

Portland State University

PDXScholar

Engineering and Technology Management
Student Projects

Engineering and Technology Management

Winter 2002

Human Genomics of Biotechnology

Brian Bluelake

Portland State University

Bob Wang

Portland State University

Serin Hudson

Portland State University

Fatih Ersan

Portland State University

Aaron Freier

Portland State University

Follow this and additional works at: https://pdxscholar.library.pdx.edu/etm_studentprojects



Part of the [Genetics and Genomics Commons](#), and the [Technology and Innovation Commons](#)

Let us know how access to this document benefits you.

Citation Details

Bluelake, Brian; Wang, Bob; Hudson, Serin; Ersan, Fatih; and Freier, Aaron, "Human Genomics of Biotechnology" (2002). *Engineering and Technology Management Student Projects*. 1578.

https://pdxscholar.library.pdx.edu/etm_studentprojects/1578

This Project is brought to you for free and open access. It has been accepted for inclusion in Engineering and Technology Management Student Projects by an authorized administrator of PDXScholar. Please contact us if we can make this document more accessible: pdxscholar@pdx.edu.



Title: Human Genomics of Biotechnology

Course Title: Management in ETM

Course Number: EMGT 520

Instructor: Kogaoglu

Term: Winter

Year: 2002

Author(s): Bluelake, Wang, Hudson, Ersan, Freier

ETM OFFICE USE ONLY

Report No.:

Type: Student Project

Note:

Abstract

EMGT 520 with Prof. Kocaoglu

Strategy and Policy Issues

HUMAN GENOMICS OF BIOTECHNOLOGY

By Team #4
Brian Bluelake
Bob Wang
Serin Hudson
Fatih Ersan
Aaron Freier

February 27, 2002

Biotechnology is the term for the techniques of managing biological systems for human benefit. [1] A biological system can range from a single cell organism to different types of plants, animals, and to the very complicated human being. Biotechnology includes a great range of scientific and technological disciplines and has a great variety of important applications in biology, medicine, agriculture, and various industries. In our report, we shall only focus on one of the most active frontiers of today's biotechnology – human genomics.

I. Human Genomics And Some Related Basic Concepts

To understand what human genomics is, it is necessary to introduce some basic terminologies and concepts first.

1. Cell

Cell is the basic unit of all life. Namely, all living things are made of cells. [1] A typical human body contains several trillions of cells of different types, such as skin cells, nerve cells, blood cells, and muscle cells. All cells are enclosed by a thin covering, called membrane. Inside the membrane, most cells in a human body have two main parts: a core, called nucleus, and the rest outside the nucleus, called cytoplasm. Figure 1 depicts a typical cell.

Cells can divide and become more cells. This replication contributes to both growth and the rejuvenation of the body. The trillions of cells now in your body have developed from just a single cell. If your memory ever fades, you know that cells can also die.

2. Chromosome

Inside the nucleus of a typical human cell, there are 46 (23 pairs) thread-like structures called chromosomes. Human chromosomes contain two sets, one from each parent. Each set has 22 autosomes and an X or Y sex chromosome. A female has a pair of X chromosomes, and a male has an X and Y pair. Figure 1 also shows the chromosomes in the nucleus.

3. DNA (deoxyribonucleic acid)

Chromosomes roughly contain even parts of protein and DNA. In a chromosome, two DNA strands are twisted together to form an entwined spiral, called double helix, as shown in Figure 2.

At a more basic level, each DNA strand is a polymer of repeating nucleotides. Each nucleotide consists of a simple sugar, a phosphate group, and one of the four nitrogenous bases – adenine (A), thymine (T), cytosine (C), and guanine (G). [2]

Weak bonds between complementary bases, A-T and G-C, hold the two DNA strands together. Each of these linkages is called a base pair (bp). It is this specific base pairing that ensures the replication of DNA. As you can image, unzipping the double helix provides unambiguous templates for producing exact copies of the original DNA.

The particular order of bases in a DNA strand is called the DNA sequence.

