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Introduction and Overview

The Controversy over Patenting DNA

Since 1976, the United States' Patent and Trademark Office (PTO) has issued over 16,000 patents on isolated and purified deoxyribonucleic acid (DNA) sequences or on processes used to identify, isolate, copy, sequence, or analyze DNA sequences (PTO 2002). In 1999 alone, the office received over 3,000 patent applications pertaining to DNA sequences or DNA-related technologies (Enserink 2000). Although the practice of DNA patenting is scarcely more than a couple of decades old, it has created an enormous controversy. The storm began brewing in 1994, when the National Institutes of Health (NIH) applied for patents on thousands of gene fragments in an attempt to undercut private efforts to patent these DNA sequences. The PTO rejected these applications, however (Zurer 1994).

During that same year, over thirty organizations representing indigenous peoples announced formal declarations objecting to gene patenting, the ownership of life, and the commercial exploitation of indigenous peoples. These organizations were responding, in large part, to the NIH's patent applications on viral genes taken from the Hagahai people in Papua, New Guinea and natives of the Solomon Islands as well as the Human Genome Diversity Project, aka "the vampire project" (Taubes 1995; Crigger 1995). While the NIH's applications did not seek patents on human genes, these organizations nevertheless argued that the patents would harm and exploit indigenous peoples and violate their cultural values. Researchers claimed that these patents could deter scientific progress and that the NIH, a government agency, should not be involved in any attempt to exert proprietary control over DNA: the NIH

should encourage public dissemination of DNA and not private control. In defense of its patent applications, the agency claimed that it hoped to encourage private investment in the development of vaccines based on these viral genes and that it intended to grant nonexclusive licenses to companies. In 1995, the PTO awarded the NIH a patent on a viral gene taken from residents of Papua, New Guinea. Responding to objections from researchers as well as the public, the NIH withdrew its request to patent viral DNA sequences taken from residents of the Solomon Islands, although it retained the Papua, New Guinea patent at the request of clinicians working with that population, who felt that the population could benefit from research and royalties generated by the patent (Resnik 1999b).

In 1995, the PTO awarded the NIH and Genetic Therapy Incorporated patents on techniques for modifying cells ex vivo. Opponents of this patent argued that it was too broad and that it would stifle research (Beardsley 1994). The patent even drew Congress' ire, which considered but rejected a measure that would have prevented many types of gene patents (Kevles and Berkotwitz 2001). On May 18, of the same year, about 180 religious leaders, led by biotechnology critic Jeremy Rifkin, held a press conference in Washington, DC, objecting to biomedical patenting. In their "Joint Appeal against Human and Animal Patenting" (1995) these leaders denounced all attempts to patent nature. Some of the members of the Joint Appeal compared gene patenting to slavery, while others claimed that gene patents treat human beings as marketable commodities (Joint Appeal 1995; Andrews 1995; Peters 1997; Hanson 1997; Rifkin 1998). Religious leaders and organizations also took their mission to stop gene patenting beyond the Joint Appeal and published articles and editorials on the subject (Christian Century 1995; Land and Mitchell 1996). For Rifkin, the Joint Appeal vindicated ideas he had voiced for years. Since the 1970s, Rifkin has been the biotechnology industry's gadlfy. He has written books denouncing attempts to modify, engineer, patent, or own living things. His Foundation on Economic Trends, a Washington-based nonprofit organization, champions Rifkin's admonitions and concerns about the biotechnology revolution (Rifkin 1983, 1985, 1998, 2000).

From 1995–1999, the controversy continued as researchers, scholars, and government officials objected to private efforts to patents DNA technologies and DNA sequences. During this period, a handful of genomics companies, such as Celera Genomics, Human Genome Sciences, Genset, and Myriad Genetics were created with the explicit mission of marketing genetic information for use in diagnosis, therapy, and drug discovery. Their business plans called for DNA patenting, protein patenting, and the commercialization of genomics information services (Fisher 1999; Wade 2000a,b,c; Marshall 1999a,b,c; Wicklegren 1999). Many pharmaceutical and biotechnology companies, such as Incyte Pharmaceuticals, Glaxo Welcome, Millenium Pharmaceuticals, Genentech, Perkin Elmer, and Monsanto, also took an interest in

gene patenting and bought gene patents or reached licensing agreements with companies conducting genetic research.

