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PATENTING HUMAN GENES
THE ADVENT OF ETHICS IN THE POLITICAL ECONOMY OF PATENT LAW

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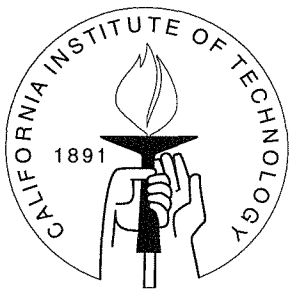

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Patenting Human Genes

The Advent of Ethics in the Political Economy of Patent Law

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Just as the development of technology is a branch of the history of political and economy, so is the evolution of patent law. The claim is well illustrated by the attempts mounted in recent years in the United States and Europe to patent DNA sequences that comprise fragments of human genes. Examination of these efforts reveals a story that is partly familiar: Individuals, companies, and governments have been fighting over the rights to develop potentially lucrative products based on human genes. The battle has turned in large part on whether the grant of such rights would serve a public economic and biotechnological interest. Yet the contest has raised issues that have been, for the most part, historically unfamiliar in patent policy -- whether intellectual property rights should be granted in substances that comprise the fundamental code of human life. The elevation of human DNA to nearly sacred status has fostered the view among many groups that private ownership and exploitation of human DNA sequences is somehow both wrong and threatening, an unwarranted and dangerous violation of a moral code.

Attempts to patent human DNA rest legally on *Diamond v. Chakrabarty*, the U.S. Supreme Court's decision in 1980 that allowed the patenting of living organisms modified, and hence made, by man. The court imposed no limits on what might be patentable, though a later ruling by the appeals board in the U.S. Patent Office held that patents could not be obtained on a human being. A biological material in its natural state remained for the law a "product of nature" and as such was also not patentable. However, once a biological substance was isolated from the body by human artifice, it became patentable because it was no longer in its natural state. Following *Chakrabarty*, cDNA copies of complete human genes with known functions were routinely patented. Such copies do not occur naturally; they are man-made. The issue of patents on them did not break substantially new legal ground or provoke widespread reactions.

On June 20, 1991, however, Dr. J. Craig Venter, of the National Institute of Neurological Disorders and Stroke (a division of NIH), filed a 400-page patent application at the U.S. Patent

and Trademark Office (PTO) for 337 human genes.[1] Venter's lab had used commercially available automated sequencing machines to sequence random fragments of human cDNA that they took from a commercially available "library" of cDNA clones from the human hippocampus (a part of the brain). cDNA is made from messenger RNA (mRNA); it is thus the part of DNA that figures in the creation of proteins. Such DNA is estimated to account for about 3 to 5 percent of all human DNA. It is the part of our DNA that is most likely to be useful for understanding diseases or normal functions, and is most likely to lead to lucrative products.[2] Venter and NIH sought patent protection for all cDNA sequences his lab had obtained that had no match in public DNA databases.

What was controversial about his patent application was that, while he was applying for patent protection on only a fragment of human DNA, such patent protection seemed likely to give him control over the entire gene that the fragment identified. Venter had sequenced just enough of each gene--150-400 base pairs,[3] which scientists termed an "expressed sequence tag," or EST — to establish its unique identity. Ventner claimed that the ESTs would have utility "as diagnostic probes" for the presence of particular types of mRNA in specific cell types and as DNA markers for mapping locations of genes on chromosomes. He made no attempt to tie sequences to any function or disorder, or even to map the locations of most ESTs on chromosomes. Venter and his colleagues were able to churn out sequences at an unheard-of rate. Another researcher could then use the EST to locate the same cDNA from the same or another cDNA library.

