells from the adult bone marrow have been used for at least a decade in the treatment of cancers and leukemias. Stem cells from the umbilical cord and fetuses are also being harnessed for transplants. The use of these stem cells in the treatment of diseases is accepted. The use of stem cells for human therapeutic cloning remains controversial when it involves the use of human embryonic stem cells, because this entails producing human embryos (whether through somatic cell nuclear transfer or in vitro fertilization), then destroying them to obtain embryonic stem cells. There is currently a lot of debate as to whether this area of human therapeutic cloning should also be banned.

The third issue is whether it is ethical to produce and/or use living human embryos for the

preparation of HESC lines. This question is related to whether a fertilized egg should have the same moral status as a baby and what sorts of protection, if any, a human embryo should have and in what ways, if any, it is ethical to use. The answer to these questions depends on one's concept of when life begins. According to Catholic tradition, life begins at conception, when the egg meets the sperm. If this is the case, then the inner cell mass that is harvested from the embryos at the blastocyst stage is not just a mere cluster of cells with no moral status, but a human being with a right to life. A more detailed discussion of the ethical aspects of cloning will be the topic of a separate article. Suffice it to say that some theologians feel that the moral status varies according to the stage of development of the embryo. Some Catholic moral theologians do not consider the human embryo in its earliest stages to constitute an individual entity (Margaret Farley's testimony to the National Bioethics Advisory Commission, 1999). Other religious traditions (Protestant, Jewish, Islam) support a view that does not assign full moral status to the early embryo (Rabbi Elliot Dorff, M. Tendler, L Zoloth, A. Sachedna testimonies to the National Bioethics Advisory Commission, 1999).

Christopher Reeve, the popular American actor who suffered a spinal cord injury after a fall from a horse, is one likely to benefit most from progress in the field of stem cell-based therapies. In his Senate testimony in 2000 he said, "Is it more ethical for a woman to donate unused embryos [for research] or to let them be tossed away as garbage when they could help save thousands of lives?" This is a dilemma between man's commitment to cure the disease and his commitment to protect human life. The Declaration on the Production and the Scientific and Therapeutic Use of Human Embryonic Stem Cells (Catholic Information Network, August 25, 2000) states that "A good end does not make right an action which in itself is wrong."

In the Philippines, the Guidelines on Assisted Reproductive Technology Research of the Philippine Council for Health Research and Development (PCHRD) state that "the intentional creation of human zygotes, embryos or fetuses for study, research and experimentation or for commercial and industrial purposes are prohibited and embryos formed by in vitro fertilization shall be given the respect commensurate to their status." This implies that human embryos cannot be created solely for research purposes and that human embryos created by IVF have rights similar to those of the unborn child. Moreover, the fertility experts who are active in the practice of assisted reproductive technology or in-vitro fertilization (IVF) here in the Philippines, are not interested in carrying out human reproductive cloning nor in doing research involving the derivation of HESCs. Although the possibility of doing research on

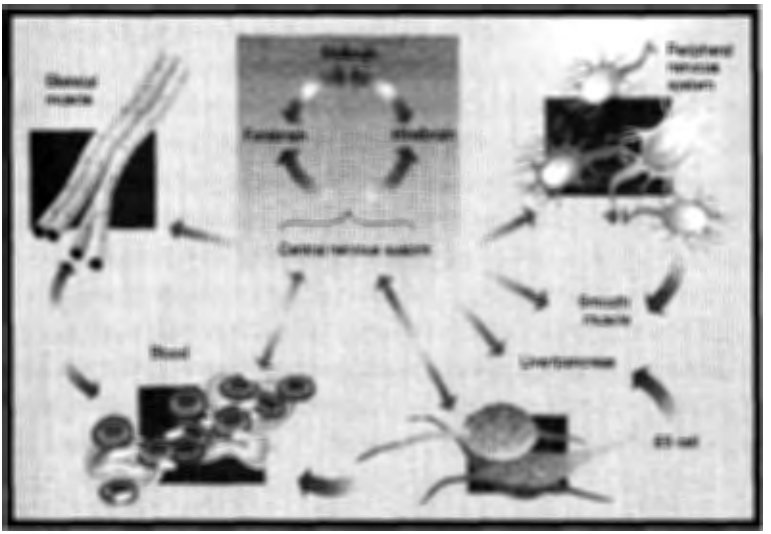

Figure 7. Plasticity of adult stem cells. Source of figure: McKay R (2000) Stem Cells Hype and Hope, Nature 406:361-364.

human embryonic stem cells in the Philippines is nil, the fertility clinics do have frozen embryos in storage. These are a potential source of human embryos for laboratories in other countries engaged in the derivation of HESCs. It may thus be prudent for the Philippines to have clear guidelines on the disposition of such embryos and look into the need and possibility for regulation.

Given that there are a number of ethical issues that have yet to be resolved with regard to the use of embryonic stem cells in human therapeutic cloning, what are the alternatives available? The most promising to date, is harnessing more uses for adult stem cells. Recent studies have shown that they may be more plastic than previously believed. That is, hematopoietic stem cells have been shown to generate not only the different mature blood cell types but may also be coaxed under highly specific growth conditions to become muscle cells, liver cells and/or nerve cells (Figure 7). A few news articles have also featured that direct injection of human adult hematopoietic stem cells directly into the myocardium of two men who have suffered severe cardiac damage have resulted in development of cardiac muscle cells in the area of injury and recovery of cardiac function. The long term effects have yet to be assessed and more studies need to be done.

CONCLUSION

Man has derived a number of benefits from the application of the cloning technology to both animal cloning and human cloning. That human reproductive cloning, including applications of human therapeutic cloning which involves the destruction of human embryos, should be banned at this time cannot be overemphasized. On the other hand, there should be continued support for the use of adult stem cells derived from bone marrow, umbilical cord and peripheral blood for therapeutic purposes and renewed interest in researches that explore the plasticity of stem cells.

ACKNOWLEDGEMENTS

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Invited Commentary on Cloning and Stem Cell Research

Fr. Daniel Paul Kroger PhD, Professor & Chairperson, Theology & Religious Education Department, De La Salle University

I come from the field of moral theology. It is an academic discipline which claims to have some wisdom in doing ethics and in interpreting religious beliefs.

The presentations on the Human Genome and on Cloning articulately pointed out some essential facts for those who are not particularly well versed in the fields of microbiology and/or genetics. The presentations have been helpful in giving accurate information on the current state of biomedical technology with regard to human cloning and the issues associated with stem cell research. This "Round Table" is a wonderful opportunity for all present to share their knowledge—whether one belongs to the government, academia, medicine, science, or one of the social or legal or ethical fields that are associated with human genetics, cloning and stem cell research technologies.

Ultimately, the fundamental ethical issue that is involved in human cloning or stem cell research is a philosophical one. This question cannot be completely answered solely by science or medicine, nor for that matter by theology, philosophy, law or social science. Indeed, this question is very, very troubling and lies at the heart of the topics that have been presented here this morning.

The question is, "What is the moral status of the human embryo and what obligations do researchers face?" Or, to phrase it another way, "What obligations do we have to the human embryo?"

First, I trust we all realize that there is no question that the human embryo, even as a single cell zygote, *is* human life. If it were not human life, it would never become human life. While twinning does occur in the zygote stage, we realize that each one of us is a biologically unique individual. Even if we are only one-tenth of a percent different genetically, from other human beings, we are nevertheless unique. Thus, one of the fundamental questions raised here with regard to the moral status of the human embryo is *what do we owe that embryo in terms of respect?* Is the embryo a

unique individual with the same right to life as a developing fetus? Is it to be accorded the same respect and care as a newborn baby, a mature adult or a senior citizen? The question is a difficult one; many have expressed conflicting, heated views on the matter.

The Catholic ethical approach operates fundamentally along the lines of what ethicists call a "safe-side" argument. This form of argumentation dominates Roman Catholic thinking on this subject. That is why even those who disagree with official Roman Catholic teaching and question its "safe-side" position still take into account the importance of this argument. This "safe-side" argument leads many Catholics, some Protestants and some people of no religious persuasion at all, to argue that because we do not know the moral status of the embryo, we do not have the right to do anything, which will harm it. A few years ago, I summarized the Catholic "safe side" argument in an article which argued that fertility enhancement by means of In Vitro Fertilization (without donor gametes) *can be* a moral choice for informed Roman Catholic couples, despite the official church teaching to the contrary.[1]

Allow me to state my interpretation of the safe-side argument by phrasing it this way: "The lack of moral certainty that the pre-embryo is a person does not justify acting as if it surely was not a person. Rather, the scientific data support the view that profound respect is due the human embryo since it is human life with the inherent potential of becoming a human person." The Catholic Church argues that because the human embryo is human life it is a human person. Ultimately, the "safe-side" argument does not answer the fundamental issue that is involved in human cloning or stem cell research: "Is the human embryo a person?" Instead, the safe-side argument takes a precautionary philosophical stance on that matter; one who accepts that stance ought to act accordingly.

It might help to point out that in any bioethical question concerning the embryo, there are always elements that pertain to the level of biological science. Biology tells that all the cells in an embryo, from its beginnings as single-cell zygote through its development into the ball of cells of the pre-blastocyst stage, have the same, unique genetic code. Some claim that the biological cell mass from the blastocyst stage is simply biological material that is not much different from other cells in any other stage of the process by which we humans develop. Yet, genetics points out that these early cells are different and have the capability of developing, given the right conditions,

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[1] *Daniel Kroger, "In Vitro Fertilization for Fertility Enhancement," MST Review, Vol. 3:1 (1999), p. 48-70.*

into another human being who is going to be only one-tenth of one percent different from you or me.

The biological aspect seems to point out that there is some value in the so-called safe-side argument. Nevertheless, the biological aspect also brings to the fore, other questions. Why are so many fertilized human ova simply lost, wasted, washed out through the menstrual flow? Why don't they implant? Why is this? For those who hold traditional views that humans have a physical body and a rational soul, still more questions are posed by biology. Does God put a soul in each human embryo and then let it go to heaven? The biological evidence also indicates that the moral status of the embryo in its earliest stages is not as certain as that of a person. Identical twinning can occur. Does the soul twin too?

There is also a relational aspect. Many argue that human dignity cannot be evaluated solely on the basis of biology. That is true, but it is also important to point out that there is more to human dignity than the relational. There is more to our value as persons than whether we can relate to someone else or not. That is why the autistic child still has dignity. That is why senile senior citizens are still treated with respect, even though they can no longer remember the names of their immediate relatives or spouses. There is a relational aspect that goes with all human life, we need to remember that. But the relational aspect does not constitute the totality of human value. We need to remember that.

Another element that should be pointed out in this process of embryonic development is the potentiality that lies within this embryo. The embryo, given a chance, the right conditions, a little luck, and proper genetic make-up, can develop into a full-grown adult human being. That is a potential that somatic cells, say the epithelial cells that one finds in the mouth cavity, do not have. The somatic cells do not have that possibility and yet the embryo does.

A fourth aspect, equally important, of the human embryo, is the symbolic factor. For those of you who are physicians, during your human anatomy course in medical school, you knew that a certain respect should be paid to the cadaver you were dissecting. I trust that this was carefully drummed into you as young medical students. Those of us who are not in the medical field are more familiar with animal anatomy—we dissected fetal pigs and cows, and things of that nature. We may crack jokes about animals we dissected, but we know we must give special respect to the human cadaver. A person whose body is mutilated in war should still be buried with respect. Such practices indicate that the human

body constitutes something deeply symbolic for us as human beings. Like stepping on your wedding ring and smashing it in front of your spouse, there is something of a similar symbolic nature when you are dealing with the human embryo, the human fetus, and the human cadaver.

