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**by**

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When ancient scholars, such as Aristotle, pursued the study of science, their initial intention was to acquire a deeper understanding life through the obtained knowledge of nature. However, in contemporary society, the study of science has become a pathway to obtain a comfortable lifestyle and the original purpose for the study of science barely remains. Science, as a key to the understanding of the physical forms around us, has opened the door for the development of technology. Aiming at improving individuals' lifestyles, technology has advanced rapidly in recent decades. Doubtlessly, the swift changes of technology can be considered as a progress in the perspective of technology itself. Yet, whether or not these changes are advancement for mankind is still in question.

While the knowledge in understanding life forms at the molecular level is increasing, the technology to help acquire further discoveries and to manipulate life forms at the molecular level is also changing rapidly. In 1953 when Francis Crick and James Watson constructed the double-helix DNA model, the research on molecular biology has gone into a different stage (Flynn 100). Now, at the transition state of two centuries, DNA chip technology is a new technological change of the 21st century. It is a monumental step in not only molecular biology, but also the medical field, and technology as a whole.

DNA chips and gene chips are the common names of DNA microarrays. A DNA chip is a technical tool for obtaining genetic information by using DNA-covered silicon, glass or plastic wafers (Wortman 51). This new technology for decoding the secret of life is based on the principle of base pair hybridization between complementary DNA strands and gene expression.

A gene is a piece of DNA that carries the information about our bodies and how they function (Keefer par. 4). Genes constitute only a tiny fraction, a mere 3 percent, of our

DNA. Scientists estimate that we have from 80,000 to 100,000 genes (Casey par. 12). DNA is the chemical that stores coded information on the functioning of an organism. DNA has a double helix structure; two strands are connected in helical shape. The two strands are held together by four different chemical building blocks that are called base pairs. The base pairs are the chemicals: adenine (A), thymine (T), guanine (G), and cytosine (C). A is always paired with T and G is always paired with C (Campbell 282). Each person's sequence of DNA bases - the order of As, Ts Cs, and Gs along a single DNA strand - is different. This is what makes each person unique. Yet, we differ by only or two tenths of one percent of our DNA (Casey par. 12).

Based on the principle of base pair hybridization between complementary DNA strands, in the first step of DNA microarray, the two strands of DNA are first separated into single-stranded DNA. This single-stranded DNA is called the probe. The probe is first robotically attached onto a glass surface or silicon chip. The chip is then incubated with the target single-stranded sample. The target single-stranded sample is mRNA, which is messenger RNA that carries the genetic instruction for producing proteins in an organism (Campbell 296). The target samples are labeled with fluorescent markers (Kim; Yang). The numerous sites where the target samples search for matching partners are called the "affinity matrix" by David J. Lockhart in his article, "Genomics, Gene Expression and DNA Arrays" (827). If the sequence of the base pairs of the probe and the target single-stranded DNA match, they come together to form a double-stranded DNA. The chip is then washed to get rid of the unwanted segments of DNA that did not bind or match (Kim; Yang). An automated instrument or an optical microscope is then used to read the chip for the result through fluorescent detection. The resulting fluorescent image is scanned by a laser beam and analyzed by a computer. The intensity of fluorescent light varies with the strength of the hybridization, or the matching of the probe and the target (Prakash par. 4). Gene expression is analyzed through the intensity of the fluorescent results (Schemm 11).

A gene's expressivity is "the degree and manner in which the gene manifests itself" (Keefer par. 12). "A gene may express itself differently in one individual relative to

another, which possibly [leads] to a more severe genetic condition in that individual” (Keefer par. 12). Also, a gene may express itself in one condition, but may be turned off in a different condition. For instance, in the fluorescent result, if the color of the spot is red, then the mRNA that is marked with red is highly expressed. This mRNA corresponds to one of the genes in the DNA. Thus, this gene that the mRNA corresponds to is turned on in this condition tested. On the other hand, if the color of the spot is yellow and there are two types of mRNA tested, one labeled in red and the other labeled in green, then the result is a combination of the two types of mRNA. The presence of the two types of mRNA is in one-to-one ratio. Thus, the two types of genes that correspond to the two types of mRNA express at the same level under the condition tested. Further, if there is no fluorescent result on the tested spot, then the gene corresponds to the mRNA tested is said to be not expressing under the condition tested. Therefore, using DNA chips to detect the gene expression through analyzing the fluorescent intensity, the functions of various genes can be identified (Kim; Yang).