Ventner seemed prepared to seek patents on the vast majority of human genes, or at least a substantial fraction of the of he 100,000 genes estimated to be contained in the human genome. At a Congressional briefing on the Human Genome Project that summer, Venter mentioned in passing that the NIH planned to file patent applications for 1000 such sequences a month. "I almost fell off my chair," said one briefing participant.[4] Venter and NIH's dramatic move may be partly due to Venter's no-nonsense attitude. He later explained: "I turned 21 in Vietnam. So, in that situation, I saw that there is too little time in life to waste on B.S. approaches. So, in that sense, I am impatient. I want to constantly be moving forward with the discovery of new things, and I'm frustrated with how long it takes new ideas to become part of the general thinking."[5]

Venter attributed the idea for patenting the ESTs to Max Hensley, a patent attorney for Genentech, who apparently suggested the idea to Reid G. Adler, the director of NIH's Office of Technology Transfer, who in turn convinced Venter. Adler apparently felt that if NIH could patent these DNA sequences, there would still be an incentive for companies to develop products using them because NIH could grant the companies exclusive or partly exclusive licenses under the Federal Technology Transfer Act of 1986.[6] If the sequences were published without being patented, they would be in the public domain, and companies would thus be without that incentive to develop products from the sequence information.

Others, however, argued that NIH patents on ESTs would inhibit industrial development of products from them.[7] Bernadine Healy, the director of the NIH, later testified: "NIH is amenable to not enforcing any patent rights that may issue to partial sequences of unknown function, except in the unusual situation where the licensing of such rights is necessary to provide for the development of a therapeutic agent that might not otherwise come to market."[8] Healy also stated: "The NIH is doing this in a socially responsible way for the purposes of assuring that products that are life-saving remedies and therapies that are derived from this basic knowledge will be developed in the interest of our mission, which is science and the pursuit of health."[9] She said that it was important for NIH to be at the table.

The debate that ensued turned in part on technical legal issues of patentability. Considerable emphasis went to the patentability of sequences that were merely fragments of genes of unknown function. Venter's approach raised questions about the "non-obviousness" and "utility" of the sequences that had not been raised by earlier gene patents. The international Human Genome Organization (HUGO) later argued: "Several uses have been suggested for genes and gene fragments to get past the utility requirement for patent protection. For any random gene, gene fragment, or collection of genes or gene fragments, it is easy to give a list of potential uses without knowledge of their true biological functions.... In all important cases the development of a truly useful tool for these purposes will require the investment of considerable further effort and creativity, far more than that invested in finding the initial fragment."[10]

Patent attorneys were divided over the patentability of ESTs. Steve Bent, of the firm Foley & Lardner in Washington, thought that the patent issued would be restricted to the ESTs

themselves. He said, "I don't want to say that NIH is wrong, but my feeling is maybe they entered the patent process too early."[11] Max Hensley, the Genentech attorney who suggested EST patenting, nonetheless was uncertain about its success. He said, "the tummy feel to this is not quite right. You ask, 'Where's the beef?'... If it was 10 or 50 genes a year, I could make that fly. But when you start talking about 20,000 genes, a buzzer goes off and you wonder, How will I get that by a judge?"[12] But he also pointed out: "If these things are patentable, there's going to be an enormous cDNA arms race."[13]

Ventner and NIH responded to the legal unhappiness. In February 1992, they filed a second patent application (technically a "continuation in part" (CIP) for the first application, both adding to and modifying the initial application[14]), for 2375 additional ESTs, also from brain tissue, in concert with publishing new EST data in the February 13 issue of *Nature*.[15] This time the patent claim included the ESTs and the full genes, but not the proteins made from the genes, in contrast to the wider claim in the previous patent application. Stephen Raines, vice president for patents at Genentech, said, "it is a little dangerous to ask for the world. As the claim gets narrower, that usually helps support the argument of patentability."[16] The CIP also reportedly removed the process of producing the cDNA sequences from the patent claim.[17]

* * *

The utility requirement for patents has traditionally been relatively easy to meet. As Rebecca S. Eisenberg, a law professor at the University of Michigan, later wrote: "The utility requirement is rarely invoked in practice, perhaps because few people go to the trouble and expense of seeking patents on useless inventions, and no one is likely to care much if they do.... It is the as yet undiscovered utility of the sequences, rather than the uses that are disclosed in the patent application, that makes NIH's patent claims worth fighting about."[18]

The stakes in undiscovered utility were high, both scientifically and commercially, the NIH/Ventner move divided government officials, who recognized that the issue went beyond legal technicalities to questions of political economy. While NIH pursued the patents, James Watson, then head of NIH's genome project, and David Galas, head of the Department of