We need to keep some of these ideas in mind. Many of us in the field of ethics sometimes question the designation of the term "therapeutic embryonic cloning," or "therapeutic embryonic stem cell research." We might ask "therapeutic for whom?" Such therapeutic cloning would be potentially good for the patient. Is it therapeutic to the embryo? No. "Patay kaagad." Do you see the difference?

If we are to follow the safe-side argument, we need to think about the terminology we use—whether *therapeutic* is indeed the right term to use or whether it is a euphemism to hide behind. Note the complexities? That is what I am trying to raise. It is not just a question of life or when life begins. We know that and we know that conception is a process, not just a single moment.

The ethical, the legal and the social implications are grave. The safe-side argument used by the Roman Catholic Church is but one argument. Some are committed to the absolute inviolability of every embryo. I questioned that also. I do not think that the embryo is absolutely inviolable. There may be sufficient reason to make determinations that will indeed be detrimental to the embryo for the purpose of some other good. This is where we need to proceed with great caution. Research projects on human embryos need to be reviewed. Social scientists, lawyers, doctors, microbiologists, geneticists—all need to work together to try to work out some consensus that will allow for socially acceptable, understandable, scientifically-accurate, wise decisions on projects involving human embryos.

A paper from the University of Louvain (in Belgium) is worth mentioning. This is the same university which first came up with the idea, now enshrined in the Catholic tradition, that human life begins at conception. The idea was a 19th Century ethical argument. Now, this same catholic university founded in 1450, has posted a page on its web site concerning fundamental approaches for the utilization of human stem cells in research and their applications in medical therapy. There is a lot more stuff on the Internet.

I invite you to ask questions about the ethics of stem cell research, in vitro research and so

forth. Just ask your questions with a sense of respect for your colleagues. The social scientist, the lawyer, the ethicist, the medical people, and the biologists all have something to offer on this question. The questions arising from genetics and biotechnology raise issues about who we are as human persons.

Excerpts from the Open Forum

Virgilio Novero MD, Associate Professor, Department of Obstetrics and Gynecology, UP College of Medicine, University of the Philippines, Manila

. . . The only aspect of cloning that intersects with stem cell research is cloned embryo stem cell research. So in fact, in our discussions here, we should not even be talking about non-cloned embryo stem cells. If our topic was purely on cloning, we should not be talking about non-cloned stem cells.

. . . I would also like some clarification on the idea of "conception" as mentioned by Fr. Kroger and Atty. Ochave. We all recognize the value of life from "conception". Scientifically however, conception does not have a very clear definition. While we have very clear scientific definitions for fertilization, embryo development, cleavage, implantation, etc., conception is still a very vague term.

. . . I would also like to react from the point of view of a clinician practicing in-vitro fertilization. First of all, I would like to state that I am a devout Catholic as are most of the IVF doctors in the Philippines. We know our limitations. In fact, the basis for our choice to practice in-vitro fertilization here in the Philippines is that we know when to stop and up to what point we can go.

... There were a few who may unfortunately have put IVF in the same category as cloning. We recognize the controversies involved in IVF. These include the disposal of extra embryos, the involvement of third parties, the use of donor embryos or donor eggs and donor sperms and surrogacy, all of which are not practiced here in our country. It has to be emphasized that IVF and cloning are entirely different entities with a few common characteristics.

Dr. Mojica-Henshaw, Lecturer on Cloning and Embryonic Stem Cells

. . . I think it all boils down to the fact that we define cloning as the production of genetically identical cells and organisms. It includes anything that can divide by itself and since stem cells are highly proliferative, then we consider that as part of therapeutic cloning.

It was more of a blanket definition. Somatic cell nuclear transfer or the cloned embryo was specified as part of either human reproductive cloning or human therapeutic cloning according to the original intent or purpose. Human cloning, as we defined it here, is not just the creation of an entire, new human individual but covers even just the use of human genes as well. More specifically, cloned embryos fall under human reproductive cloning.

Dr. Monzon, Lecturer on Ethical, Legal and Social Issues

. . . In response to Dr. Novero's question, IVF is related to cloning because spare IVF embryo cells are used as source stem cells. We are not, however, saying that IVF and cloning are equal. In in-vitro fertilization, it has to be acknowledged that a baby is created without the sexual act or the conjugal union of the husband and the wife, which makes it immoral.

For Catholics, there is a very nice and informative encyclical which I recommend, "Donum Vitae", an "Instruction on Respect for Human Life and Its Origins and on the Dignity of Procreation". The general teaching is that if reproductive technology becomes a substitute for the conjugal act, meaning that the conjugal act no longer becomes necessary for a couple to have a baby. That is immoral. If it helps or improves the chance for the realization of a baby, then it is assisted reproductive technology.

Dr. Renante Bases, Komisyon ng Karapatang Pang-tao (Commission on Human Rights)

I am certainly glad that I am with the "pro-life" group. I am happy that the draft demonstrates absolute observance of human rights. My comments will focus on the human rights implications of (1) stem cell research and (2) in-vitro fertilization as practiced in the clinics.

The Philippine Commission on Human Rights defines human rights as the enduring and inalienable right to life, to dignity and to development. Now, using embryos in the stem cell research would interfere with "development", thereby violating both the right to life and the right to development. The normative content of this may be found in the Universal Declaration of Human Rights and in the International Convention of Civil and Political Rights of the 1987 Philippine Constitution. If the right to life of the embryo has been violated, it constitutes murder. As I understand, the process of IVF involves the initial selection of 24 ova,

which are fertilized and allowed to grow. From these 24, 3-4 healthy embryos are selected. What then will happen to the 20 other embryos? I understand that these may be stored, frozen in nitrogen for future use. But I don't think these clinics are going to keep these embryos in storage for very long. They eventually dispose of these. And that is mass murder of 20 embryos. It is a blatant violation of human rights and the right to life.

Another key issue is advocacy. It is very important to educate and inform the public, the academe, the officials, the doctors, the professionals, the lawyers about this topic because we must admit, many know very little about the human genome and the implications of the Human Genome Project.

DNA Forensics, The Human Genome Project and Human Rights

Maria Corazon A. De Ungria PhD

INTRODUCTION

'The Human Genome Project has been an amazing adventure into ourselves to understand our own DNA instruction book, the shared inheritance of all humankind'

Francis S. Collin

The Human Genome Project provides us with wonderful opportunities to get to know ourselves and those around us. The Project's scope was not only limited to sequencing the entire human genome, but included animal, plant and microbial genomics as well as environmental research. Overall, the Human Genome Project has accelerated the pace of scientific research, making use of the information generated and the tools developed, to improve our quality of life.

One field greatly influenced by the Human Genome Project is forensic science, particularly in the field of forensic DNA technology. Forensic science is defined as 'the application of scientific principles and technological practices to the purposes of justice in the study and resolution of criminal, civil and regulatory issues' (American Academy of Forensic Science 2003). Advances in DNA technology has led to methods of human identification that surpassed earlier forensic techniques, e.g. fingerprint analysis and serotyping, in terms of sensitivity, specificity and robustness. The use of modern DNA technology has revolutionized human identification, particularly in criminal investigations (Moenssens et al. 1995; Swanson et al. 1996; Asplen 1999; Kluger 1999), law enforcement using criminal databanking (Asplen 2000; Guillen et al. 2000; Ban 2001; Schneider and Martin 2001), human rights advocacy through exoneration of convicted criminals using DNA evidence (Huff 2002), resolution of disputed parentage cases (Bjerre et al. 1997;

Carracedo 2002; De Ungria et al. 2002; Morling et al. 2002), and identification of human remains in mass disaster cases and those found in unidentified graves (Whitaker et al. 1995; Corach et al. 1998; Miller 2001; Calacal et al. 2003).

The ability to identify persons using forensic DNA tests relies on the uniqueness of the total genetic make-up of each individual (except identical twins), which is contained in most cells. A person's DNA profile serves as his 'DNA print', which may be used to identify him and/or trace his activities, e.g. crime scene evidence. Current techniques to generate and analyze DNA profiles are capable of analyzing even minute amounts of crime scene evidence, hence the immense impact of DNA technology in forensic investigations. Unlike proteins, DNA is very stable and may be isolated from living and deceased individuals as long as biological samples are not exposed to adverse environmental conditions and/or microbial contaminants that can degrade DNA. Many laboratories also use automated methods of detection, which makes DNA testing more routine and less prone to human error through computer-assisted analysis.

Currently, there are four DNA testing laboratories in the Philippines, namely: the DNA sections of the National Bureau of Investigations (NBI) and the Philippine National Police (PNP), the Institute of Pathology, St. Lukes Medical Center (SLMC) and the DNA Analysis Laboratory, Natural Sciences Research Institute of the University of the Philippines, Diliman (UP-NSRI). The routine operations of the four laboratories differ because of variation in their objectives and mandates. NBI and PNP concentrate on criminal cases due to their roles in law enforcement, albeit both sections accept civil cases, provided the proper requirements are met. SLMC only accepts paternity cases for private clients following hospital policy of non-involvement in high-profile cases. UP-NSRI undertakes forensic researches on validation of methods, quality assurance procedures and training since the laboratory belongs to the academic community of the University of the Philippines. In addition, UP-NSRI accepts civil and criminal cases as part of its extension work to the community. The types of cases accepted by each of the laboratories are listed in Table 1.

This paper presents a basic background of forensic DNA testing, the current state of the technology in the Philippines and a discussion of areas wherein policies and legislation are needed to further maximize the utility of forensic DNA as a powerful tool for human identification, whilst respecting the fundamental human rights of individuals and communities alike.

Table 1. Cases accepted by forensic DNA laboratories in the Philippines

Cases	NBI	PNP	SLMC	UP-NSRI
Criminal Cases	Yes	Yes	No	Yes
Civil Cases	Yes	Yes	Yes	Yes
Mass Disaster	Yes	Yes	No	Yes

DNA FORENSICS

The method of fingerprinting an individual using his DNA, termed 'DNA fingerprinting', was invented by Sir Alec Jeffreys in 1984 at the University of Leicester while he was studying the human myoglobin gene (Jeffreys et al. 1985). The technique developed, called Restriction Fragment Length Polymorphism (RFLP), utilizes a special class of enzymes (restriction enzymes) that cut human DNA based on specific recognition sequences located on the target DNA. These recognition sites may be used to analyze variations in length (length polymorphism) or sequence (sequence polymorphism) in different individuals. Length and/ or sequence polymorphisms are reflected in banding pattern variations of samples from different sources.

However, due to the requirement for considerable quantities of intact, high molecular weight human DNA and the long turn-over time from sampling to generation of RFLP-DNA test results, other less tedious techniques were developed. These include the reverse dot blot methods for the characterization of human leukocyte antigen DQ (HLA-DQalpha) and other polymarkers namely low density lipoprotein receptor (LDLR), glycophorin A (GypA), hemoglobulin G gammaglobulin (HBGG), D7S8 and group specific component C (GC); sequencing of mitochondrial DNA; and amplification of non-coding regions of the human chromosome, e.g. Variable Number Tandem Repeats (VNTRs) and Short Tandem Repeats (STRs) via the Polymerase Chain Reaction (PCR). A comparison of these markers is summarized in Table 2.