Private efforts to profit from genomics research were part of a massive increase in private funding of biomedical research and development (R & D) that has taken place in the last two decades. Private funding of biomedical R & D rose from $2 billion per year in 1980 to over $50 billion per year in 2000 (Beardsley 1994; Resnik 1999a). Although government funding still plays an important role in biomedical R & D, private funds now account for more than 60 percent of all biomedical R & D, including a large portion of genomics R & D (Resnik 1999a). As money continued to pour into privately funded genomics research, many people in the research community worried that private efforts to patent or control DNA would hamper scientific innovation and discovery (Marshall 1997; Heller and Eisenberg 1998; Reynolds 2000; Gosselin and Jacobs 2000; Guenin 1996; Caplan and Merz 1996; Merz et al. 1997).

Many scientists, clinical researchers, and organizations continue to oppose various types of DNA patenting. For example, the Council for Responsible Genetics drafted a Genetic Bill of Rights that opposes the patenting of human genes (Council for Responsible Genetics 2000). The United Nations Educational, Scientific and Cultural Organization (UNESCO) declared its opposition to human gene patenting several years ago (UNESCO 1997). Many indigenous groups have signed formal declarations against animal or human DNA patenting (Resnik 1999b). The Foundation on Economic Trends remains firmly opposed to all forms of gene patenting (Rifkin 2000).

Early debates about DNA patenting focused on fundamental questions about whether any patenting of DNA should be legal. While many people still oppose all forms of DNA patenting, these arguments have so far not swayed legislators, judges, or patent offices. Accordingly, debates about gene patenting have shifted away from general concerns about patenting toward more specific issues related to patenting (Barton 2000; Resnik 2001a,b; Caulfield and Gold 2000a,b; Heller and Eisenberg 1998). Many people have raised objections to specific patenting policies, such as allowing patents on sequences tags (ESTs) or single nucleotide polymorphisms (SNPs); patenting the use of genes to diagnose diseases; and patenting genes related to research on the human immunodeficiency virus (HIV) (American Society of Human Genetics 1991; Human Genome Organization 1995; Marshall 1997; Council on Ethical and Judicial Affairs 1997; Reichhardt 1998;Reynolds 2000; Marshall 2000a). Others have objected to the effects of patents on agricultural biotechnology and global trade (Poland 2000; Barton and Berger 2001; Shiva 1996). Most of these specific concerns address potential, undesirable social consequences of patenting and restrictions on access to genetic information. These critics argue that some types of DNA patents may hinder the progress of science, medicine, or agriculture.

Many government researchers, such as Francis Collins, Director of the National Human Genome Research Institute (NHGRI), which funds the Human Genome Project (HGP), have expressed dire concerns about private control of genetic information (Marshall 2000b,c,d,e). In response to concerns raised by researchers about speculative and broad patents on DNA sequences, PTO decided to raise the bar on DNA patents by clarifying the conditions that must be satisfied before a patent may be awarded. The PTO issued new utility guidelines in December 1999, which made it clear that inventors must state definite, specific, and plausible uses for the sequences of DNA that they plan to patent (Patent and Trademark Office 1999; Enserink 2000; Resnik 2001a).

During the 1990s, a rivalry developed between public and private efforts to conduct genomics R & D. The human genome, the holy grail of biomedicine, occupied ground zero in this conflict. The two principal players were Collins and Craig Venter, the (then) maverick CEO of Celera Genomics, which launched a private effort to sequence and map the human genome (Kevles and Berkowitz 2001). The public effort consisted of a consortium of universities and research centers, led by Collins and the NHGRI. Using a shotgun approach to gene mapping and sequencing as well as supercomputers and automated sequencing machines, Venter promised to sequence the human genome ahead of the HGP's schedule (Marshall 1999b; 2000b,e). Traditional clone-by-clone methods, used by researchers in the HGP, sequence DNA one sequence (or clone) at a time. The shotgun method breaks DNA into its various parts, sequences them all at once, and then uses supercomputers to reassemble the parts. Many scientists doubted whether his shotgun approach would work and feared that it would produce a genome with missing pieces or pieces that are out of place. Venter was vindicated in February 2000, when Celera produced a high-quality data set for the entire genome of the fruit fly, *Drosophila melanogaster* (Pennisi 2000a,b; Adams et al. 2000).

Access to genetic information was one of the key issues in this public-private conflict. The NHGRI wanted all researchers to have free access to genetic data as soon as it is checked for accuracy and quality; Celera planned to eventually allow all researchers free access to data through its website but would also charge corporations or research institutions a fee for an early look at genetic data. Although Celera did not plan to patent large portions of the genome, it planned to patent some specific genes or DNA sequences with practical applications. Celera planned to make most of its money through selling information services related to its genomics databases. (This business strategy proved to not be very profitable.) The NHGRI, on the other hand, hoped to undercut private patenting efforts by placing as much genetic information as possible in the public domain (Marshall 2000b,e).