In 1996, a biotechnology company in Santa Clara, California, Affymetrix, introduced the first commercial version of DNA chips, which the company dubbed GeneChip. GeneChip is a glass wafer that contains as many as 16,000 different DNA strands with an area of less than 1.5 cm<sup>2</sup> (“Visualize: DNA Chips” par. 2; Abbott par. 5). Though GeneChip is not installed in a computer, it uses technology for creating silicon computer chips to create DNA probes (Junarkar “‘GeneChip’ Encodes DNA on Silicon” par. 8). Today, there are many companies that provide DNA-chip products and services. With the development of new fabrication methods, many types of chips have been developed. For instance, Nanogen, Inc. creates NanoChip, a type of DNA chip that uses electrical charges to hold the probes. According to David Cameron’s article published in *Technology Review* in September 2001, NanoChip provided by Nanogen “is currently the only DNA chip on the market using microfluidics – the channeling of fluids on a chip surface” (par. 2). The size of NanoChip is only 0.7 cm<sup>2</sup>, smaller than a regular postage stamp ([Nanogen](#)). While standard DNA chips are already equipped with probes when they come into the hands of the researchers, NanoChip is blank and is to be customized by the researchers according to their needs. Using NanoChip, the whole process only

takes about 15 minutes (Cameron pars. 8-9). With the increasing number of companies entering the biochip business, the market is expected to grow to \$10 billion within the next five to ten years according to Alexandra Stikeman in the article "Biochips Go Big Time" (Stikeman par. 2). Through the estimated market growth, it is evident that even though DNA chip technology is still at its infancy, the development of this technology is changing swiftly.

Technology is developed with the purpose of providing benefits to human beings. As one of the modern technologies, DNA chip technology has evolved based on the many promising applications and benefits that it brings to the medical field and scientific research. One of the most important contributions of DNA chip technology that is related to every individual is the improvement in the health care system. Common gene mutations can alter people's predisposition to disease or their reaction to drugs. Predisposition to most disease is affected not by a single gene, but several. Conversely, each disease-related gene can have many possible mutations. Therefore, each mutation has to be searched for individually (Abbott par. 2). As one of its applications in the medical field, a piece of DNA chip can tell an individual what diseases or disorders that he/she might develop in the future. An individual's possibility of developing cancer can be detected much earlier and easier by detecting the gene activities using DNA chips.

According to the American Cancer Society, one out of every two men and one out of every three women in the United States are likely to get cancer at some point in their lives, and about 560,000 Americans were expected to die of the disease in 2001 (Wortman 52). Looking at such statistics, "as many as 500 research laboratories in academia and industry are already employing DNA chips to develop sweeping new genetic pictures of different cancers" (Wortman 52). As Kathreena M. Kurian points out in "DNA Chip Technology" published in 1999, a group of researchers "has used DNA chip technology to screen individuals for mutations in the breast cancer gene BRCA1" (270). Further, Affymetrix markets a type of GeneChip that is called p53 chip. "The p53chip includes over 400 mutations that have been found to be associated with tumors and has been marketed to determine individuals with increased cancer risk" (Kurian 270).

As National Cancer Institute director Richard Klausner points out, "DNA chips are potent weapons against cancer" (Wortman 51).

Not only can DNA chip technology make the detection of cancer earlier and easier, it can also distinguish the genetic differences between similar cancers. For example, the two different types of leukemia that are different genetically are distinguished using this technology ("Visualize: DNA Chips" – View the Visual Image par. 1). Furthermore, lymphoma is a relatively common cancer of the white blood cells that affects more than 15,000 people in the United States each year. Using the DNA-chip approach, in 2000 researchers at the Stanford University School of Medicine discovered two genetically distinct classes of disease within a type of lymphoma that were previously classified as one cancer ("Visualize: DNA Chips" par. 3). Pat Brown is a Stanford University School of Medicine geneticist who helped invent one of the two main types of DNA chips. He says, "cancers with different clinical outcomes have different molecular subtypes" (Wortman 53). Before the two different types of lymphoma were discovered using DNA chips, patients were given standard chemotherapy, but only 40% of them responded rapidly to the treatment (Wortman 53). As a powerful tool in diagnostics, DNA chips' applications range from detecting mutations in HIV-1, the virus that causes AIDS, suspect genes in breast and ovarian cancers, cardiovascular diseases, Alzheimer's disease, diabetes, hypertension, schizophrenia, and manic depression (Junarkar "'GeneChip' Encodes DNA on Silicon" par. 12; Casey par. 16).