Table 2. DNA markers used in forensic DNA Analysis

Characteristics	HLA-DQ and PM	Mitochondrial DNA	VNTR	STR
Target DNA	nuclear	mitochondrial DNA	nuclear	nuclear
Number of copies per cell	2	>1000	2	2
Number of genetic markers	HLA + 5 PM	2 sites	>10	>40
Size of DNA fragment	200-300 base pairs	400 base pairs	400-1000 base pairs	100-400 base pairs
Detection method	PCR and slot blot hybridization	Sequencing & laser detection	PCR and DNA hybridization	PCR and silver stain or laser detection

Of these, forensic DNA testing using STRs is currently the method of choice for most forensic DNA laboratories worldwide (Butler 2001) including those in the Philippines, because of the relative ease of use, shorter time for analysis and less stringent requirement for high quality DNA. STRs are characterized by 2-6 base pair (bp) core repeat units and allele size range of approximately 100-400 bp. Smaller target fragments are more easily amplified via the Polymerase Chain Reaction (PCR), are suitable for amplification from minute and/or degraded DNA sources and provide more interpretable output which is particularly important in analysis of mixed samples, e.g. vaginal smears in sexual assault cases. Each laboratory in the Philippines tests from 9-20 STR markers in casework analysis depending on the amount and state of biological samples submitted and the purpose of the analysis. The four DNA forensic laboratories in the Philippines use different sets of STR markers, reaction conditions, instrumentation and detection systems.

In addition, the UP-NSRI DNA laboratory is also working on methods for typing mitochondrial DNA, which while not as discriminating as STRs, can be invaluable in analyzing skeletal remains from disaster sites or those collected from unidentified graves (Holland et al. 1993; Goodwin et al. 1999; Stone et al. 2001).

THE HUMAN GENOME PROJECT

Since its inception in the mid-1980's, forensic DNA technology developed rapidly, feeding from information and technology that came about because of the Human Genome Project. The availability of a human genome reference sequence provides an unprecedented biological resource from which an unlimited amount of information may be sourced. Information include identities of putative polymorphic genetic markers for development of new systems for human identification and sequences which may be used for the synthesis of human-specific probes. For example, 50,000 dinucleotide STRs (2 bp) and 300,000 trinucleotide (3bp) and tetranucleotide (4bp) STRs have been identified (Li 1997). Putative human-specific DNA probes targeting the flanking regions of these genetic markers are identified based on the absence of sequences that are homologous with other organisms. These DNA probes identified 'in silico' are then tested in the laboratory against a wide range of non-human DNA to evaluate its specificity for human DNA. Moreover, the availability of genomic sequences of other organisms allow direct comparisons of genes in humans and other animals thus providing remarkable insights into human evolution.

In addition, studies on human diseases and their association to alterations in the human genome sequence have given us a better understanding of human mechanisms to preserve normal bodily functions. At the population level, the effect of mutations and natural selection on the viability and distribution of certain gene types (alleles) have significant effects on the statistical analyses of forensic data (Triggs and Buckleton 2002). Hence, the association of certain DNA sequences with diseases or gene functions excludes these as useful markers for forensic purposes (Council of Europe 1991). This may be one reason why many laboratories have stopped using HLA-DQ alpha and Polymarkers for forensic applications.

One goal of the Human Genome Project which has significantly contributed to the advancement of forensic DNA technology is the study of human genetic variation within and across populations. Interestingly, 99.9% of human genomic sequence is similar (Office of Science US Department of Energy 2003). This confirms genetic data in many modern populations (Butler and Reeder 1997) that show similar gene types amongst people of the same race, e.g. Caucasians, Africans and Asians. This is important in making basic assumptions for statistical evaluations of forensic data. For example, the frequency of the DNA profile generated from casework evidence is determined using reference databases relevant to the case at hand (Evett and Weir 1998).

The remaining 0.1% of human genome sequence estimated to vary amongst individuals includes polymorphic regions, e.g. VNTRs, single nucleotide polymorphisms (SNPs) on mitochondrial and nuclear DNA and STRs. This portion of the human genome is the heart of forensic research, in its goal to develop new and more sensitive systems for human identification.

In addition, powerful analytical and computational tools were developed to complete the Human Genome Project, which have considerable impact on forensic DNA technology, particularly in the areas of DNA sequencing, multiplex DNA fragment analysis, population databanking and statistical analyses of forensic data.

HUMAN RIGHTS

Ethical, legal and social issues have been raised in forensic research and the conduct of forensic DNA tests. Clearly, misuse of genetic material and information derived from studying human DNA has ethical implications for individuals and communities. Article 10 of the Universal Declaration on the Human Genome and Human Rights, states:

'No research or research applications concerning the human genome, in particular in fields of biology, genetics and medicine, should prevail over respect for human rights, fundamental freedoms and human dignity of individuals or where applicable, groups of people'.

Focus on ethical issues in forensic DNA technology is underscored by its significant contribution in assisting criminal investigations, and to some extent, in reforming the criminal justice system through post-conviction DNA tests. DNA has unique properties that differentiate it from the earlier types of physical evidence, e.g. fingerprint analysis and serotyping (Kimmelman 2000). Firstly, DNA is predictive for sensitive information, e.g. predisposition to certain types of diseases. Secondly, methods are available to amplify minute amounts of DNA contained in trace evidence, e.g. sloughed skin, hair strand, perspiration from fingerprints, which has significantly increased the types of crime scene evidence that may be submitted to the laboratory for testing. Thirdly, DNA profiles are shared amongst biological relatives hence the DNA profile of a convicted offender also contains incomplete information about his non-offending relatives. Hence, DNA holds a special place as a powerful and sensitive tool in human identification, and human rights

concerns must be addressed for the effective use of the technology at the service of society.

Major areas of ethical concern in the use of forensic DNA technology include 1) acquisition of informed consent prior to the collection of biological sample, 2) privacy and confidentiality of genetic information, 3) storage and destruction of stored DNA/bodily tissue/ relevant genetic records particularly those in criminal databases, and 4) unauthorized/illegal third party access to DNA and relevant genetic records.

Human samples are required for any one of the following reasons: 1) for the conduct of DNA tests, e.g. comparison of suspect DNA with crime scene evidence or comparison of DNA of alleged father and child in disputed parentage cases; 2) for the establishment of population databanks to study the distribution of polymorphic gene types in a given population, and in mass disaster identification; and 3) for the establishment of databanks of convicted offenders and crime scene samples which are used in law enforcement.

INFORMED CONSENT FOR PRIVATE AND CIVIL CASES

In all situations, it is important that informed consent is obtained prior to collection of any biological sample as stipulated in Article 5b of the Universal Declaration on the Human Genome and Human Rights:

'In all cases, the prior, free and informed consent of the person concerned shall be obtained. If the latter is not in a position to consent, consent or authorization shall be obtained in the manner prescribed by law, guided by the person's best interest'.

The process of obtaining informed consent varies depending on the purpose of the collection. For example, in civil or private disputes, e.g. questioned parentage cases or identification of human remains, it suffices that all parties involved willingly submit themselves for sampling. The informed consent of the legal guardian in behalf of a minor must also be obtained prior to the conduct of DNA tests.

In the Philippines, laboratories hold pre-testing orientations with all parties concerned to inform them of the procedures, limitations and significance of DNA testing, as well as to answer questions. In these interviews, relatives, friends and lawyers, if any, may also be present. Testing is conducted upon the request of one or both parties, with or without a Court Order.

INFORMED CONSENT FOR POPULATION DATABANKING

The development of automated systems for the simultaneous analysis of different STR genetic markers has paved the way for large-scale population databanking efforts in Europe (Martin et al. 2001; Schneider and Martin 2001), US, Iceland and New Zealand (Harbison et al. 1999). Population databanks are important in studying the utility of a genetic marker for forensic casework and in generating frequencies of alleles in a given population which are needed for statistical analyses of forensic data. Individuals volunteer their samples for the establishment of population reference databases for forensic applications.

In the Philippines, the National Ethics Committee organized by the Philippine Council for Health Research and Development of the Department of Science and Technology has issued National Guidelines for Biomedical/Behavioural Research for the conduct of scientific research involving human participants (National Ethics Committee 2000). In the said document, specific guidelines on obtaining informed consent to protect the rights and welfare of human participants were provided. Sections relevant to population databanking include:

'The rights and welfare of human participants in medical research shall be adequately protected by a legally effective informed consent which contains a fair explanation of the research proposal in a language the participant understands, including the purposes of the research and the identification of any experimental procedure (Section A1) and assurance that any inquiry concerning the procedure will be answered at any time during the research (Section A2). Informed consent shall be obtained from all human participants of research or from his/her authorized representative (Section B1).'

The rights of indigenous communities to their genetic resources, which include the DNA of the people, are protected by virtue of Republic Act 8371 or The Indigenous Peoples Rights Act (1997). It states:

'Access to biological and genetic resources and to indigenous knowledge related to the conservation, utilization and enhancement of these resources shall be allowed within ancestral lands and domains of the Indigenous Cultural Communities/ Indigenous Peoples only with a free and prior informed consent of such communities, obtained in accordance with customary laws of the concerned community (Chapter VI Section 35).'

To date, SLMC and NBI have constructed population databases using data generated

from casework samples. NBI and UP-NSRI (Halos et al. 1999; Tabbada et al. 2002) use anonymized samples from the Philippine Red Cross (convenience sampling) and from volunteers who agree to provide samples for databanking and research purposes. In addition, the members of the UP-NSRI DNA lab collect samples from various indigenous communities. Theoretically, some tribal communities may form 'pockets of populations with distinct genetic characteristics' or subpopulations due to their geographic isolation and/or cultural practices with respect to formation of families, thus affecting the genetic composition of a given community. Studying the genetic variations within subpopulations is essential in applying the appropriate statistical principles for the correct interpretation of forensic DNA typing results (US National Research Council II, 1996). In all instances, informed consent of all human participants is obtained prior to sample collection.

INFORMED CONSENT FOR CRIMINAL CASES AND INCLUSION IN CRIMINAL DATABASES

Different legislations for the collection of samples from suspects and convicted offenders exist worldwide (1998; Harbison et al. 1999; Schneider and Martin 2001). In some countries such as the United Kingdom (UK), the United States (U.S.), Austria, Germany, Finland, Denmark and Switzerland, samples are collected from individuals who have been arrested for serious crimes such as sexual assault and homicide, although the types of crimes included vary across countries (Moenssens et al. 1995; Schneider and Martin 2001). When a subject, e.g. a man suspected of committing a serious crime, refuses to submit himself for sample collection, police investigators are permitted by some legislation, e.g. New Zealand Criminal Investigations (Blood Samples) Act (Harbison et al. 1999; 2002a), to apply for a compulsion order from the High Court. The Court will only issue a compulsion order if the police officer can show reasonable cause. This is particularly important because judgment of the existence of a reasonable cause for collecting a sample from a suspect is the Court's jurisdiction. Moreover, compulsion orders are issued only for 'serious offences', which are defined by law. Once granted, the compulsion order allows authorized individuals 'to exert reasonable force' in collecting biological samples. The argument is that an individual suspected of committing a serious crime with reasonable cause has forfeited some of his rights. He must be subjected to DNA tests to evaluate his involvement in a serious crime and convicted if found guilty, for the protection of the community. This is a clear application of Article 9 on the Universal Declaration on the Human Genome and Human Rights:

'In order to protect human rights and fundamental freedoms, limitations to the principles of consent and confidentiality may only be prescribed by law, for compelling reasons within the bounds of public international law and the international law of human rights.'