In June 2000, the two sides agreed to cooperate and announced that the entire human genome had been sequenced and would soon be mapped and

analyzed (Wade 2000c). They used data generated by both the clone-by-clone and shotgun methods to complete this task. In February 2001, the public consortium and Celera published versions of the human genome in the journals *Nature* and *Science,* respectively (Marshall 2001; Venter et al. 2001). Under the terms and conditions negotiated between *Science* and Celera, nonprofit researchers are allowed to download pieces of Celera's DNA sequence from its website, provided that they agree not to commercialize or distribute the data. Researchers who plan to use the data for commercial purposes must negotiate an agreement with Celera (Marshall 2001).

As an epilogue to this story, it is worth noting that Venter resigned as CEO of Celera in January 2002, to form another company, because he disagreed with the company's new business strategy. Celera is now pursuing drug development instead of selling access to data, as its main business objective. On August 16, 2002, Venter announced his plans to form a genome sequencing company, which will sequence human, animal, and plant DNA for a fee. He hopes that in ten years advances in sequencing technologies will allow his company to be able to sequence a person's entire genome for several thousand dollars, which would represent a dramatic cost-reduction. Currently, the cost of sequencing a human genome would run at least into the millions of dollars. Unlike his earlier company, Venter's new company will be nonprofit. Venter also now plans to release all data to the public at no cost. He has also established two foundations, the Center for the Advancement of Genomics, which explores ethical and policy issues related to genomics, and the Institute for Biological Energy Alternatives, which develops microorganisms that produce energy alternatives to fossil fuels (Pollack 2002).

The United States was not the only country debating DNA patenting. In Europe, researchers and the public also expressed concerns about patenting genes and life forms (Kevles and Berkowitz 2001). In France, legislators adopted a measure declaring that human genes (in their natural state) are not patentable, which brought the country in conflict with other members of the European Union (EU) (Balter 2000). Denmark, on the other hand, ruled that there is no compelling argument against gene patenting (Knoppers 1999). Switzerland considered but ultimately rejected an initiative that would have forbidden the patenting of transgenic plants, animals, or their components parts (Schatz 1998).

The European Commission, a division of the EU which makes policy for the European Patent Convention (EPC), ruled that the EPC can refuse to award patents on inventions that infringe on human rights or violate human dignity (European Commission 1998). The EPC's patent laws, unlike U.S. patent laws, declare that patents should not be granted for inventions that are contrary to the public morality (Brody 1999). Although gene patents remain legal in countries that accept the EPC, it is not clear whether gene patents are contrary to the public morality or violate human dignity (Crespi 2000).

Overview of the Issues

Although DNA patenting is a highly technical topic far removed from ordinary, human concerns, it is not entirely surprising that it has generated so much controversy, since a great deal is at stake in this issue. As mentioned earlier, private companies have invested billions of dollars in genetic research with the expectation that they will be able to obtain the intellectual property protection afforded by patents. Genomic R & D has had a significant impact on the world's economy and has played a key role in advances in pharmaceuticals, medicine, biotechnology, and agriculture (Rifkin 1998; Enriquez 1998; Biotechnology Industry Organization 2001a). It was clear that industrial biotechnology had come of age when the announcement by then President William Clinton of the United States and Prime Minister Tony Blair of the United Kingdom (UK) of an agreement to make data from the human genome available to all researchers sent the NASDAQ composite tumbling over 200 points (Berenson and Wade 2000). The NASDAQ contains many biotechnology companies, including Celera, and investors speculated that this announcement would undercut private efforts to profit from genomics. During the slide, Celera's stock dropped 5.2 percent and Incyte's dropped 12 percent. As an aside, Wall Street probably overreacted to this announcement because it only restated previous commitments by these governments to make genetic data publicly available, and biotechnology companies have taken these commitments into account in their business plans (Langreth and Davis 2000). However, the episode shows that even if investors misunderstood the significance of the announcement, proprietary interests in DNA and other biological materials have important implications for business and investing. Moreover, disputes about intellectual property rights in biotechnology can exacerbate the high volatility of biotech stocks.

The issues involve much more than money, however. Genetics and genomics are foundational disciplines in many different areas of biology, biotechnology, and agriculture, and have an important bearing on psychology, sociology, and anthropology (Kitcher 1997). The free and open exchange of information is vital for discovery and innovation in basic and applied research (Resnik 1998b,c). Practices that can inhibit access to genetic data and genetic technologies, such as patenting, can therefore be an impediment to the progress of science. Likewise, genetics and genomics now play a vital role in diagnosing, treating, and preventing human diseases and in agricultural biotechnology (Collins and McKusick 2001; Barton and Berger 2001). Now that researchers have completed their study of the human genome, it will be possible to understand the genetic basis of health and disease. Still, this genetic information is of little use if it is not available to clinicians and medical researchers. If gene patenting were to restrict access to genetic information and genetic technologies, then this would threaten the progress of med-

icine and the promotion of health. The same points apply to restrictions on access to genetic information that could affect agriculture. Thus, basic researchers, applied scientists, and clinicians are key stakeholders in the gene patenting controversy.