With the potential of providing a great advance in diagnostics, DNA chip technology also helps develop suitable treatment, drugs, and therapy for diseases. New therapies and drugs can be developed with the finding of cancer-associated genes. Tens of thousands of people are hospitalized each year as a result of toxic responses to medications that are beneficial to others (Casey par. 23). Also, it has been estimated that adverse drug reactions caused 100,000 deaths in the U.S. in 1994 (Harrop par. 3). As Marc Wortman points out in an article published in 2001 in *Technology Review*, "DNA chips help identify all the potential drug targets for a given type of tumor" (55). Instead of the traditional trial-and-error methods for finding new drugs, drugs can be developed to

target specific genes and unwanted side-effects can be eliminated using DNA chips. As one researcher points out, "DNA-chip-based diagnostics will very soon become routine technology" and currently untreatable forms of cancer may, one day, no longer mean death sentences (Wortman 53). Overall, medical diagnostics can be simplified and made more reliable by finding the most fundamental cause of diseases at the genetic level. In the future, an individual's illness can be easily diagnosed to its fundamental cause, which is the change in the gene expression or activity by giving the doctor a small sample of DNA, such as a drop of blood, to be analyzed on a DNA chip.

In addition, on the scientific research aspect, the study of genetics can be done faster and easier. As the "lab on a chip" technology, DNA chips allow researchers to perform what once would have been thousands of separate experiments all at the same time. Alison Abbott points out in an article published in 1996 in *Nature*, on a 1.5 cm<sup>2</sup> DNA chip, 16,000 different DNA strands can fit together (par. 5). Large numbers of genetic mutations can be detected and searched simultaneously in a short period of time, while traditional methods can only search each mutation individually. Says Sarah Harrop, recent advances in [DNA] chips... [cut] down what would previously have been several weeks' worth of work into a single afternoon" (par. 2). Also, the process of determining the functions of specific genes can be expedited. For instance, using the DNA chip technology, the Biochemical Genetics Lab of National Institutes of Health is currently searching for gene expressions and thus the functions of tested genes, under conditions of low oxygen and gamma radiation (Kim). As David Mack, the vice president of genomics research of Eos Biotechnology Company, points out, "the ability to generate the human genome on a chip today is incredible" (Wortman 55). Overall, DNA chips allow us to learn about DNA in a much faster and easier way and thus, lead to the development of revolutionary new ways to diagnose, treat, and someday prevent the thousands of disorders that affect us.

However, there is no one-sided coin; controversial issues concerning the use of DNA chip technology are an area that cannot be ignored. As one of its applications, DNA chip technology improves the methods for genetic testing. Concerns on the impact of DNA

chip technology are mainly ethical issues surrounding genetic testing. These issues include discrimination, eugenics, and an individual's take on his/her genetic information. "As more ethnic-specific mutations are identified, risks of ... discrimination have become a concern not only for the individual being tested, but also for every member of that person's ethnic group" (Grody 65). For instance, the breast cancer mutations, BRCA1 and BRCA2, are found in the vast majority of families of Ashkenazim tested. The inherited propensity to get breast cancer has led some people to call it a "Jewish disease" (Pollack 194).