Interestingly, the DNA sections of NBI and PNP have not encountered a criminal case wherein a suspect refused to provide a sample. Routinely, samples are collected in these laboratories in the presence of legal counsels for the best interest of concerned parties.

To date, a legislation-backed national strategy, which outlines the role of various government agencies, e.g. local health and police units, crime scene investigators, health professionals and forensic scientists, is lacking in the Philippines. Firstly, inadequate collection and storage procedures limit the utility of forensic DNA test results by delaying criminal investigations, which may then lead to the loss of important evidentiary samples. Secondly, types of crimes wherein sample collection is made mandatory need to be defined to insure that costly DNA tests are conducted on relevant cases. For example, samples in drug trafficking cases do not normally contain biological material needed for the conduct of DNA tests. Thirdly, the possibility of 'using reasonable force' in cases where suspects refuse to provide samples even if ordered by Court must also be clarified. It has been argued that the collection of biological samples from a suspect violates his constitutional rights against self- incrimination as stated in Article III Section 17, Philippine Constitution (de Leon 2002) which states:

'No person shall be compelled to be a witness against himself.'

Legal arguments have been made to support or negate this claim. And although the Supreme Court has ruled in favor of the admissibility of DNA evidence in Court in People of the Philippines vs. G Vallejo (2002b) the question of the use of 'reasonable force' during sample collection must be addressed. Is the use of 'reasonable force' permissible in the Philippines? In the same case, the Accused claimed that he was tortured by policemen during interrogation. Already, there have been studies that report various forms of torture of suspects and inmates by investigating officers to obtain a confession and/or inflict punishment (FLAG and FIDS 2003). Claims of torture, if applied to the collection of biological samples 'using reasonable force', could provide obstacles for the admissibility of DNA evidence in Court. To protect the rights of the individual, the Criminal Investigations (Blood Samples) Act of New Zealand placed rigorous requirements on police investigators collecting blood samples (Harbison et al. 1999). It is likely that similar precautionary measures might have to be incorporated in the appropriate legislation in the Philippines.

Besides using an individual's DNA profile in a current investigation, many countries have enacted legislation for the incorporation of offender and crime scene profiles into DNA

databases for the purpose of criminal investigation. Unlike population databanks, criminal databases contain the DNA profiles of convicted offenders of certain types of crimes (convicted offender database) and crime samples (crime scene database) to facilitate the early detection, arrest and conviction of offenders (Harbison et al. 1999). In addition, criminal DNA databanks are expected to act as a deterrent to recidivism (Moenssens et al. 1995). For example, the U.S. National DNA Databank called CODIS (Combined DNA Index System) contains DNA profiles of offenders convicted of certain serious crimes and crime scene evidence from all 50 states, albeit states vary in the types of crimes that are included in the database. From 1998 to January 2003, the US Convicted Offender Database contained more than a million DNA profiles. In New Zealand, the success rate of linking crimes to individuals and crime to other crimes is 32% and 14%, respectively. In a one-year period (1998-1999), investigations of more than 300 unsolved crimes were completed using offender and crime scene databank hits. Likewise, the UK reported over 700,000 profiles in its criminal database by the end of 1999, with around 700 matches achieved per week (Martin et al. 2001). The utility of criminal databases in identifying suspects and linking crimes has had considerable impact on the investigation and resolution of many crimes, particularly homicides, sexual offenses and burglaries (Harbison et al. 1999).

UK legislation, enacted in 1995, is the most permissive to date and allows the collection of samples from all suspects who had been arrested for 'any recordable offence' (Guillen et al. 2000), which is generally understood to be a crime that could attract a custodial sentence (Martin et al. 2001). Apparently, including the DNA profiles of suspects increases the capability of criminal databases to link crimes and persons because of the recidivistic nature of many offenders. Databanking shows that many individuals convicted of major crimes were linked to earlier commission of minor offenses. Hence, earlier convictions of these individuals would have prevented the commission of the more serious crimes. The pace of investigation is accelerated leading to considerable overall government savings due to a decrease in investigation, prosecution and incarceration costs brought about by early resolution of the case (Martin et al. 2001). However, there is the danger that databanking empowers police officers to conduct 'investigative arrests'. For example, if the DNA profile from an evidentiary sample matches the DNA profile of an individual who was never convicted of a crime but whose DNA profile was retained in a criminal database, police officers in the UK have the power to obtain a sample from the person to further their investigation. This in turn may result in people being investigated, and potentially arrested on less than probable cause. Clearly, if proper guidelines are not put in place, the power of police officers to conduct 'investigative arrests' may potentially lead to discrimination based on 'genetic characteristics'.

Such a situation is not in keeping with Article 6 of the Universal Declaration on the Human Genome and Human Rights which states:

'No one shall be subjected to discrimination based on genetic characteristics that is intended to infringe or has the effect of infringing human rights, fundamental freedoms and human dignity.'

To date, there is no criminal database in the Philippines. However, NBI, PNP and UP-NSRI have stored DNA samples and records of suspects and convicted offenders involved in various cases submitted to these laboratories. Hence, there is a need to formulate guidelines for the proper handling and storage of genetic samples and DNA records of these suspects, until the appropriate legislation is enacted in the Philippines.

In addition, the impact of DNA evidence on criminal investigations (Huff 2002) highlights the need for strict observance of quality assurance and proper analytical procedures in generating and interpreting DNA data. The need for high laboratory standards and peer review is stipulated in Article 5d of the Universal Declaration on the Human Genome and Human Rights:

'In the case of research, protocols shall in addition be submitted for prior review in accordance with relevant international research standards or guidelines.'

Due to the complexities of forensic DNA testing, errors of independent DNA analysts or laboratories are not easily detected by the judiciary/legal profession in Court. Such errors, if they exist, may only be detected if concerned parties decide to have two independent laboratories conduct separate DNA tests. Independent testing is very expensive and may not be possible in cases where DNA extracted from evidentiary samples is limited. In this respect, laboratory accreditation is needed to demonstrate compliance with standards and assure quality control of procedures used for DNA testing, ensuring that forensic DNA testing results are free from error. In the U.S., government laboratories conducting forensic casework must be accredited by agencies such as the American Society of Crime Laboratory Directors (ASCLD) and the American Association of Blood Banks (AABB).

Although the importance of laboratory accreditation is evident, forensic DNA laboratories in the Philippines have not been accredited, mainly because of the absence of a national accreditation agency, the expense if accreditation is conducted by an international agency, the requirement for extensive documentation of routine laboratory procedures and the relative novelty of forensic DNA technology in the country. The Philippine government should assist existing laboratories address this issue so as to maximize the potential offered by forensic DNA technology as recommended in Articles 13 and 18 of the Universal Declaration on the Human Genome Project and Human Rights which state:

'The responsibilities inherent in the activities of researchers, including meticulousness, caution, intellectual honesty and integrity in carrying out their research as well as in the presentation and utilization of their findings, should be the subject of particular attention in the framework of research on the human genome, because of its ethical and social implications. Public and private science policy makers also have particular responsibilities in this respect (Article 13).'

'States should make every effort, with due and appropriate regard for the principles set out in this Declaration, to continue fostering the international dissemination of scientific knowledge concerning the human genome, human diversity and genetic research and, in that regard, to foster scientific and cultural cooperation particularly between industrialized and developing countries (Article 18).'

STORAGE AND SECURITY OF GENETIC MATERIAL AND DNA PROFILES

Issues such as security, confidentiality, disclosure, sample storage or destruction and removal of DNA records from criminal databases need to be incorporated in the appropriate legislation/policy. Improper sample storage, unauthorized third party access and use of biological samples for purposes other than law enforcement and forensic research purposes is not in keeping with Article 7 of the Universal Declaration on the Human Genome and Human Rights which states:

'Genetic data associated with an identifiable person and stored or processed for the purposes of research or any other purpose must be held confidential in the conditions set by law.'

The Canadian DNA Identification Act (1998) prescribes the removal of all records when

the conviction of an individual is quashed and a final acquittal entered or when the person is discharged provided certain conditions are met. In addition, DNA records of convicted young offenders are not included in the Convicted Offenders database, but are placed in a special repository established by the Commissioner of the Royal Canadian Mountain Police (1985). All records are destroyed after five years, provided the youth offender is not convicted of another crime. In the UK, Austria and Norway, the record of a convicted offender is permanently retained in a criminal database even after the person's release from incarceration (Schneider and Martin 2001). Although an individual has already served his term, his DNA record may be kept and stored for matching to any DNA profile which may be generated in future crimes, making him 'a suspect for life'. Notably, data in some countries, e.g. UK and U.S. (1994), show that many offenders are re-convicted of other crimes after their release from incarceration. Maintaining a permanent catalogue of offender DNA profiles has been shown to be an important law enforcement tool in catching repeat offenders and accelerating the resolution of a significant number of crimes.

Besides DNA records, another important concern is the storage of biological samples (from convicted offenders), which may be used for purposes other than law enforcement, e.g. testing for genetic diseases and 'abnormalities'. Third parties such as employers, insurance companies and private detectives may potentially seek access to genetic material and information contained in databanks to use to their advantage (Kimmelman 2000). Guidelines to restrict access to stored genetic material/bodily substance must therefore be prescribed in legislation (1998; 2002a).

Legislation in the US (Moenssens et al. 1995), UK (1995), Canada (1998), New Zealand (2002a), Austria, Finland and Switzerland (Martin et al. 2001) clearly prescribe that the collection and testing of biological sample are exclusively for law enforcement. Additional DNA tests are not permitted so as not to generate sensitive genetic information that could be prejudicial to the persons concerned. Furthermore, laws exist that prescribe the destruction of stored bodily substances of adult and youth offenders. In Canada (1998) and in some U.S. states (1994), stored bodily substances of youth offenders are immediately destroyed together with their records following prescribed procedures to facilitate immediate rehabilitation. In the case of adult offenders, the Canadian Identification Act mandates the destruction of bodily substances one year after a person has been discharged absolutely, or after three years if the discharge is conditional, provided the person is not convicted of a new offence (1998). Germany, Denmark and Switzerland also have specific laws which

provide guidelines on the destruction of biological samples after the release of the convicted offender (Schneider and Martin 2001). Interestingly, in the Netherlands, Norway and Belgium, biological samples are immediately destroyed after the generation of the offender's DNA profile to remove all possibilities of conducting additional DNA tests for purposes other than forensic identification.

The retention or destruction of biological samples is an area of contention in many countries. The destruction of biological material while retaining genetic records will limit the utility of criminal databases by restricting DNA profiling to include only genetic markers which are currently available. Firstly, future DNA tests using new genetic markers may invalidate current databases. New and more sensitive DNA technologies are likely to be developed in the future and scientists foresee the need to continuously validate existing databases using these more advanced technologies (Schneider and Martin 2001). If offender samples are not available for re-testing, then criminal databases must always use the same genetic markers, regardless of future discoveries of better and more discriminating genetic markers. In addition, post-conviction DNA tests on stored evidentiary material and convicted offender samples have led to exonerations of individuals awaiting execution or already serving life sentences (Connors et al. 1996). With the use of more advanced methodologies, it was shown that the convicted offender DNA did not match that of the case sample. In 2002, 26 years after the reinstatement of the Death Penalty in the US, Ray Krone became the 100th person to be exonerated from Death Row (Democracy Now 2002). In countries like the Philippines where the Death Penalty is implemented, the need to retain crime scene and offender samples outweighs ethical issues with regard to the retention of biological samples, provided the proper security measures in the storage of biological samples are observed.