Genetics and genomics also have important implications for society and culture. Since the discovery of the structure of DNA in 1953, genes have acquired a great deal of cultural and social significance and symbolic value (Nelkin and Lindee 1995). Since many people readily accept genetic explanations of human personality, behavior, and physiology, and genetic tests can be used in medicine, insurance, employment, or the criminal justice system, our treatment of genes has ramifications for human rights, privacy, and dignity. Although few people would equate a person with a set of genes, many people believe the genes have some fundamental connection to the person or self. Since genetics and genomics play key roles in biology, medicine, and agriculture, our attitudes toward genes and DNA have implications for our views of humankind's relation to nature. Since researchers may use DNA sequences from all over the world, genetics and genomics also have important implications for cultural exploitation. Furthermore, since genetically engineered crops or animals could affect the health and safety of other species, including humans, genetics and genomics have important implications for public health and the environment. Thus, virtually all people who are concerned with the cultural, social, and environmental consequences of bioscience and biotechnology, such as religious leaders, politicians, environmentalists, consumers, humanists, indigenous people, and ethicists also have a stake in the DNA patenting dispute.

DNA patenting raises a number of different legal, ethical, philosophical and political issues. These questions range from very broad concerns about public policy, such as "What is the justification of the patent system?" and "What is the difference between a product of nature and a product of human ingenuity?" to narrower questions, such as, "Are isolated and purified DNA sequences products of human ingenuity?" and "What is the correct way to interpret the scope of a DNA patent?" Although most of these questions are framed in terms of specific laws or policies and have a legal context, in order to answer them, one must often examine the moral and philosophical arguments used to justify policies and frame legal questions and issues. For example, U.S. statutes and court decisions provide a basis for the legal distinction between a product of nature and a product of human ingenuity, but to interpret or evaluate this distinction one must have some grasp of its moral and philosophical implications. Although the courts operate according to legal rules and procedures, they must frequently interpret concepts and terms from ordinary language and address public policy arguments. The line between law and ethics that seems so clear in the abstract becomes quite murky when one examines a real world legal issue with moral, social, and economic implications. Although

this book does not seek to render a legal analysis of DNA patenting or offer legal advice, it will be necessary to engage the legal issues that raise moral and ethical concerns. One goal of this book is to provide a moral analysis of DNA patenting that can be used to interpret patenting laws or to suggest changes in the laws.

My Approach: A Moral Analysis

What makes an analysis of a practical problem a *moral* analysis as opposed to some other type of analysis, such as a political, legal, or economic analysis? A moral analysis, according to many, attempts to understand whether a particular action or policy is right or wrong, all things considered (Fox and DeMarco 1990; Baier 1958). It attempts to determine whether there are good reasons for performing an action or instituting a policy. Thus, a moral analysis may consider and critique economic, legal, political, social, religious, and scientific perspectives related to the particular question at hand. A moral analysis of a practical problem takes all relevant factual and normative considerations into account, considers the relevant interests at stake, examines the issue from different perspectives, and attempts to reach a fair and impartial decision (Rachels 1993). It attempts to give a well-reasoned analysis of a practical problem, and involves the kind of self-reflective and critical discussion associated with the Socratic method used in philosophical debate and legal argument. Thus, to understand whether DNA patenting is morally justifiable, one must address the economic, scientific, social, political, legal, and religious aspects of the issue.

There are two basic viewpoints one may consider when conducting a moral analysis (Frankena 1973; Pojman 1995). According to consequentialist approaches to morality, an action or policy is justifiable insofar as it is likely to yield the greatest balance of good/bad consequences (outcomes or results) for all relevant parties. Utilitarianism is the most influential consequentialist theory in ethics. According to this view, one should act so as to maximize utility and minimize disutility. There is considerable debate among utilitarians about how one should define or measure utility. Early utilitarians, such as John Stuart Mill ([1861]1979), equated utility with happiness; modern utilitarians define utility in terms of welfare or the satisfaction of preferences (Scheffler 1988).