Also, the widespread use of DNA chip technology for genetic testing can lead to insurance and employment discrimination. Insurance companies may refuse health insurance for certain individuals based on the genetic test, which shows possible diseases that an individual might develop in the future. For instance, Ashkenazi Jewish women might be denied for health insurance because of the discovery of a higher possibility of gene mutations that lead to breast cancer (Grody 65). Insurers' access to genetic information "[violates] rights of privacy, prevents patients from getting needed help, and lead to widespread discrimination against applicants" (Keefer par. 2). In addition, an individual may be refused for an employment opportunity because of the genetic test that predicts personality traits or future behavioral disorders. Health insurance costs have become increasingly a large portion of employers' expenses. Therefore, employers may use employees' genetic information based on the genetic screening to eliminate prospective employees and hire those without evidence of genetic susceptibilities to disease (Arras 482).

Another concern regarding the application of DNA chips is that eugenics practice may be taken to a more subtle level based on specific gene selection and replacement at the molecular level. As Eileen P. Flynn points out in the book Issues in Medical Ethics, "the goal of eugenics is to improve the human gene pool by eliminating negative characteristics and breeding in such a way as to maximize the chances for creating superior human beings" (107-8). Such practice takes place at the expense of the harmony of the human community. Human rights are possessed by all persons, yet "eugenics tends

to cancel out the right of the less than perfect individual to existence" (Flynn 108). Through genetic screening, privileged groups might act on their prejudices against others. In seeking to build a better society, eugenics might try to eliminate defect members from the human gene pool. DNA chip technology allows the screening for all sorts of traits. Therefore, the parents of the fetus are given "new eugenic options for avoiding offspring with [minor] traits that many would not consider serious enough to justify termination" (Grody 66). DNA chip technology as a tool that speeds up research on genetics "may ultimately create an entirely new kind of racism or discrimination and eventually alter human beings to conform to a new techno-politics of hierarchical gene structures" (Mander 177).

In addition, an individual's take on his/her genetic information is one of the serious issues. "One of the most common ethical and legal questions is whether and to what extent a person is responsible for something. We ask whether alcoholics are responsible for their addiction and for the consequences of acts committed while they were inebriated: (Arras 486). However, as the knowledge on genetics increases with the help of technology, genetics is frequently used as an explanation or excuse for individual behaviors or traits. As John D. Arras points out in the book Ethical Issues in Modern Medicine, "the genome project will enhance the tendency to give genetic explanations for individual and group differences" (486). Therefore, whenever "a genetic correlate is suggested for some ethically, legally, or economically consequential outcome, there will be a temptation to explain it as fundamentally ... genetic, and hence is outside the individual's responsibility or capacity to control" (Arras 486). A positive genetic test may result in the stigmatization of the individual tested (Veatch 219). Thus, the individual might not be as motivated for life. On the other hand, with a negative genetic test, an individual might not care as much for the well-being of the body because there is no possibility of developing certain diseases based on his genetic information.

The former president, Bill Clinton says, "[DNA] chips will offer a road map for prevention of illness throughout a lifetime" (Kurian 270-1). Yet is the elimination of illness from life really a progress to mankind? Based on the desire to obtain a

comfortable life, the answer might be yes. However, looking at a deeper level, the elimination of illness perhaps is a loss for an individual's learning opportunity in elevating one's spirituality. In some cultures, illness is considered as a learning experience. Through that experience, one develops empathy and understanding for others when others are experiencing similar situations. For instance, oftentimes, in shamanism, a shaman experiences a major illness or physical sufferings before he becomes a healer. Such experience is said to "breakdown the ego, to restructure the personality, and to open new doors of perception" (White "Shamanic Healing" 31).

Furthermore, throughout life, we learn from mistakes. In some Eastern philosophies and religions, especially Buddhism, illness is said to be caused by the karma from an individual's previous lives in the reincarnation. Karma is the force that propels the law of cause and effect. As Edward J. Thomas points out in the book The History of Buddhist Thought, an individual "is born again ... in [certain] states, according to his karma" (110). Thus, illness in one's present life is the fruit of deeds done in previous lives. Experiencing illness gives an individual the opportunity to learn to be more mindful and responsible for his own actions in present life. Overall, experiencing illness not only is a pathway to be a better person, but it also is a collective experience of mankind that strengthens humanity. Therefore, DNA chip technology as a tool to prevent illness is not a beneficial application to mankind in this aspect.