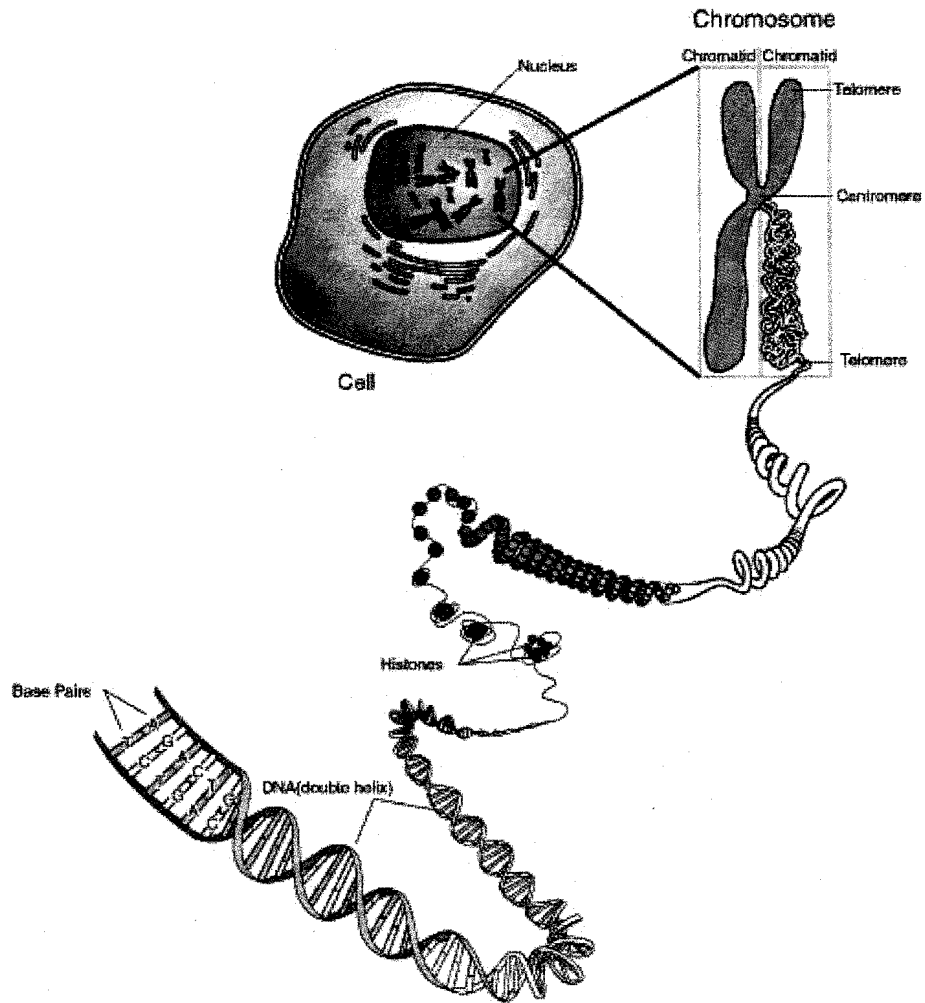


Figure 1. Illustration of a cell and its fine structure.

The exact amount of each of the nucleotides and the precise order in which they are arranged is unique for each kind of living thing and for each individual in a particular type of species. It is this DNA sequence that spells out the exact instructions required to create a unique individual with his or her own traits. In a human cell, there are about 3 billion base pairs.

4. Gene

A gene is a specific sequence of nucleotides in a DNA that encodes instructions on how to make a protein. At the molecular level, genes are responsible to synthesizing proteins in a human cell that determine all personal features such as sex, height, color of the eyes, and hair color of a human being. Therefore, gene is the basic unit of heredity.