Energy's genome project, both strongly opposed the move. Watson called cDNA patenting "outrageous"[19] and "sheer lunacy."[20] Watson said that "virtually any monkey" could perform this type of research. "What is important is interpreting the sequence.... If these random bits of sequences can be patented, I am horrified."[21] Galas said: "There is no coherent government policy, and we need one--quick--since the sequence is just pouring out.... It would be a big mistake to leave this one to the lawyers."[22] Adler claimed that NIH would continue to pursue the patents through litigation only if industry showed interest in licenses from these patents; then, companies could pay for the legal costs related to their licenses: "It will be the company bearing the cost, not the taxpayer." He set up a November 14th meeting with industry representatives to "announce that this invention is ready for licensing."[23] (As of May 1992, one company apparently had a license application on file at NIH, although the patent application had not yet been decided on.[24])

Stakes in the issue were evident to interest groups outside the government. Many scientists strongly dissented from NIH's move. Maynard Olson, a molecular geneticist then at Washington University and a member of the advisory panel to the Human Genome Project, said, "I think it's a terrible idea.... If the law is interpreted to give intellectual property rights for naked DNA sequences, then the law should be changed. It's like trying to patent the periodic table.... Patent law wasn't designed to be a kind of lottery where one guesses every large number of letters that might be the right combination."[25] George Annas, a lawyer and medical ethicist at Boston University, said: "This is not science. This is like the gold rush. That's why there are no scientists saying this is a wonderful thing."[26]

Biotech companies were also divided on the issue. The Association of Biotechnology Companies (ABC) in Washington, DC, which represented 280 companies and institutions[27], issued a statement in May 1992 that supported the NIH patent application, but argued that the NIH should not attempt to award exclusive licenses for the ESTs (as opposed to the full cDNAs or the proteins).[28] Lisa Raines, vice president of the Industrial Biotechnology Association (IBA), which represented 125 companies[29] and 80% of U.S. investment in biotechnology[30], said that U.S. biotech companies support the NIH patent application "for the purpose of preserving NIH's

options."[31] However, in June 1992, an IBA committee recommended opposition to the NIH patent. The IBA committee argued that product development would require "more meaningful and costly scientific work" than the EST sequencing and that it would be "unfair to permit the Government to exercise complete control over a product to whose development the Government contributed little." In addition, the committee suggested that issuing the NIH patents would increase costs of product development as well as risks of future patent infringement litigation. Companies would be encouraged "to abandon current research efforts that are aimed at product development in favor of routine genetic sequencing for the purpose of staking claims to as much of the genome as possible."[32] Richard Godown, president of the IBA said: "If somebody spends a lot of time and money to discover the whole gene and its function, and then discovers they've got to deal with somebody who owns a patent to part of it, suddenly the commercial possibilities become clouded."[33] Moreover, the Pharmaceutical Manufacturers Association, which had 100 member companies[34], actively opposed the NIH patent in a May 28, 1992 letter to Louis W. Sullivan, the Secretary of HHS, saying that "a governmental policy of ownership and licensing of gene sequences would inevitably impede the research and development of new medicines in this country."[35] In August 1992, Adler conceded that "it is clear that the trade associations are not interested in exclusively licensing sequences of unknown function, assuming that they are patentable, as an incentive for product development."[36]

Foreign governments were apprehensive that their biotechnology enterprises would be competitively disadvantaged by NIH patents on ESTs. Government officials in France, Italy, and Japan announced their countries' opposition to such patents early on.[37] The French Academy of Sciences issued a statement on January 13, 1992 condemning "any measure which, answering purely to a logic of industrial competition, strove to obtain the legal property of genetic information data, without even having taken care to characterize the genes considered."[38] In March 1992, the British retaliated against the NIH: the Minister of Science, Alan Howarth, announced that the MRC would also seek cDNA patents. He said, "a decision by the UK Medical Research Council (MRC) not to seek patents when researchers funded by public bodies in other countries have or may do so could place the UK at a relative disadvantage."[39] However, Howarth also claimed that the UK was attempting to negotiate an international agreement not to

patent "genome sequences of unknown utility identified as a result of publicly funded research."[40] In 1992 July, the MRC applied to the European Patent Office (EPO) and the U.S. PTO for patents on about 1200 ESTs, all the while claiming that it opposed EST patenting.[41] (In October 1993, the MRC announced that it would not apply for any additional EST patents. David Owen, the MRC's director for technology transfer, explained: "By filing a patent, we felt that we would get a seat at any table where the issue was discussed. We've now got places in the most important discussions on the patent issue--in the patent offices of the world and in a public inquiry for the US Congress by its Office of Technology Assessment."[42])