Due to the sensitivity of situations involved in forensic DNA testing, e.g. disputed parentage and criminal investigations, privacy of genetic information is adhered to by all forensic DNA testing laboratories in the Philippines. Identities and records are held confidential and DNA testing results are only released to the parties concerned, and to the Court, if any, that ordered the conduct of the tests. Notably, each laboratory has set procedures to restrict access to case files in print and electronic forms although the four laboratories differ in some aspects of access to genetic information. The DNA laboratories of UP-NSRI and SLMC restrict access to genetic information in their own laboratories. The DNA sections of PNP and NBI on the other hand, may provide information to their superiors, based on the Principle of Chain of Command, if the common good requires it. This is of

particular importance since NBI and PNP are involved in criminal investigations which may affect local and national security.

CONCLUSIONS AND RECOMMENDATIONS

Forensic DNA technology is now available in the Philippines. The same technology has been in use in many countries for years and shown to be a powerful tool for human identification in the resolution of criminal, civil and private disputes. The Human Genome Project has accelerated the development of DNA forensics particularly with regard to providing us with a better understanding of how we are alike and how we differ. The study of human genetic variation in an individual and at the population level, which is among the objectives of the Human Genome Project, forms the very foundation of DNA forensics.

Because DNA forensics is about human identification, the main ethical concerns involve genetic privacy issues and third party access to 'one's DNA' which was previously the sole realm of the individual. However, the considerable contribution of DNA forensic technology to the protection of a child's best interests when disputed parentage cases are resolved early, as well as to societal protection through quick and reliable identification of suspects should outweigh the threat of government intrusion into one's genetic privacy. The challenge now is integrating forensic DNA technology in a way that maximizes its use, by effectively accelerating the fair administration of justice and the early resolution of civil cases while respecting human rights. Cultural and constitutional rights to privacy must be properly addressed and guidelines must be formulated to prevent potential abuse by the different 'key players', i.e. from law enforcers, medical professionals, forensic scientists, members of the executive, judicial and legislative branches of government, within the system. Clearly, a national strategy, which defines the responsibilities of each 'key player' or government agency, backed by the appropriate legislation, must be put in place. Only in so doing will the Philippines reap the maximum benefits of forensic DNA technology as well as ensure that the rights of the Filipino people are protected.

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Invited Commentary on DNA Forensics

Raquel B. del Rosario-Fortun MD FPSP, Associate Professor, Department of Pathology, UP College of Medicine, University of the Philippines Manila

I will just give you some observations, the fruit of a modest eight years of experience in forensic pathology in the Philippines. Specifically, I would like to give you some perspectives on the Philippine situation when it comes to the forensic applications of DNA analysis. This may sound promising if you are the optimistic type but unfortunately, the outlook for forensic application of DNA analysis still looks bleak.

Time and again, I say that Forensic Medicine in the Philippines is in the infancy stage when it comes to science-based criminal investigation. But then, I check myself and think that maybe, we have not even reached the infancy stage. Perhaps we are but a fetus as we are only just beginning. It was impossible to conduct the level of investigation we did for the children of the Asosacion de Damas Filipinas for the Ozone Disco fire victims eight years ago in 1996. The Damas investigation is probably a good sign that we are on our way to progress. But still I am firmly rooted in place. I do my reality checks constantly and I will tell you how it is in the Philippines. For one thing, the science behind the forensic application of DNA analysis is still being challenged. The validity of the technology is questioned even though it has been successfully used in other countries since the 80's. Why can't we just look at the experience of the rest of the international forensic community, learn from them and try to catch up?" It is as if we are trying to reinvent the wheel. Fortunately, some local court decisions have lately given it due recognition and acceptance and it is now admissible as evidence.

The line of attack against forensic DNA testing abroad has by now shifted to issues involving the quality and methodology of the laboratory work. The lack of quality assurance in the laboratories is a current concern, and so is the statistical interpretation of data

But by and large the problems plaguing us in the Philippines are still very basic. For one thing we lack personnel who are adequately trained and are knowledgeable in the recognition, collection and preservation of evidence. Physical evidence in many cases is not obtained at the crime scene at all and the few samples actually obtained are improperly stored and transported. Chain of custody which is very, very critical, is often overlooked.

Hence there are criticisms easily raised regarding contamination, switching or loss of samples. At the laboratory level other valid issues are the absence of peer-reviewed procedures and inadequate validation studies.

What then is the current situation in the Philippines? Dr. De Ungria has already given you a considerable amount of information but allow me to highlight a few more of the problems we face. In many situations in the Philippines, one practically needs a court order for a DNA test to be done. The idea here is that all the necessary forensic tests should have been done right at the beginning, after the evidence is collected and while the investigation is ongoing. Why wait for a court order? Our legal proceedings are so slow that that may be a good 7 to 10 years after the crime. Will there still be samples to go back to that are available for analysis by then?

Another problem is that our investigation system tends to be prosecution-based. Worse, to be frank about it, we could even very well be *prosecution-biased*. As a forensic specialist, I deal with both sides—meaning— I am neither pro-prosecution, nor am I pro-defense. Of the cases referred to me, those coming from the defense sometimes can be more frustrating. I was once involved in a sensational case from the south, in which the family of one of the accused was requesting that DNA analysis be done. This was an alleged rape-murder with multiple suspects. The parents of the accused had the money, they could afford to have the test done and they wanted the analysis in order to prove their son's innocence. But since we were on the side of the defense, it was very difficult to get even a presentation in court of the evidence. They made a big deal about it in Cebu and I wondered what the fuss was all about because to my knowledge, the defense has every right to examine the evidence. When the evidence was finally brought out in court it consisted of pieces of clothing allegedly found on the body of the victim, all dumped in a recycled plastic bag, unsealed and badly labeled. Among the pieces of clothing was the underwear allegedly found on the victim's body. Not surprisingly, it was moldy and the alleged stains found earlier were either indistinguishable from the molds or gone because huge portions had been cut-out of the garment. (Reportedly, an outdated test for semen was attempted and much of the sample was unfortunately lost due to this.) We could not even touch the evidence and quite predictably, the motion of the defense to independently have the evidence examined was denied.

In the case just cited, someone was willing to foot the bill but the DNA analysis still could not be done. In many other cases though, the cost of the test is simply out of reach of

the interested parties. If you watch "C.S.I." on cable TV, you marvel at their state-of-the-art crime laboratory and you wonder who pays for those tests that they do. Forensic science is definitely not just for those who can afford it. Whether a test should be done in a case or not must not be dependent on the victim's capacity to pay. A crime lab, in other words, must be state-funded.

A well-supported, topnotch crime lab in the Philippines will not solve all our problems however. The quality of any forensic laboratory work including DNA analysis depends on what is obtained from the crime scene in the first place. The term "crime scene" includes the body. If the investigation is botched right at the level of the crime scene investigation and the autopsy, an expensive state-of-the-art laboratory becomes worthless. The lack of public education also has to be addressed. An appreciation of forensic science must be taught to the public because that is where the victims come from. If you have a rape survivor for instance, she should know that she should not take a bath, she should have herself examined and have the evidence taken from her body right after the assault rather than cry rape ten years down the line.

Finally I will leave you with this. The catch phrase right now seems to be DNA analysis: DNA this, DNA that. Let me point out however, that in forensic science we employ a lot of techniques, and DNA analysis is but one of them. It is not always applicable to all forensic issues. Demonstrating the presence of someone's DNA somewhere is one thing; explaining how it got there is another. The test is expensive and it is not simple. Mere acquisition of the so-called "DNA machine" (as some are wont to boast) is not enough to declare that the technology is here, alive and well. The bottomline is you must have the *right people* to make the technology work, and you must also know *when* to use this technology.

Genetic Testing and Research

Eva Maria C. Cutiongco MD

The discovery of genes linked to diseases like cancer and other neurodegenerative disorders has ushered in a new form of testing, genetic testing, that enables one to know with fair amount of accuracy if one has the disease or will be at risk of developing the disease. It is important to realize however, that not all genetic testing is the same and that a genetic test is more than just any other laboratory test. It is set apart from other forms of tests because it is context specific, which addresses the question of why a test is being done on a patient at this particular time.

Genetic testing is part of a broader testing service which encompasses patient identification, education and referral accompanied by the delivery of test results and their interpretation to those tested. There are significant concerns, which need to be addressed with regard to the recognition of risks, appropriate referrals and the delivery of accurate and balanced information to patients.

Genetic testing can be classified into two areas : clinical testing and research testing. Clinical testing is done for the purpose of prevention, diagnosis, or treatment as part of patient care. The results of such testing are reported to the health care provider. Research testing, on the other hand, is done for the purpose of understanding a condition better, or developing a clinical test. Results in this form of testing are usually not given to patients.

There are three kinds of genetic tests available: cytogenetic, molecular and metabolic or biochemical tests. A cytogenetic test studies chromosomes, their structure, function and abnormalities. A molecular test studies a gene directly or indirectly by looking at variations in the nucleotide base sequences. A biochemical or metabolic tests looks at the presence of by-products of metabolic pathways either being abnormally high or low. These genetic tests have several uses. They may be used as diagnostic tools or screening tools in presymptomatic individuals, i.e. those people who are now unaffected, but will be affected later in life, or those predisposed to develop the disease. The latter refers to people at risk but not assured of being affected. Such tests can be used prenatally and postnatally. The tests are also useful in identifying carriers with reproductive risks or people themselves at risk of developing disease.

These different forms of genetic tests can target individuals, families, well-defined and even entire populations. The different uses of genetic tests can be broadly categorized as diagnostic, carrier, prenatal or predictive testing; newborn screening is a form of genetic testing as well.

Diagnostic testing is applied to a patient who is already symptomatic to confirm or rule out a clinical impression. A positive result raises the possibility that other blood relatives may carry the abnormality. Carrier screening refers to the detection of recessive mutations in healthy, asymptomatic individuals for purposes of reproductive planning. Carrier screening is a form of testing wherein individuals are screened for a condition that is present in the family. It can also refer to population-based screening of large numbers of individuals who have no family history but are at risk because of the high prevalence of the disease in the population. Prenatal diagnosis is the detection of a mutation in a fetus through DNA or biochemical analysis. Predictive testing is applied to primarily late-onset dominant disorders such as familial cancer syndromes, Alzheimer's disease or Huntington's chorea. This is the most problematic from a psychosocial and ethical standpoint. Newborn screening is the identification of all newborns at risk for a defined set of disorders where early detection leads to treatment and prevention of mental retardation and death.

Genetic testing and its applications help patients in reducing morbidity and mortality through close surveillance of high-risk individuals. Likewise, it eliminates the need for extra surveillance in individuals with no increased risk. However, there are disadvantages that have been recognized in association with such forms of testing. These include the psychological impact of knowing one has a life-threatening condition, the possibility of insurance and employment discrimination associated with disease risk and family discord that may arise. It is therefore of primary importance that pretest counseling and informed consent are clearly in place before any such form of testing is carried. Pretest counseling should address risk perception, expectations and support systems, implications of testing versus not testing, methods used to obtain specimens and associated risks, test accuracy in terms of sensitivity and specificity, the chance that the test will be positive, plans for conveying the test results and lastly, the level of confidentiality.