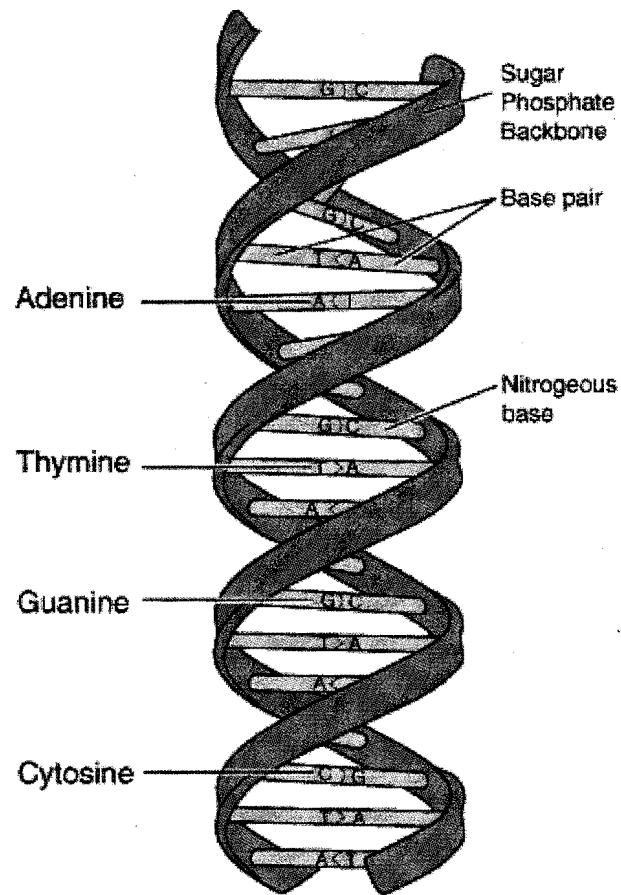


Figure 2. Illustration of a double-helix DNA

It was just less than two years ago when scientists found that there are about 30,000 – 40,000 genes in a human cell. [3] An average gene consists of ~3,000 bases. Therefore, genes only count for approximately 2% of the DNA. [3]

5. Genome and genomics

The genome is an organism's complete set of DNA. The human genome is the full complement of the DNA in the 23 pairs of chromosomes, or the approximately 3 billion base pairs in a human cell. The genome is the master blueprint of all actions during the lifetime of a cell. It is the complete set of code of life. Human genomics is the study of the entire human genome. The very first step is to find the precise sequence of the 3 billion base pairs in a human cell.

II. Human Genomics and The Human Genome Project (HGP)

The genetic revolution has its beginnings about a century ago with the rediscovery of Gregor Mendel's "transmission of characters in pea plants" [4] in 1859. His first generation hybrid's fertile and large tasty seed characteristics were reproduced the following year.

In the 1953, James Watson and Francis Crick discovered the structure of deoxyribonucleic acid (DNA), the molecule of heredity, to be in a double helix form. [5] This breakthrough directed focus on bio-molecular inheritance and cellular function.

With the DNA structure revealed, scientists had the beginnings of new questions, possibilities and research to learn how the genes of life forms (plants, animals and humans) evolve, interact, react, exchange information, live and die as complex organisms.

In the mid-1980's, Department of Energy (DOE) first initiated the effort of mapping the entire human genome. National Institute of Health (NIH) then joined in the 1990s to form and coordinate the US Human Genome Project. Now, the HGP collaboration involves 20 groups from the United States, the United Kingdom, Japan, France, Germany and China to produce a draft sequence of the human genome [6].

“The project originally was planned to last 15 years, but rapid technological advances have accelerated the expected completion date to 2003. Project goals are to

- *identify* all genes in human DNA,
- *determine* the sequences of the 3 billion chemical base pairs that make up human DNA,
- *store* this information in databases,
- *improve* tools for data analysis,
- *transfer* related technologies to the private sector, and
- *address* the ethical, legal, and social issues (ELSI) that may arise from the project.

To help achieve these goals, researchers also are studying the genetic makeup of several nonhuman organisms. These include the common human gut bacterium *Escherichia coli*, the fruit fly, and the laboratory mouse.” [6]

International Human Genome Sequencing Consortium, primarily funded by US government, makes their findings to the public for the benefit of the entire world. In 2001, this consortium published the draft of DNA sequences of the human genome in a paper entitled “Initial Sequencing and analysis of the human genome.” [3]

One of HGP's initiatives was to disseminate its finding to the private sector, educational institutions and other governmental systems. “By licensing technologies to private companies and awarding grants for innovative research, the project is catalyzing the multibillion-dollar U.S. biotechnology industry and fostering the development of new medical applications” [6].

In the private sector, Celera Genomics, a company led by J. C. Venter, took a slightly different and faster approach to DNA sequencing. Celera's business model is based on selling its genomic expertise and database to identify pharmaceutical objectives, assist in

drug designs targeting specific diseases, and minimize drug side effects. Celera was also able to produce a draft of DNA sequences of the human genome and published its results in February 2000. [7] The two versions of human genome maps agree well with the Celera's draft having slightly more details. Aach et al compared the two human genome maps. [8]. It is worth noting that Celera has the full access of the HGP's data while its own data is less freely available to the public.