In April 1992, James Watson resigned as head of the NIH genome project, pointing to the NIH attempts to patent ESTs.[43] (Watson, however, was also under fire for conflict of interest: he owned shares in a biotech company and refused to sell them. The attack on Watson for conflict of interest was led by Frederick Bourke, a businessman who aimed to form a private company to sequence the nematode genome--a project that the NIH was already pursuing in collaboration with the British.[44])

In the meantime, Venter himself, along with three dozen other scientists at a human genome meeting in Brazil in May 1992, signed a resolution that opposed the patenting of "naturally occurring gene sequences," while supporting the patenting of specific uses for sequences. Venter said he supported the NIH patent application only because it stimulated debate; he hoped the patent would not be issued.[45] (Venter, however, did stand to gain if a patent were issued. Under the terms of the Federal Technology Transfer Act of 1986, he would be personally entitled to at least 15% of any royalties accrued from licensing of patents, with the majority of such royalty income designated for funding of research in his laboratory.[46])

In July 1992, Venter announced that he was leaving the NIH to head a new private, nonprofit research center called The Institute for Genomic Research (TIGR) [initially referred to as the Institute for Genomic Research (IGR)]. TIGR received $70 million as a 10-year grant from a New Jersey venture capital group called Healthcare Investment Corporation, which had also created several biotech companies, including Genetic Therapy Inc. The chair of Healthcare Investment Corporation, Wallace Steinberg, asserted that American scientists needed to patent

genes before their European and Japanese competitors beat them to it: "I suddenly said to myself that if this thing doesn't get done in a substantive way in the United States, that is the end of biotechnology in the United States."[47] While TIGR itself would be nonprofit, a new biotech company, called Human Genome Sciences Inc. (HGS), was created to develop and market products resulting from TIGR's research. TIGR and the new company would be set up in Montgomery County, Maryland, near NIH.[48] Venter took 30 NIH researchers with him[49] and said TIGR would "do the genome project," beginning with a scaled-up continuation of his project to sequence random ESTs.[50] He predicted that TIGR would discover "a majority of human genes within the next 3 to 5 years at a pace of up to 1000 genes per day."[51]

Even critics wanted to see the NIH EST patent application legally decided. "We need a definitive answer," Paul Berg said. "Withdrawing the patent would resolve nothing."[52]

On August 20, 1992, the expedited decision of the U.S. PTO was announced. The initial review concluded that the patent claims were "vague, indefinite, misdescriptive, inaccurate and incomprehensible."[53] The PTO rejected the patent claims mainly because they did not meet the standards for "nonobviousness" and novelty. (In contrast, most of the public criticism of the patent application had focused on utility as the problematic criterion.) The PTO claimed that the sequences were obvious for a surprising reason. Molecular geneticists had traditionally regarded a 15-base pair sequence (or "15mer") as the minimum length of DNA sufficient to identify a gene. (However, many researchers already had come to believe that a longer stretch of DNA was in fact necessary for this purpose.[54]) The PTO examiners searched through conventional databases of DNA sequences and found that randomly selected 15mers from the Venter application sometimes occurred within published sequences of human or nonhuman DNA. Hence, they concluded: "It would be obvious for someone ordinarily skilled in the art" to find Venter's ESTs using one of these published 15mers as a probe.[55] Thus, ironically, while most of the scientific and biotech community was urging that the patents be denied because short fragments of genes with completely unknown functions should not be patentable, and if patented, might hinder the elucidation of full gene sequences and functions, the PTO effectively argued that previous publication of even smaller fragments had already undermined the patentability of Venter's fragments.