Since genetic testing is relatively new, the development of standards, regulations and guidelines to ensure accuracy, validity and precision of laboratory procedures and to ensure that other quality assurance issues are addressed is of paramount importance. The evaluation of a genetic test will include analytic validity, clinical validity and its clinical utility.

cultural and societal practices as well as religious beliefs.

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Invited Commentaries on Genetic Testing and Research

Romulo S. de Villa MD PhD, Chairman, Department of Biochemistry and Nutrition, Far Eastern University-Nicanor Reyes Memorial Foundation

I will be short and brief. Before I proceed with my reaction, may I request Dr. Cutiongco to give an update on the susceptibility gene mutations for breast cancer BRCA1 and BRCA2.

Dr. Cutiongco

The paper by Matsuda et al, which looked at 256 cases of undulated breast cancer patients among Filipino women and matched them with about 346 controls showed that about 5% will have the BRCA1 and BRCA2 mutations. The BRCA2 mutation is more common than the BRCA1 mutations and we think that it is probably a founder effect mutation.

Dr. De Villa

I am interested in breast cancer genetic studies because I know that breast cancer is the number one *cancer* among women in the Philippines. I have always thought that there may likely be a big genetic component here. We now know that BRCA3 and BRCA4 have been identified. Who knows if BRCA5 will be discovered in the Philippine population.

In a world wherein lives have been prolonged to the point that people with genetic defects are able to reproduce, I think the prevalence of these genetic disorders in society will increase. As we have mentioned, certain mutations are already being screened for in certain groups, because there is increasing incidence of those particular genetic disorders in those particular populations.

It is good to know that newborn screening has been implemented and is being done in our country. It has contributed significantly to reducing the rates of mental retardation in our country. And I think this should be encouraged particularly among pediatricians because they are the first contacts of patients and parents in these kinds of cases.

Now, I would like to emphasize the point that genetic testing is not, as we mentioned, just any ordinary laboratory test. Genetic testing without counseling is like going through a well-lit

busy street with your eyes closed. Guidelines for genetic testing should address not only quality standards but also include provisions for counseling, because of its implications for the patient, the family and even for society.

I fully agree with the guidelines that have been presented for genetic research and will support its implementation in the Philippines. The genetic information of an individual is private and personal property. Thus, there is a need for consent whenever publicizing the information to protect the genetic privacy of the individual. We have to be concerned not only with personal privacy but with genetic privacy as well. The permanency of genetic information however, may change. With the development of gene therapy, we may be able to alter the set of genes that we have.

In summary, in genetic testing and genetic research, there must be (1) proper counseling; and (2) adequate protection of genetic privacy.

Florante E. Trinidad MD MPH DFM CESE, Chief, International Relation Division, Bureau of International Health Cooperation, Department of Health

I would like to highlight six issues in the field of genetic testing and research, which I believe require pro-active intervention.

First, there is a need for the Department of Health, in collaboration with other stakeholders, to develop formal structures for the evaluation of potential genetic screening and research testing programmes to ensure that the programmes address local health needs in a cost-effective manner. These regulatory structures should also be charged with addressing, on a regular basis, the ethical legal and social implications of genetic screening, research and testing programmes as well as the development of appropriate regulations.

Second, when genetic testing services are not part of universal health services, but instead are available only to those who can pay for them with out-of-pocket funds, the clearly inequitable result could be a concentration of genetically transmitted diseases among the poor in society. This would further exacerbate inequalities in our country by creating a genetic as well as a social and economic underclass. The ideal situation would be the introduction

and the integraton of genetic testing and screening programmes into universal health services, available to all and not only to the private health sector. The introduction of genetic testing and research programmes should not be left solely to the private sector where profit potential may be the primary motivation and in which testing may not represent a good use of limited health resources.

Third, as we introduce genetic testing programmes, we should simultaneously build capacities for high quality genetic counseling.

Fourth, the populations of developing countries are especially vulnerable to economic exploitation by much richer, more developed countries or multinational corporations in the field of genetic research and development and use of genetic databases. Companies performing genetic research oftentimes have research agendas which may be in conflict with the needs of developing countries. The international consensus is that research which does not have potential benefits for their populations should not be done in developing countries. Genetic and other research in developing countries should be directed at health problems in those countries. In order to prevent exploitation, there must be reasonable assurance that the benefits of the research will be available to the research participants at the very least, and to the broader community in which the research was conducted.

Fifth, there is greater potential for genetic discrimination by insurers in countries with significant private health insurance compared to those with a national health service that is made available to all. Hence, the ideal situation would be for a country to have clear and enforceable legislation prohibiting the use of genetic tests in health insurance and the use of genetic information by insurance companies in setting health insurance rates for individuals or groups and in decisions to offer or deny health insurance. There should also be clear and enforceable legal prohibitions on the use of genetic information in employment decisions.

Sixth, low education levels and limited familiarity with genetic medicine and research present special obstacles to obtaining truly informed consent from the population or study subjects. In many cases genetic tests are offered before any effective therapeutic interventions have been developed for those found to have a genetic risk. It is then especially important for patients and individuals to understand this fact as well as the potential longer-term psychological,

emotional, and social consequences of learning genetic risks in the absence of therapeutic means for eliminating the condition.

In conclusion, the reality is that as far as the Department of Health is concerned, health programs on communicable diseases and basic public health measures are often of greater priority than most, if not all— genetic services. I look forward to the day when the DOH can be given sufficient budget in order to protect and promote the people's right to health, accord the proper value to the dignity of every human being and guarantee full respect for human rights including the right of the unborn, from the moment of conception, to life.

Excerpts from the Open Forum

Cecilia V. Tomas MD, Professor and Chairman, Department of Physiology, UP College of Medicine, University of the Philippines Manila

I would just like to make a comment regarding genetic research. Indeed, I welcome fora such as this as they will hopefully enable us to establish implementing guidelines especially in the field of genetic research.

During the past couple of years, we have reviewed a lot of protocols submitted for approval by the ethics reviews committee and the truth is, we were caught off-guard. It was difficult for us because there are currently no institutional guidelines on these areas for us to follow. We know that informed consent is a very important aspect of research. The process has to be explored and studied in depth especially since many of our people need to be educated regarding genetics. It is not simply a matter of giving consent. We feel that people should be informed and educated about that which they are consenting to.

Guidelines on the storage and future use of blood and tissue samples should also be carefully studied and established. Third, the matter of collaborative studies with foreign— either multinational companies or academic institutions should also be addressed. We feel that we should develop our own capabilities to do genetic testing here, so that there will be no need to send samples abroad while also minimizing the transfer of technology.

Dr. Cutiongco, Lecturer:

The scientists must be able to discern 'honest-to-goodness' collaboration. The field of genetics remains to be an extremely expensive field at this time. It remains prudent in certain cases to send out samples for genetic tests for very rare conditions. The Philippines indeed must start offering genetic tests for the more common disorders. It will be impossible to have everything available.

Cynthia P. Saloma PhD, Associate Professor, National Institute of Molecular Biol-

ogy and Biotechnology, University of the Philippines Diliman

. . . We should be concerned with Filipino interest. We have limited resources— limited financial resources and limited support from the government. We should therefore maximize our resources.

. . . The idea is to make a stand calling on the government and the nation to set goals for the development and progress of scientific research, rather than ask the government to set up a new agency and spend money on cement to build mere physical structures. We should use the money to develop existing resources, improve laboratories and train better personnel, so that we can do the basic science competently and proficiently. In connection, I would like to point out the relative importance of non-human resources, such as natural resources in relation to genetics.

Another byword currently used in the field is pharmacogenomics, which by studying genes that affect an individual's response to drugs, hopes to design better, more effective drugs.

. . . The approach of many companies and research laboratories abroad now is comprehensive. For instance, genetic research has gone beyond gene studies to include investigations into protein expression to determine possible, more specific targets for drugs. And it so happens that our country lies in the area of highest biodiversity in the world. One would think that we would have a competitive advantage as our country would probably be considered an important potential source of lead compounds for many diseases like cancer and infectious diseases. As such, medical researchers and commissions should be aware than in fact, many multinational drug companies have come to the Philippines to conduct clinical researches through clinics for the purpose of conducting pharmacogenomic studies. They come here with a lot of money to test their drugs or their products for the purpose of finding out whether this particular population will respond to their drugs. We should be aware of this so that we can protect our rights as patients, as researchers and as scientists.

Science is a profit of human efforts and his works, human benefit. It is essentially a humanist effort.

Dr. Padilla, Moderator:

. . . On the one hand, we have our basic scientists and researchers, with limited money, limited budget; and on the other are the many pharmaceutical companies that have now gone into the field of genetics. In other words, NAST should not be looking only at the scientists but also at the pharmaceutical industry that may exploit and abuse genetics.

One more point that I would like to pick up from is that, as Dr. Saloma said, in other countries, they have gone beyond the field of genetics and into newer, related fields like pharmacogenomics, proteinomics, functional genomics, comparative genomics, etc. We really do have to fast track a few things because it is a pity that we are lagging behind other countries in the region. Even if we have the people and the expertise of the scientists, we do need a lot of support, not necessarily just from the government but from other agencies as well.

Ethical, Legal and Social Implications of the Human Genome

Victoria Edna G. Monzon MD

The US Human Genome Project is a thirteen-year effort which started in 1990, coordinated by the US Department of Energy and the National Institute of Health with international collaborations. Its estimated cost was $3 billion and it was completed this year, two years ahead of the original plan.

When the completion of the project was announced, patients, physicians and scientists received it with great excitement and expectations and the hope that this would lead to revolutionary ways of diagnosing, treating and preventing thousands of genetic disorders. However, just like any new explosion of knowledge, genetic science must be examined critically and subjected to careful scrutiny and ethical criterion.

As is, science can tell us a great deal about the treatment, cure and prevention of genetic disorders but it cannot help us distinguish between right and wrong. It can tell us what can be done but it cannot guide us as to what ought to be done. It cannot dictate moral criteria for obtaining the good for mankind.

It is therefore the task of ethics to define the constraints of good and bad, the right and wrong use of knowledge and the proponents of this project recognized this need and for this reason has allocated some of its fundings for ethical research.

The Human Genome Project per se is not unethical. What may potentially be unethical will be the abuse of the technology and the knowledge, the means used, the applications and circumstances in which it is applied.

Ethical implications of certain medical applications of Human Genome Research

Genetic Testing

Gene tests can be used to diagnose disease, confirm diagnosis, confirm the presence of disease in an asymptomatic individual and predict the risk of future disease in a healthy individual or his/her progeny.

Progress in knowledge of the genetic basis of diseases has not produced similar progress on their cures. As a result there are now more genetic tests available that can predict the probability of death from diseases for which we have no cure, or predict disorders which may only manifest during adulthood, hence most people would prefer not to know. Revealing information about the possibility of future disease may have significant emotional and psychological effects. Moreover, the absence of privacy and confidentiality and legal protection can lead to discrimination and stigmatization in employment and insurance. Pre-natal screening intended to detect fetal abnormalities may go along with the offer of abortion or in-vitro fertilization. Pre-implantation screening to detect known risk of genetic defects, which will result in the destruction of defective embryos is inconsistent with the recognition of the dignity of the human person. In vitro embryos are subjects to quality control and discarded if deemed unfit for implantation. They have come to be manipulable (? Is there such a word?) products of technical expertise rather than the fruit of unconditional self-giving.