To date, Celera and International Human Genome Sequencing Consortium are still in competition to produce the first high quality DNA sequence of human genome by 2003. In addition to human genome, the International Human Genome Sequencing Consortium is also sequencing many forms of viruses, bacterium, some plants and animals, plus some human bacterium, in hope to learn more by comparison and to find more applications.

The "draft sequence data are mostly in the form of 10,000 base pair-sized fragments whose approximate chromosomal locations are known" [6]. The finished high quality sequence is 63% completed with the goal of 100% completion by 2003. What's left is to close gaps, reduce ambiguities and achieve a high quality DNA sequence with no more than one error for every 10,000 bases. The finished sequences that have been completed for the human chromosomes are: 5, 16, 19, 20, 21 and 22. [6]

With the constant upcoming of new information, our understanding of living organisms, including human life, keeps changing. New sciences are created and new technologies are needed to support or refine the genome science. Focus is now on "increasing our ability to prevent, treat and diagnose disease, to engineer new life forms for food and medical uses; and, ultimately, creating the ability to replace or correct detrimental genes" [6].

With continued research and refinement, understanding the genome may "resolve which human characteristics are innate or acquired and how the interplay between heredity and environment contributes to defining susceptibility to illness. Such an understanding will make it possible to study how genomic DNA varies among patient groups, and especially the role of such variation in the causation of important illnesses and responses to pharmaceuticals" [6].

III. The Impacts And Anticipated Benefits Of Human Genomics

The human genome project has a goal of producing a high quality set of DNA sequence data in 2003. Unprecedented details for human genome information will become available in the very near future. Much more about human genomics still remains to be discovered. Even today, the significant impacts of human genomics can already be seen.

1. Impact on the science of human biology

The human genome project will provide the entire map of DNA sequence in a human cell. With all genes in a human cell being identified, our understanding of human genetics

will be pushed to the molecular level at its entirety. The complete DNA sequencing will provide a base for understanding human biology. It will change the way of biological research. With the entire DNA sequence, scientists can approach questions systematically by studying all of the genes in a genome. In the past, researchers were only able to study a few genes at a time.

In the decades to come, we shall be able to search for answers, at the molecular level, of profound questions such as, how we develop from an embryo to adult, how human beings work biologically, and what are the causes when things go wrong in our body. Genomics will undoubtedly move the science of biology into a new height.

Furthermore, the progress in human genomics has been creating new branches of science. For example, the complete sequence of approximately three billion base pairs is a massive quantity of data. The need for handling biological data with computer science and information technology gave birth to bioinformatics to manage and analyze this data. Proteomics is another new branch of science that is the study of protein expression and function. After all, genes only store the blueprint of life but genes are “lifeless.” Proteins are the products of genes and they carry out the primary functions of a cell in response to intra-cellular and extra-cellular signals. The proteins exhibit what life really is.

2. Impact on medicine [9]

Even though it still sounds like a fairy tale, human genomics will ultimately provide detailed information how all genes function normally or abnormally. Such knowledge will revolutionize medicine. Instead of treating the symptoms of a disease, the new era of molecular medicine will pinpoint specific genes for the cause of a disease by gene tests. Once the gene with problems is identified, a disease can be treated by replacing the defective gene by gene therapy. It is also possible to use highly targeted pharmaceuticals produced based on human genomics to directly cure the disease at its molecular foundations (pharmacogenomics).

(1). Gene tests: The ultimate gene tests should include the full DNA test of a patient and a library of DNA data of family members, relatives and others. Such a gene test will pinpoint the defective genes responsible for the patient's disease utilizing the data bank. It will be the ultimate diagnostic tool for any disease.

At its current level, gene testing is still immature. Nevertheless, various DNA-based tests can be used with some uncertainty to diagnose a disease, confirm a diagnosis, or predict a future disease in a healthy individual. For example, some gene tests can detect mutations associated with specific genes relevant to colon cancer in some patients. Even with severe limitations, these tests can currently be used to make risk estimates in presymptomatic individuals with a family history of the disorder. It is only a matter of time for more tests and more accurate tests become available.