Today, technology is changing so fast that we are not even sure if it is still in the control of our hands. With DNA chip technology at the forefront of current technological development, the serious ethical issues should be taken into consideration by society. Perhaps some might say, as long as "[DNA chip] technology remains available to benefit the greatest number of" people, it should be allowed to develop without questioning (Grody 67). The invention of airplanes doubtlessly has brought great benefits to the majority in society. Yet, as it is evident from the September 11th incident, only a few individuals using this technology caused a great destruction to mankind. So who is to say technology in the future will not be used inappropriately by a small number of individuals that might lead to perhaps the destruction of Civilization? Doubtlessly, technology itself

is neutral and "worries about discrimination and other potential abuses of [DNA chip] technology should be directed not at the science itself but at the societal setting of its application" (Grody 67). Therefore, the moral and ethical standards of society as a whole and of individuals in society should be re-evaluated, before this powerful technology is manipulated at the expense of humanity.

## **Bibliography**

1. Abbott, Alison. "DNA chips intensify the sequence search." Nature 379 (1996): 392.
2. Affymetrix. 7 Feb. 2002. <<http://www.affymetrix.com>>.
3. Arras, John D. and Bonnie Steinbock. Ethical Issues in Modern Medicine, 4th ed.. London: Mayfield Publishing, 1983.
4. Cameron, David. "DNA Chip Gives Positive ID." Technology Review. 14 Sept. 2001. 12 Dec. 2001 <<http://www.techreview.com>>.
5. "Living Array Speeds Gene Research." Technology Review. 4 June 2001. 12 Dec. 2001. <<http://www.techreview.com>>
6. Campbell, Neil A., Jane B. Reece, and Lawrence G. Mitchell. Biology, 5th ed.. Menlo Park, California: Benjamin Cummings, 1999.
7. Casey, Denise K. "Genes, Dreams, and Reality: The Promises and Risks of the New Genetics." Human Genome Project Information. 15 Jan. 2002. 7 Feb. 2002. <<http://www.ornl.gov/hgmis/publicat/judicature/article3/html>>
8. DNA Chips and Microassays. 6 Nov. 2001 <<http://www.science.uwaterloo.ca/~bpbobech/welcome.html>>
9. "Ethical, Legal, and Social Issues." Human Genome Project Information. 15 Jan. 2002. 7 Feb. 2002. <<http://www.ornl.gov/hgmis/elsi/elsi.html>>.
10. Farkas, Daniel H. "Bioelectronic DNA Chips for the Clinical Laboratory." Clinical Chemistry Vol. 47 No. 10 (Oct. 2001): 1871-1872. 6 Nov. 2001 <<http://www.clinchem.org/cgi/content/full/47/10/1871/>>
11. Flynn, Eileen P. Issues in Medical Ethics. Kansas City: Sheed & Ward, 1997.
12. Friend, Stephen H. "How DNA Microarrays and Expression Profiling Will Affect Clinical Practice." British Medical Journal (BMJ). 319 (13 Nov. 1999): 1306-7.
13. Grody, Wayne W. "Ethical Ramification of Genetic Analysis Using DNA Arrays." DNA Arrays: Methods and Protocols. Ed. Jang B. Rampal. Totowa, New Jersey: Humana Press, 2001.