Genetic engineering, which looks to a future in which designer babies will be produced according to parental specifications correspond to eugenic ideology and eugenic practices.

Gene Therapy

Somatic cell gene therapy alteration is morally acceptable provided it is for therapeutic purpose only and not purely experimental. Somatic cell therapy is an extension of standard medical practice and may be similar to organ transplantation to which the same medical and ethical parameters apply. Medical interventions are ethically acceptable when they comply with the principles of autonomy, beneficence, non-maleficence and justice.

Germ-line cell transfer raises some ethical issues in that its effects are cumulative, specific and impact generations as yet unborn. It entails intergenerational consequences. Currently germ-line alteration in humans is considered unethical by most in the scientific and religious communities. However, germ line alteration aimed at the prevention or transmission of genetic disease that does not interfere with the origin of human life may be considered acceptable.

Cloning

The real issue in cloning concerns its immediate product. Though cloning and fertilization are different processes of human reproduction, the immediate product of both processes is the same scientifically; a human being and embryo begin immediately at fertilization or cloning (or should we rephrase to: a human being and embryo are both conceived at the time of fertilization or cloning OR for a human being and embryo, life begins immediately at the time of fertilization or cloning). While recognizing human life in the case of cloning is more difficult because the embryo is made in a "dishuman" (is there such term?) way without uniting sperm and egg, the resultant being has the same dignity as any other human life. On the basis of its having been produced in an abnormal way, supporters of therapeutic cloning say that an embryo produced through somatic nuclear cell transfer is not really an embryo at all. If this were true, then one wonders why we should be concerned about reproductive cloning. If the cloned embryo is not, at the time of implantation, a real human embryo, then what was implanted could never turn out to be a human baby.

Some have suggested that human beings should be cloned, but only allowed to develop until the embryonic stage for use in research. Through these means, the embryos could be sources of genes, cells or tissues for experimental purposes. Embryos, babies and adult are merely three terms we use to distinguish between stages of biological development. These terms should not be used to obscure the moral complications of how we treat human lives at different stages of development. All three are human beings who deserve equal respect.

Creating embryonic clones for purposes of research is even worse then creating them to be born, in that the harm done is intended rather than unintended.

Another major factor in the cloning controversy has to do with the way human cloning affects the family. It will upset traditional family patterns. To what extent do children have a right to have a mother and father? Would a clone be a sibling or a child of the original? Men are the earlier potential loser, they would no longer be necessary for reproduction if it is done through cloning. If an artificial uterus is eventually perfected, women might not be necessary either.

Clones would first have to suffer the notoriety of being born through somatic cell nuclear transfer. Their future would be shaped by someone else's past. Property interests would be at stake. Who owns a clone? The cloned, the clone or the cloner? In the commodified world of biotechnology, the one with the most investment is likely to win. In this case the cloner would own

the clone. Prospective parents might be able to purchase a clone but it is the market that will determine the selling price.

On August 12, 2003, an article in the Mayo Clinic Proceedings authored by physicians from different centers in the United States suggested a comprehensive ban on human cloning; claiming that a ban on research cloning is needed to safeguard against reproductive cloning because a partial ban would be unenforceable and violations would go unnoticed.

Conclusion

The ethical issues involved in the Human Genome Project may be summarized into the following basic ethical principles:

Beneficence

This signifies an obligation to provide benefits or to seek the good of patients. The HGP has as one of its goals the pursuit of genetic research to improve health care. It may lead to revolutionary ways of diagnosing, treating and preventing thousands of disorders. It may allow for more accurate and faster diagnosis of disease caused by genetic factors. It may help discover drugs that suit individual idiosyncrasies. Our role is to evaluate the benefits versus the risks and harm that the technology may entail.

Non-Maleficence

No harm should be done to patients or subjects of research. In the case of genetic testing wherein many tests are available but no treatment is possible, the question "what benefits will it have for patients?" must be raised. The psychological impact of these tests may be considerable, possible devastating as in cases where no cure is possible or children are tested and adult onset disease is discovered. We are not only made up of genes. We know that environmental factors play key roles in determining whether a given probability will become a certainty. One possible future use of the information gained from the HGP would be the abortion of "defective" children or embryo found in vitro to have genetic disorders. The danger of eugenics has to be safeguarded.

Respect for person

On the basis of biological data, we know that from the moment the human embryo comes into existence, we are dealing with a new human being who has the capacity to grow and develop like all other human beings. As a human being, justice demands that it be recognized as one with inalienable human rights among which, is the right to life.

Autonomy

Each human being must be given due freedom for self-determination and allowed to exercise his/her personal values and decisions so long as they are not contrary to natural law.

Privacy and Confidentiality

We know that DNA can provide knowledge into many aspects of a person and his/her family including susceptibility to particular diseases, legitimacy of birth, sexual orientation and behaviors. Access to collected samples stored in databanks and genetic information should be limited and safeguarded by the proper ethical guidelines. They should not be made publicly accessible without consent. Genetic mapping may become source of stigmatization and social discrimination by government, insurers, employers and schools. How will the individual's privacy be protected?

Informed Consent

Articles 1 & 6 of the *"Universal Declaration on the Human Genome and Human Rights"* endow all human beings recognition as persons and as such, cannot be used as experimental subjects without their free and informed consent.

Justice

Who will benefit from this project? Will everyone have access to such highly sophisticated health care? Will this further widen the gap between the rich and the poor? In a developing country like ours where millions of people do not even have access to adequate, basic health care and medical treatment, human genome sequencing may not be the most relevant and practical way to provide better treatment options for our people.

Human beings should not be used as means to our own ends. They should not be the subjects of experiments, nor destroyed to save somebody's life. Human clones should not be used for those needing transplantable organs. They should not be made to substitute for children who died. They should not be cloned for posterity for love of oneself. Doing research on human embryos for cloning is wrong. Even if the end is justifiable, the means would not justify the end.

We therefore believe that human cloning should be banned. However, further research and adequate funding should be allocated for adult stem cell research.

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Invited Commentary on the Ethical, Legal and Social Implications of the Human Genome

Atty. Jose Maria A. Ochave LLM

I am glad that Dr. Monzon discussed the element of beneficence. In novel science and new technology, the issue of beneficence is usually forgotten. People end up scaring themselves without actually studying the science or technology, as in the debate regarding the use of biotechnology in the agricultural field. We do not want the same thing to happen in the use of genetic technology in the medical field.

It must be emphasized that while there are ethical and legal considerations when one embarks on biotechnology research, there are similar ethical and legal issues as well in *not* doing such type of research.

We should caution ourselves against promising more than the technology can actually deliver. As proponents of certain technologies, we sometimes forget that there are equally important considerations other than the technology that we are promoting.

I will now address the issue of respect for the human person. The constitutional provision for the rights of the unborn states that the "State shall equally protect the rights of the mother and of the unborn child upon conception". It is definitely an anti-abortion provision. However, there are some issues. For example, in in-vitro fertilization, when does conception begin given that the first few cells are outside the womb? The constitutional provision speaks in terms of balancing the rights between the mother and the unborn child during conception. Is the 'cell', which is outside the mother's womb in the first few days, covered by the said provision of the Constitution?

The next issue is prior and informed consent. If we go into the public arena and talk about prior and informed consent, we must remember that many people already have preconceived notions and interpretations of this term. It has been used in the context of treaties like the Basel Convention on Transboundary Movement of Hazardous Wastes, the Wildlife Act and of course, Executive Order 247, on bioprospecting. So when we go to the

public and talk about prior and informed consent, we had better be clear about what we mean by the term.

Dr. Monzon is right. In a developing country like ours, the real issue with regard to biotechnology is access and ownership. In a country where only about 5 patents are issued to Filipinos for every 650 patents given every year to foreigners, do we go into strict intellectual property protection (IPR) of technology? There has been much talk about IPRs recently. My suggestion is to sit back and find out whether a strict IPR regime, particularly as regards patents, is really in our national interest, whether it will truly encourage and not in fact, discourage, the exchange of information among our researchers.

Now, let me talk briefly about forensic DNA testing. Dr. de Ungria is right! The law is very slow in taking into account developments in science and technology. In fact, it was only in 2001 when the Supreme Court first recognized the admissibility of DNA evidence. Up to now, there is disjunction, a lack of congruence between the legal and the scientific communities. As you know, many lawyers entered law school because we wanted to avoid science and math. Therefore, it takes a lot of effort to educate us about new sciences. This was evident during a seminar that Dr. de Ungria recently had with several judges. Lawyers, and in particular, judges, think in terms of "black or white" because they have to make decisions on whether one is guilty or not "beyond reasonable doubt". Scientists, on the other hand, think in terms of probabilities —— one in one billion, one in one million. But what do such statistics mean to a lawyer or to a judge?

I am however, pleased to inform you that the Supreme Court has now taken notice of developments in genetics. In fact, in a speech given by one of the Associate Justices during the recently held Asia-Pacific Judicial Educators Forum, he made mention of a "fourth wave" in technology, and he meant developments in biology and biotechnology. The Philippine Judicial Academy, the education arm of the Supreme Court, also sponsored a DNA forensic seminar the other week and a seminar on Biolaw will be held sometime in September this year.

As you can see, there is a lot of interest in DNA among lawyers. Our concern however, is maintaining a healthy balance by ensuring that things do not swing to extremes such that everything becomes solely about DNA and genetics to the detriment of the truth-seeking function of judges and advocates. We saw this happen with Children's Rights. In 1990, it was

difficult for us to file a case involving child abuse, particularly sexual abuse. Much progress has been made since but it came to a point that child abuse had become so 'mainstream' that it now became difficult for the accused to prove himself innocent of charges of child sexual abuse. So much so, that I suspect that many of the convictions which were eventually reversed by the Supreme Court were cases of alleged child sexual abuse or incestuous rape. There is often the tendency in the legal community to swing from one extreme to the other. In child abuse, the sole testimony of the child, if credible, is enough to convict the accused, and this has led to some questionable convictions. The entry of DNA analysis as evidence is a welcome development if only to provide an additional instrument for the accused to prove his innocence.

Now for the "watch-outs". First, I hear that a bill on cloning has been filed. Although I agree with banning human cloning, my sense is that this is not the time to go into statutory regulation of this technology. My suggestion is to go slow with statutory regulation because it is very difficult to amend a statute if it later proves to be imprecise or inaccurate. The way to proceed is to come up with guidelines, which everybody in the scientific community should comply with and which can be presented to the public for their education as well.

There is also a need to touch base with the legal and political communities because, as I have mentioned, people scare very easily with new technologies. So, the earlier we inform and educate the public about what genetic technology is, its benefits as well as its potential risks, the better for everyone.

Second watch-out: Sometimes, scientists can be more popish than the Pope. Although I do not have first-hand knowledge about the drafting of E.O. 247, I have discussed the issue with people who were involved in the drafting process. When I asked those involved about who included academic research agreements in the coverage of the E.O., I was told that it was actually the scientists who insisted on its inclusion because they thought that its exclusion would give rise to loopholes for commercial research agreements. As a result, our own local scientists suffered from their inability to comply with E.O. 247 because of their limited resources.