(2). Gene therapy: Gene therapy, or gene transfer, is to replace “bad” genes with normal genes. It is still in its very early stage although it is already very controversial

ethically. Nevertheless, it holds the potential to treat or cure disease or enhance particular traits. Currently, gene therapy serves as a clinical trial for giving some participating patients the last chance of survival.

(3). Pharmacogenomics: Pharmacogenomics is a new branch of science that blends pharmacology with human genomics. Its goal is to correlate DNA variants with individual responses to medical treatments and to customize drugs for such individuals. Human genomics will provide detailed information on particular genes of a group of individuals for a disease. Such right-on-the-target information will lead to new drugs specifically designed for such a disease. These highly targeted drugs will not only have high efficiency to cure the particular disease, but also eliminate or reduce side effects and adverse reactions that kill more than 100,000 people each year.

3. Impacts on other fields

Progress in Human genomics will have to be accompanied by progress in genomics of other biological systems. As current frontier medical research is often first done on animals rather than human beings, results in genomics of other biological systems will be useful to human genomics. Furthermore, genomics of animals, plants, and microbials have their own significance as well, such as [9]

- (1). Breeding healthier, more productive, disease-resistant farm animals,
- (2). Growing disease-, insect-, and drought-resistant crops,
- (3). Growing more nutritious produce,
- (4). Incorporating edible vaccines into food products,
- (5). Developing new energy sources (biofuels), and
- (6) Developing new cleanups for toxic waste.

With commercial incentives, the development of genomics of other species seems to get exotic. It was reported recently that Fugu (puffer fish), a Japanese Sushi delicacy, will be sequenced. [10] Fugu, a Sushi delicacy, enjoyed by thousands particularly in Japan, also claims about 100 diners' lives every year from its highly potent neurotoxin when prepared improperly. It is the only food forbidden to be served to Japan's royal family. May the emperor of Da Nippon enjoy Fugu one day!

IV. Ethical Issues

Human genomic technology's greatest obstacle may be the ethical acceptance and regulated use by the public. Having a globally accepted governing set of laws, regulations, guidelines and disciplining actions is an impossibility. Even nationally, this is a challenging task. Despite the differences in religion, politics, and social groups, biotechnology and its implications, especially in the human genome aspect, will continue to advance. What is needed is a managing mechanism to guide and direct the human genome application.

Since this is a new field with so many unknowns, caution must be used in the application of old laws and ideologies in maintaining a healthy progressive balance between science

and humanity for the near future. Yet, hindsight is a good starting point to anticipate possible ethical confusion and ineffective regulations. These issues have to be addressed in depth before social and regulatory factions play catch up in the wake of genomic havoc.

Currently still in its infancy, genetic coding is still a developing science. There are relatively safe assumptions being made, but time and continued research will validate or dispute these assumptions. Presently, caution should accompany the genetic information used for diagnosing or treating ailments. Stigmatism, mental health, employment and institutional acceptance are all serious concerns, should erroneous hereditary information be made use of.

An important aspect of this new field is the continued physician-patient relationship. Part of the physician's duty is to respect and maintain the patients' confidence in treatment and personal information. With genetic tools, physicians will be able to provide more effective care, treatments and cures with minimal side effects. But the genetic information gathered could have negative implications for the patient and their genetic relatives. What is at stake here is the ownership and proper dissemination of the genetic data.

The balance of private versus public best interests lies on the shoulders of the physicians. Arbitrary laws that are enforced by removed governing bodies compound this juggling. Patient expectations and trust are important for the physicians to remain in business. The public's interests and safety are paramount as well. But where the two equally meet, may never satisfy all effected parties.

A question for genetic advancement is, to treat or not to treat? Which is more valuable, individual treatment or public welfare? There is a need for public protection and individual care. Those threatened of exposure may forego medical treatment or withhold information about their conditions. The practice of medicine and the physician's duty is to provide care, treatment and if possible, a cure to ailments. The physician, individual and the public's economic and social wellness may be jeopardized without a firm hand to guide and protect each best interest while advancing the knowledge and science technology of human genome.