The PTO also concluded that the sequences were not novel because the DNA was taken from a commercially available "library." Bernadine Healy, the director of NIH, commented on this during the gene-patent hearings organized by Senator DeConcini in September: "Taken to its logical extension...the PTO's reasoning would deny novelty to virtually all products isolated from expected sources of biomolecules in nature, such as blood, saliva, or tissues."[56] Craig Venter, also testifying at the hearings, argued that patent law should be changed to permit future patenting of DNA sequences that contain previously published fragments.[57] Healy agreed: "The PTO's position here suggests the need to at least consider a legislative remedy and international agreement that prior publication of partial gene sequences not preclude a subsequent patent on the full genes and/or partial genes with known function."[58] Senator Pete Domenici (R-NM) planned to introduce such a bill.[59]

Sen. Mark O. Hatfield (R-OR) had already introduced a bill to impose a 5-year moratorium on patenting animals. Although Hatfield's bill did not refer to gene patenting, Hatfield argued in speeches that gene patenting raises the "specter of removing the building blocks of life from the common possession of us all and shifting them to the private use and profit of researchers or corporations." He also said that biotechnology generally has reduced man to a "biological machine."[60] Hatfield's bill, reconstituted as an amendment to the NIH reauthorization bill, providing a 3-year moratorium on patenting of both living organisms and "genetic matter" did not advance. Hatfield withdrew the amendment after reaching an agreement with Senator Dennis DeConcini (D-AZ), chair of the Senate Subcommittee on Patents, Copyrights, and Trademarks, and Senator Edward M. Kennedy (D-MA), chair of the Senate Committee on Labor and Human Resources, that they would each schedule hearings on gene patenting. Hatfield, DeConcini, and Kennedy also requested a report from the Office of Technology Assessment (OTA) on legal, ethical, and economic issues raised by human gene patenting.[61]

The hearings, in September 1992, enlarged the issue before the government to include ethical considerations. Such considerations had been advanced earlier -- by critics of genetic engineering such as Jeremy Rifkin and his allies as well as by a variety of clerics, a number of whom had been recruited by Rifkin -- in connection with the *Chakrabarty* decision and then with

the patenting of animals. The issue of patenting DNA sequences prompted a reconsideration in an ethical framework of whether human genes should be patented at all. Andrew Kimbrell, the policy director and attorney for Jeremy Rifkin's Foundation on Economic Trends, argued in favor of a moratorium on gene patenting such as Senator Hatfield had suggested, saying, "We are right in the middle of an ethical struggle on the ownership of the gene pool." Kimbrell also took the opportunity to review innovations in patenting of biological entities since the 1980 *Chakrabarty* Supreme Court decision, which included the patenting of human cells and of entire mammals. Kimbrell referred to these innovations as the "the children of *Chakrabarty*" and suggested that the *Chakrabarty* decision be effectively reversed by legislation: "We need Congress to intercede to decide where this ethical and legal free-fall ends." Before *Chakrabarty*, "[w]e never allowed the patenting of animals. It was tried. They tried to patent hybrid chickens and the answer was no. We have never allowed nature itself to be patented because that is our common heritage."[62]

Kimbrell added:

> "There is little question that, unless stopped, the patenting juggernaut will continue to transgress into life in all its forms. As research continues in cell analysis and in the deciphering of the human genome, corporations and researchers will fight for patent ownership of commercially valuable genes and cells held to be the key to health, intelligence or youth. As there are advances in reproductive technologies human embryos may be up for patent grabs. Animals with increasing number of human genes will be patented. Genetically engineered human body parts will almost certainly be patented. And looking into the more distant future perhaps a genetically altered human body itself may be patentable. As patenting continues, the legal distinction between life and machine, life and commodity will begin to vanish."[63]