The right, if not the obligation, of the Filipino scientists to do research has to be respected but sometimes in the scientists' eagerness to prove to people that there is nothing to worry about what they are doing, they tend to be more popish than the Pope. Be very, very careful because seemingly simple statements that you incorporate in regulatory

guidelines may have meanings that are far more reaching than you imagined. It may even be used against you, to stop, limit or stifle research.

Be aware that the conception of ethics in the Filipino setting may differ from that in many of our references, which are mostly Western in origin. Issues, such as the primacy of the right of choice in reproduction, may not be applicable or acceptable to our people. My suggestion is that our ethics should be defined by our own social and cultural menu. Rather than mindlessly borrowing ethical principles from the West, we should study the unique Philippine experience and fashion an ethical view of the world using such experience.

Finally, a number of people want to establish more regulations for science. I believe attention should be focused on building capacity for the technology being regulated. Sometimes, we are excellent in drafting regulations even when there is really nothing much to regulate. We excel in attending international conferences and take pride in saying we have very strict regulations. However, when asked what we are *actually* regulating, we are sometimes forced to admit that we have nothing much and that we are simply preparing for the time when a given technology comes, if at all.

I agree that we should address all the ethical, legal and social issues, but we also have to recognize that scientists should be allowed to do research with the least interference possible provided they do so within the limits laid down by law and ethics. In short, regulations should not stifle, but in fact encourage the safe and responsible use of technology.

The Law and Human Genetics: Opportunities for Legislative Action

Atty. Jose Maria A. Ochave, LLM

My presentation entitled "The Law and Human Genetics: Opportunities for Legislative Action" focuses on steps that can be taken by the legislature.

In exploring the possibilities of legislative action that will involve the sciences, it is prudent to start with Executive Order 247 and the experience of the academic community with respect to its implementation. From there, I will proceed to discuss possible areas for legislative action by focusing on three issues: newborn screening, the use of DNA in the judicial system, and the privacy of genetic data. These three areas, I believe, are the most urgent, timely, and pertinent, even more so than human cloning.

Although EO 247 has no direct relation to human genetics, it should serve as an illustrative example of the problems that we may encounter when we seek to regulate science without an eye on implementation. Executive Order 247 was issued by the Department of Environment and Natural Resources to prevent bio-piracy by providing for mechanisms to ensure that our biological resources are used for the benefit of the Filipino people. While the objectives were laudable, the administrative and financial burden imposed by the Order had a restrictive effect on researches conducted by Filipino scientists. It covered not only commercial researches but academic researches as well, and had strict provisions requiring prior informed consent before any collection of biological samples is done. Scientists were required to go to local communities to secure prior informed consent. It was a costly process, and given the limited budget that local scientists have, it had the unintended effect of making it difficult for our scientists to conduct research. Further, while the intention was to ensure that biological resources and knowledge about them are made available to us through Filipino scientists, it had inadvertently given foreign scientists an advantage because of their access to more substantial financial resources.

The E.O. 247 experience should serve as a reminder that if the law intervenes in areas such as research it also has the responsibility of ensuring that regulations do not boomerang on our own scientists. It should always be borne in mind that regulations always have a cost and our local scientists are operating under extremely tight research budgets.

Let me now proceed to the issues which I believe should be the focus of our immediate attention. The first is newborn screening. This should not be controversial. Newborn screening is essentially a public health program to prevent mental retardation and death. (For a more in-depth explanation of the disorders included in the screening program such as Congenital Hypothyroidsim, Congenital Adrenal Hyperplasia, Glucose-6-Phosphate Dehydrogenase Deficiency, Phenylketonuria and Galactosemia, I refer you to Dr. Carmencita Padilla.) Based on studies conducted by the National Institutes of Health, at least 10,000 newborns can be saved annually through newborn screening, a simple test which costs only Php550. When a baby is born, a blood sample is taken through a quick heel prick. The blood sample is tested for the 5 heritable conditions. If the test is confirmed positive, immediate intervention is instituted in order to prevent the ill effects of an untreated condition. Mental retardation and death are consequences which are preventable through newborn screening, which is already routine in many developed countries. In Asia, Thailand screens 87% of its newborns, while Korea screens 92%. In the Philippines, only 3% of newborns are actually screened. What we need from Congress is a very simple law, a law that integrates a sustainable newborn screening program into the national healthcare delivery system and imposes upon health care professionals the duty to inform parents of the availability and benefits of newborn screening. We are not requesting for funding. All we are asking for is a law that will: (1) require healthcare personnel to inform parents about the availability and the advantages of newborn screening; (2) authorize the Department of Health to supervise and accredit newborn screening facilities; and (3) encourage the Philippine Health Insurance Corporation to include newborn screening in its schedule of benefits. At this time, I am not sure that we can compel the Philippine Health Insurance Corporation to do this as I am not familiar with their actuarial situation, but the bill should include provisions that will encourage PhilHealth to do so. It would certainly be a welcome development if PhilHealth decides to provide the service in the immediate future. The allocation of additional funding for newborn screening research and development would be desirable, but considering our country's current economic situation, we are willing to settle for a law that will make newborn screening available to everyone simply by enforcing the health practitioners' obligation to inform. We can later look for ways to ensure that indigents will have similar access to newborn screening services.

The second issue is the use of DNA in the judicial system. DNA has been used in cases of disputed parentage. For example, in one case, the child of a dishwasher woman was "abducted" by her employer and grew up with the latter. The dishwasher woman later found out about it and wanted to regain custody of the child. The Court ruled that the child should be returned to his biological mother. This was based on a comparison of physical features of the child with the biological parents and the fact, that it was impossible for the ostensible mother to have a child since she was already of advanced age. Significantly, the Court also allowed DNA evidence to be admitted.

The next case involves an incident of rape. In this case, the Court was explicit in its decision to admit DNA evidence. In assessing the probative value of DNA evidence, the court outlined the criteria that should be taken into account. These include— how samples were collected; how they were handled; the possibility of contamination; the procedure followed in the analysis of samples; the qualification of the analyst conducting the test; and whether or not proper standards and procedures were followed in the conduct of the test. These are the minimum standards required if DNA evidence is to be admissible in court. What we ask of Congress, in so far as the use of DNA is concerned, is a law that requires crime scene investigators to collect biological samples for selected crimes. The problem that Dr. Cora de Ungria usually encounters in many of these death penalty cases is that no biological samples were even collected, or if they were collected, they were discarded simply because glass slides are in limited supply and thus have to be recycled. The law should require crime scene investigators to pay particular attention to biological evidence for selected crimes such as rape and murder, penalize anyone who will tamper with biological evidence and provide financial assistance to indigents accused of crimes to enable them to avail of DNA forensic analysis. While DNA forensic analysis may not be available most of the time, indigents should be provided with assistance in terms of resources for a credible defense.

The law should also have provisions for the establishment of a nationwide criminal database. What we have at the moment is essentially a population database. If we want DNA evidence to be used effectively in criminal investigations, we ought to have a criminal database, but this would of course require legislative funding. Parenthetically, the U.S. already makes extensive use of criminal databases, and so does the U.K.

The next item concerns the need for legislative action on the collection of genetic data, which has in fact been ongoing for some time. There should be strong legislative protection

of privacy of genetic data to prevent genetic discrimination, particularly in situations such as insurance and employment. In insurance, the law should prohibit genetic information from being considered as a pre-existing condition in the absence of a diagnosis of an actual medical illness, or used as basis for increasing insurance risk or refusing coverage altogether. Unless a person has symptoms at the time he undergoes a medical insurance test, he or she should not be discriminated against because of a mere predisposition to a genetic condition.

Finally, another area which carries the risk of genetic discrimination is employment policies. While this is not happening here yet, it is already a significant policy and legal issue in other countries. It may eventually be in the Philippines. We need a law that prohibits discrimination against employees, current and prospective, based on their "genetic status", which employers may attempt to ascertain through direct questions on medical history or using general medical release forms.

The law should also prohibit the acquisition or collection of genetic information from applicants or current employees without.their consent. The issue of consent is of critical importance and cannot be overemphasized, especially in the brave new world of human genetics.

Invited Commentary on The Law and Human Genetics

Hon. Constantino G. Jaraula, Congressman, Lone Lone District, Cagayan de Oro City and Author, House Bill 1203: "*Cloning Prohibition Act of 2001*"

Now, it says here that human cloning refers to all methods of cloning involving human genes. Is that correct? It encompasses reproductive cloning and therapeutic cloning which are 2 different aspects. In the Bill that was approved in the Lower House of the U.S. Congress, human cloning is defined as "human asexual reproduction, accomplished by introducing nuclear material from one or more human somatic cells into a fertilized or unfertilized oocyte whose nuclear material has been removed or inactivated so as to produce a living organism at any particular stage of development." Genetically, it is virtually identical to an existing or previously existing human organism.

The U.S. Senate, on the other hand, defines human cloning as 'implanting or attempting to implant the product of nuclear transplantation into a uterus or the functional equivalent of a uterus'. Other terms including somatic cells, nuclear trnasplantation, nucleus, oocyte, are also defined.

In House Bill 1203, my very poor definition of human cloning was 'a method involving the production of a group of genetically identical cells or organisms derived from a single individual. It shall encompass or include any activity or overt (?) act designed directly towards human cloning'. From a layman's point of view, I believe that life begins from the time of "bonding", that moment when the sperm cell and the egg cell meet and 'bond'. The beginning of human life must be counted from that point on because that organism is not a cat, nor a dog. It has never happened in scientific history that a human egg, fertilized by a sperm cell becomes something other than human. Therefore I maintain that life begins from that moment on.

I am emphasizing this because historically, our old civil code, the Spanish Civil Code, which was introduced in this country in 1886, considered life to begin only after you were born and cut off from the umbilical cord and thus, have human form. (you must have a human form.) In other words, being born with birth defects disqualify you from being considered

a human being under the old Civil Code.

That provision has since been amended and the new civil code states that life begins from the moment that you are born, as long as one is born alive. As such, abortion was not considered a violation of life, because as far as the Civil Code was concerned, an unborn fetus is not considered alive.

The Philippine Constitution states that both the mother and the unborn from the moment of conception must be accorded equal protection. This should be of particular relevance to medical practitioners. You are not to favor the mother at all times because that will constitute unequal protection. The Constitution mandates protection for both the mother and the unborn child from the time of conception, not two or three months later when a pregancy test shows one to be pregnant. When is that moment of conception? I will adopt Dr Monzon's assertion that conception begins from the moment of fertilization. According to Dr. Monzon, fertilization is not when an embryo is being implanted in the uterus, fertilization occurs even before that.

These are my concerns with respect to human cloning. We cannot justify as Dr. Monzon has said, scientific research and the production of spare parts—— human spare parts! What cloning involves is the production of as many human spare parts as possible to the extent that a spare part is created by killing a living organism that in and by itself is already alive. To my mind, that is murder. It is murder because it involves a helpless child who has no way of defending himself. Why should we play around with a living organism? We cannot say that the soul comes only when one is born. I believe that the soul becomes a part of the living organism from the first moment of life.

I am certain that the Congressmen and the Congresswomen here present agree with me because we should not remain uninformed and unaware of modern scientific developments. Science must be adopted and promoted but it must never be abused. Neither should it be used to degrade the individual or to violate the dignity of the human person.

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