At this time, we cannot escape our genes. What is needed is continued accuracy in isolating and treating detrimental genes. Currently, genetic coding can only tell of risks and limited certainties. We have inherent factors that may or may not develop in our lifetime. With irreversible advances to be made in the genetic progress and its accompanying technology, there may come a time when we can escape our genes.

V. Legal Issues

The current arbitrary laws have to be more solidified to gain public and private acceptance of utilizing and disseminating genetic information gained by new and upcoming technology. Patient confidentiality is being eroded by lawsuits and third party

inquiries for physicians to disclose patient information. In modern history, laws have been created that forces physicians to disclose info under such patient acts of breachment (contract and fiduciary), invasion of privacy, violation of statutes and the United States Constitution [10]. More recent mandatory disclosures include sexually transmitted diseases, violent tendencies and gunshot wounds among other seemingly public right-to-knows. These have all led to a sense of subjective set of laws concerning disclosure of medical information. The impacts of this have yet to be felt with genetic information to be gained through genome technology.

The current situation is not a suitable foundation to handle genetic information. What is needed is set regulations with little room for changes. These would only be effective if it is known under what circumstances a physician must disclose genetic information about their patients. If all parties are aware of these immovable guidelines, then all know where they stand and the consequences of their decisions.

Proper regulations need to be addressed before the time comes where they have to be reassessed in order to fix loopholes and conflicting legal issues. Past failures and historical solutions have to be reviewed and applied to a new arena. What is not ideal is having a limited number of like-minded people making the rules or interpreting them.

Strategies for addressing Issues:

Here are two generic ways of addressing the ethical and legal issues, externally and internally, created by human genome technology. By looking from the outside of the practice of medicine, autonomy and social responsibilities can be addressed [11].

The benefits and harms to patients and the public must be weighed. Fairness in distribution of available health remedies gives weight to individual protection. But social awareness of uncontrolled health and safety risks is equally important. Through increased capability for treatment and preventative measures, there is a sense of social responsibility to see that all are allowed equal opportunity to receive proper medical attention, even at the risk of some unchangeable diagnosis going unnoticed.

The social responsibility amounts to public protection, a sensitive yet important safeguard. The health of relatives and business success may depend on genetic disclosure. But also to be kept in mind is that in the past, without genetic information, society moved on without fearing about their neighbors' inherent possibilities. This molehill should not be generated into a mountain. Boundaries have to be concrete in what and how much genetic information should be disseminated. These boundaries will help control the technological directions of genetic science.

These issues should also be viewed internally with regards to the practice of medicine around genetic information. Curing, caring and the patient's right to secrecy and their right to disclosure of their personal genetic information should remain at the forefront of medicine. Continued medical research in the human genomic arena will only enhance these virtues. Genetic advances and treatment will be far broader if there is adequate and reliable individual protection yet with a vested interest in public welfare.

In both, the benefits and harms to the individual and their rights should be weighed against the potential benefits and harms of society. The bottom line is that genetic information is about an individual's personal being and those aspects should be weighted more heavily. The benefits of medical care outweigh potential harm to the public. What gain is there if people do not feel safe in exposing themselves to a system without protection.

VI. The Future

The "information era," even though many people have yet to fully understand and come to grips with being completely immersed in it, is going to be replaced by the emerging biotechnology. Biotechnology is showing great promise to become the next economic era. This "bio-economy" has already started, even though very few people have seen direct impacts of this new technology.

Genomics tells us who human beings are, not where they should go. What is being learned from the study of genomics is radically changing the how people think and perceive themselves and their place in the natural world. It is leading to conclusions that all species stem from the same ancient common ancestors. The future will soon show even clearer lineages as molecular archeologists study the genome sequences that are becoming available. [12]

Within a few years from now, testing a couple of drops of blood from a newborn will be able to provide a "fate map". Genetic diseases may not only be visible at birth, but gene manipulation may be able to decrease the occurrence of possible problems such as coronary artery disease. But there is the possibility that the gene associated with high blood cholesterol may be linked to some other desirable trait. It is possible that if we decrease the prevalence of these genes, that we may lose a valuable component of human capital if the numbers of such people declined. [12]