Consequentialist approaches also play a prominent role in economic theory, environmental management, medicine, and public health. Economists frequently analyze policies, technologies, and institutional arrangements in terms of their economic costs and benefits (Blaug 1980; Samuelson 1980). Scholars and policy analysts concerned with environmental considerations or public health and safety often use risk-benefit theory to understand the con-

sequences of actions or policies. Risk-benefit theories address the probability and magnitude of harms as well as the probability and magnitude of benefits (Shrader-Frechette 1991). In medicine, physicians use evidence from physical examinations, medical records, diagnostic tests, and scientific articles to assess probable risks and benefits to the patient when making medical recommendations and decisions (Sackett et al. 1997).

Nonconsequentialist (or deontological) approaches, on the other hand, hold that the morality of an action or policy does not depend on its consequences: an action or policy is, by its very nature, moral or immoral, just or unjust (Frankena 1973; Pojman 1995). Kantianism is by far the most influential deontological theory in ethics. According to the eighteenth century German philosopher, Immanuel Kant, it is wrong to treat people as mere instruments to other ends, regardless of the consequences (Kant 1981 [1985]). Another popular deontological theory known as libertarianism, holds that all people are endowed with some basic natural rights to life, liberty, and property (Nozick 1974). The sole function of the state is to protect these rights, and restrictions on natural rights are justified only to prevent people from violating each other's rights.

Many theorists, such as Rawls (1971) and Ross (1930), defend a hybrid approach and hold that one needs to balance consequentialist and deontological concerns in determining how one should act. According this balancing approach, one must weigh and consider many different moral duties and principles in order to make a moral choice. It is not my aim in this book to pass judgment on consequentialist or deontological approaches to ethics and moral reasoning. I agree with commentators who recognize that both approaches should play some role in social and political philosophy and moral argument (Rawls 1971; Feinberg 1973; Pojman 1995; Gutman and Thompson 1996). A moral analysis of a problem should consider deontological concerns pertaining to moral rights, duties, and justice and consequentialist concerns relating to probable benefits, harms, and utility. One should also consider both of these perspectives in understanding the morality of DNA patents (Resnik 1997).

In this book, I shall examine the main arguments for and against DNA patenting from both consequentialist and deontological perspectives. (Table 1.1 provides an outline of these arguments.) I will examine and critique deontological arguments for and against DNA patenting and show that they generally fail to show that DNA patenting is inherently moral or inherently immoral. Only one type of DNA patenting is inherently immoral, the patenting of a whole human genome. The morality of all other forms of DNA patenting, from the patenting of gene markers, to whole genes, to artificial chromosomes, depends on the consequences of these practices for science, medicine, agriculture, society, business, industry, and the economy.

I shall attempt to show that DNA patenting offers society many important benefits, even though it also creates some potential threats. Although it

TABLE 1.1
Arguments for and against DNA Patenting

	Consequentialist Arguments	*Deontological Arguments*
For	Patenting promotes science and technology	People have a right to patent DNA
	Patenting benefits business and industry	
	Patenting benefits medicine	
	Patenting benefits agriculture	
Against	Patenting hinders science and technology	Patenting violates human dignity
	Patenting harms medicine	DNA is God's invention
	Patenting harms agriculture	DNA is our common heritage
	Patenting harms society and culture	Patenting DNA commodifies nature

is easy to imagine and predict the various ways that DNA patents might harm society, it is not easy to assign objective probabilities to these threats. In order to suggest strategies for decision-making when we lack a great deal of knowledge about potential outcomes, I shall articulate and defend a popular principle known as the Precautionary Principle (PP). I shall apply this principle to the DNA patenting debate and argue that the most reasonable response to the various threats posed by DNA patenting is to enact various regulations and policies to regulate DNA patenting. These rules would aim to prevent potential threats from happening or minimize their impact. We should take advantage of the opportunities presented by industrial biotechnology, but we should also take precautionary measures to mitigate harmful results. Throughout this book, I will discuss policies that I think would be reasonable responses to the potential harms of DNA patenting, and I will summarize my policy conclusions in the final chapter. Since the biotechnology industry is still in its infancy and DNA patenting is quite new, we need to study and monitor the effects of various policies and update them in response to changes in science, technology, and the industry (Resnik 2001a; Schonmann 1998). I will argue that there is no need, at this time, to make any substantive changes in patent-

ing laws, since society already has the legal and regulatory tools needed to deals with the issues raised by DNA patenting.

Since this book will take a stand on a fairly controversial topic, I realize that many readers may disagree with my analysis of the problems and my proposed solutions. I do not aim to convince every reader of the truth of my views, but I do hope that even those who disagree with me will learn something from this book, that they will understand how we disagree, and that they will see where further discussion and debate may advance social policy.