14. Harrop, Sarah. "Single Nucleotide Polymorphisms Point the Way to Genetic Disease Diagnosis and Potential Cure – Are Those for Whom the Technology Should Most Help, Likely to Become Most Disadvantaged?" Derwent. Jul. 2001. 7 Feb. 2002. <<http://www.derwent.com/ipmatters/features/snps.html>>.
15. Human Genome Project Information. 15 Jan. 2002. 7 Feb. 2002. <<http://www.ornl.gov/hgmis/>>.
16. Junarkar, Sandeep. "'GeneChip' Encodes DNA on Silicon." The New York Times on the Web: Cybertimes – Technology. 15 Mar. 1997. 6 Nov. 2001. <<http://www.nytimes.com/library/cyber/week/031597genechip.html>>.
17. "GeneChip's Greatest Promise Lies in Basic Biological Research." The New York times on the Web: Cybertimes – Technology. 15 Mar. 1997. 6 Nov. 2001. <<http://www.nytimes.com/library/cyber/week/031597genechip-side.html>>.
18. Keefer, Christopher M. "Bridging the Gap Between Life Insurer and Consumer in the Genetic Testing Era: The RF Proposal." Human Genome Project Information. Fall 1999, 7 Feb. 2002. <http://www.ornl.gov/hgmis/>.
19. Khan, Javed, Michael L. Bittner, Yidong Chen, Paul S. Meltzer, and Jeffrey M. Trent. "DNA Microarray Technology: the Anticipated Impact on the Study of Human Disease." Biochimica et Biophysica Acta. 1423 (1999): M17-M18.
20. Kim, Myung. NIH: Lab of Biochemical Genetics. Personal Interview. Nov. 2001 – Feb. 2002.
21. Kurian, Kathreena M., Christine J. Watson, and Andrew H. Wyllie. "DNA Chip Technology." Journal of Pathology. 187 (1999): 267-271.
22. Lander, Eric S. "Array of Hope." Nature Genetics. 21 (1 Jan. 1999): 3-4.
23. Lockhart, David J. and Elizabeth A. Winzeler. "Genomics, Gene Expression and DNA Arrays." Nature. 405 (15 Jun. 2000): 827-836.
24. Mander, Jerry. In the Absence of the Sacred: The Failure of Technology & the Survival of the Indian Nations. San Francisco: Sierra Club Books, 1991.
25. Marshall, Andrew and John Hodgson. "DNA Chips: An Array of Possibilities." Nature Biotechnology. 16 (Jan. 1998): 27-31.
26. Nanogen. 11 Feb. 2002. <<http://www.nanogen.com>>.
27. Nystedt, Dan. "Biowell Chips Ready to Fight Piracy." The Taipei Times Online. 23 Aug. 2001. 12 Nov. 2001. <<http://www.taipeitimes.com>>.
28. Pollack, Robert. The Missing Moment: How the Unconscious Shapes Modern Science. Boston: Houghton Mifflin, 1999.

29. Prakash, C. S. "From DNA Chips to Potato Chips...: New DNA Chip Technologies Impact Agbiotech Research." Sept. 1997. 6 Nov. 2001. <<http://www.agro.umn.edu/plant-tc/listserv/1997/log9709/msg00015.html>>.
30. Robinson, Alan. "Large-Scale Gene Expression and Microarray Links and Resources." Gene Expression Links. 6 Nov. 2001. <<http://industry.ebi.ac.uk/~alan/MicroArray/>>.
31. Schena, M. ed. DNA Microarrays. Oxford: Oxford University, 2000.
32. Shi, Leming. DNA Microarray (Genome Chip) – Monitoring the Genome on a Chip. 29 Apr. 2001. 6 Nov. 2001. <<http://www.gene-chips.com/>>.
33. Stikeman, Alexandra. "Biochips Go Big Time." Technology Review. Mar. 2001. 12 Dec. 2001. <<http://www.techreview.com>>.
34. Thomas, Edward J. The History of Buddhist Thought. New York: Barnes & Noble, 1971.
35. Veatch, Robert M. Ed. Medical Ethics. Boston: Jones and Bartlett Publishers, 1989.
36. "Visualize: DNA Chips." Technology Review. Jan./Feb. 2001. 12 Dec. 2001. <<http://www.techreview.com>>.
37. White, Robert. Philosophy professor at Montgomery College. Personal Interview. 11, 12 Feb. 2002.
38. "Shamanic Healing: An Old Practice In Light of the New Science." 24 Oct. 1997.
39. Wickelgren, Ingrid. "DNA Chips: Here Come Genetic Diagnoses, at Pentium speed, for a Host of Diseases." Physician's Weekly Highlights and Analysis of Medical News Vol. XIV, No. 43 (17 Nov. 1997). 6 Nov. 2001. <[http://www.physweekly.com/archive/97/11\\_17\\_97/twf.html](http://www.physweekly.com/archive/97/11_17_97/twf.html)>.
40. Wortman, Marc. "DNA Chips Target Cancer Even Before Tumors Forms." Technology Review 104 (July/August 2001): 51-55.
41. Yang, Shutong. NIH: Lab of Biochemical Genetics. Personal Interview. Nov. 2001 – Feb. 2002.