By being able to identify the genome of each individual, our society as a whole may change drastically. The future may hold many options that seem almost unimaginable to the common person today. It would be possible to have services such as computer dating that matches genetically compatible people together, or for the government to offer tax incentives to couples that have their profiles validated before they reproduce. Even with today's technology, it would be possible to take a sample from a napkin or a stray hair to have it tested before furthering a relationship. What about insurance policies? Will it someday be legal for an insurance representative to request a DNA analysis before they will provide coverage? Will our society ever get an extreme such as the movie *Gattaca* portrays, where only the "elite", the genetically altered humans, will hold high-powered jobs and discrimination is based off of our personal genomes? This is probably not going to happen. The first few examples may come to age, but most likely, all genetic mapping will be strictly controlled. There are many laws that are in place and will be created to provide protection to individuals based on privacy.

Like any other economic eras, the bio-economy will provide new jobs and careers to support this new technology. There will many new branches of Law that are needed to provide protection to peoples rights and maintain control over the uses of genetic information. As mentioned before, many new branches of science are already being developed to study and maintain biotechnology. Law enforcement is already regularly using this technology to identify suspects involved in crime scenes. The agricultural industry has already embraced some of the early advantages of using biotechnology to produce stronger, healthier products. And the pharmaceutical industry is rapidly changing to adapt this new technology into useful products.

Genomics offers us the ability to create drugs that are more precise, safer and that have fewer side effects. There are four critical factors in new drug development: the bioavailability of the drug in the system, how quickly it is metabolized, its toxicity, and whether after all the pre-clinical test, it is effective in the human system. [13] These issues make developing and marketing new drugs very expensive and time consuming. The fact is, most drugs being discovered now, won't be tested in humans until 2005 and wont be available on the market until 2010. [14] The future of genomic technologies will provide for "mass customizing" as stated by Stan Davis in Lessons from the Future [15]. This will allow there to be mass quantities of very specialized pharmaceuticals available on the market.

It is estimated that the current genomics market of \$1.1 billion will steadily grow to \$10.6 billion by the year 2010 [14], and we are still just in the beginning of this new era. This industry has great potential to create a new way of life for every human being on this planet. These changes will affect our culture and our day-to-day activities, regardless of your opinions about biotechnology. Our understanding about ourselves and every other biological thing around us will change significantly over the next few decades. The potential of this new era is well beyond any of our best guesses.

References

- [1] The World Book Encyclopedia, Vol. 2, P326, World Book Inc., 1996.
- [2] F. Betz, Managing Technological Innovation, John Wiley & Sons, Inc., 1998.
- [3] International Human Genome Sequencing Consortium, *Nature*, 409, 860-921 (2001).
- [4] <http://www.ornl.gov/hgmis/graphics/slides/images1.html>, accessed 02-23-02.
- [5] J. D. Watson and F. H. C. Crick, *Nature*, 171, 737-738 (1953).
- [6] Human Genome Project Information Website, <http://www.ornl.gov/hgmis/project/about.html>, accessed 2-15-02.
- [7] J. C. Venter, et al, *Science*, 291, 1304-1351 (2001).
- [8] J. Aach, *Nature*, 409, 856-859 (2001).
- [9] "A 2001 Primer on Genomics and its impact on medicine and society," www.ornl.gov/hgmis, accessed 2-15-2002.

- [10] News, from www.ornl.gov/publicat/hgp/v11n3/08sushi, accessed on 2-8-2002.
- [11] Roberta Berry, "The Role of the Old Hippocratic Virtues in the Regulation of the New Genetic Intimacy", 1997, *The Journal of Legal Medicine*, Taylor & Francis
- [12] "The Crossroad of Biotechnology 2001: Vision of the future of Biopharmaceuticals", *Canadian Corporate News*, October 11, 2001
- [13] P. Doherty, "Just natural that we should shape the future", *The Australian*, August 9, 2001
- [14] R. Rosenberg, "Biotech companies face obstacles in developing gene-based drugs", *The Boston Globe*, February 7, 2001
- [15] C. Johnson, "Information age to soon yield to bio-economy, book predicts", *Fort Worth Star-Telegram*, August 23, 2001
- [16] "Genetics: From Genes to Genomes",
<http://www.mhhe.com/biosci/cellmicro/hartwell/preface.mhtml>, accessed 2-15-02