However, Kimbrell was in a minority at the hearings. He was strongly opposed by patent attorneys and by representatives of the biotech industry. For example, Genentech vice president David Beier, testifying as a representative of IBA and ABC, opposed a moratorium on human DNA patenting.[64] A key criticism came from William D. Noonan, a physician and patent

attorney who testified on behalf of the Oregon Biotechnology Association. Noonan insisted on distinguishing between issues of political economy and issues of ethics. The former had a place in disputes over patent policy; the latter, at least in the United States, did not, even though they might be legitimate in principle. Noonan argued that because of advances in human genetics, "we have to confront some of the darker questions about our human nature as we gain the power to practice eugenics on a scale and with a precision that was previously impossible." In this context, however, the debate about patenting human ESTs was a red herring:

> [T]here is nothing inherently wrong or even ethically new about patenting DNA molecules. We have been patenting chemical components of the human body for years. Patents have been issued for decades on purified proteins, enzymes, neuropeptides, and many other gene products. There is no inherent ethical distinction between patenting these molecules and a purified molecule of DNA. Promoting the development of new medical treatments ethically justifies gene patents. Patent applications have been filed in recent years on genes involved in cystic fibrosis, neurofibromatosis, Fanconi's anemia, and other diseases. These filings did not provoke the ethical outcry. It was only when the NIH filed Dr. Venter's patent applications on cDNA's of unknown function that a sustained international debate arose about the ethics of gene patents. I think we run the risk of failing to address the real ethical concerns if we become too fixated on what is essentially a problem in international scientific politics and the uncertainty about the scope of patent law. What we should instead talk about is the social impact of human genome research. Do we want to practice molecular eugenics on humans and animals, and what is the acceptable scope of such eugenic efforts? These ethical questions have nothing to do with patent law and cannot be addressed by changing the scope of patentable subject matter. The Patent Office is, of course, the wrong place to conduct any ethical inquiry."[65]

In support of biotechnology and in opposition to a moratorium, Senator Orrin Hatch (R-

Utah) warned:

> "I would be concerned about any sweeping measure which would jeopardize the jobs associated with this vital industry. Such a measure would certainly undermine our world competitiveness. Do any of my colleagues believe the Europeans and Japanese are going to slow down their efforts, let alone engage in a moratorium in this cutting edge industry? Of course not. They are going to take advantage of it."[66]

Senator Domenici added:

> "Frankly, if we are not careful, what we do at this stage might thwart the evolution of this program in America by great American scientists, universities, laboratories, pharmaceutical houses, those who manufacture technology of medicine. What we do at this stage also could indicate whether the United States of America is the beneficiary of all that will come from this in terms of economics.... It is obvious once you get into the mapping of the human genetic system and the delivery of those maps to scientists with an indication of where various disease [sic] exist that they can find a cure. We can tell them that right here--this gene we just gave you--is where schizophrenia comes from. As we continue to increase our efforts, all of the dread diseases will be located by gene. This will have a dramatic impact on the way we develop cures and [treat] diseases."[67]

Bernadine Healy also opposed a moratorium on gene patenting, saying it would be contrary to the Federal Technology Transfer Act of 1986 and would be the "death knell for the patent system in the biotech field."[68] Healy argued that the attempt to patent human gene fragments did not raise as serious ethical concerns as the patenting of entire organisms, which she personally regarded as questionable, but which had already received the stamp of approval of the U.S. Supreme Court. She also pointed out that complete human gene sequences that code for

proteins with known functions had been routinely patented without a fuss, and added: "Some have said that we should not patent our universal heritage as a matter of ethics. But the same people who are saying that--the French Government has said this many times--... [also say that] if you know the function of the gene and it has commercial value, then you can patent it. That seems to be an ethical double standard."[69]

Healy testified that the NIH ought to pursue the appeals process, because "truncating the patent process before it yields useful information would leave uncertainty and would perpetuate a policy void in patent law in the technology transfer system."[70] NIH did seek approval for an appeal. Healy later asserted that NIH's "outside patent attorney" was "very optimistic that most of the concerns raised in the preliminary finding can be met." She added: "I don't think it's a question of winning or losing. It is a question of resolving uncertainty that is unsettling to both the scientific community and to the policy makers.... It will ultimately be a decision made by the Secretary [of HHS] as to whether or not we will continue these patent proceedings."[71] In late 1992, during the governmental transition from Bush to Clinton, HHS approved the NIH appeal.[72]

However, Healy was soon succeeded in the directorship of the NIH by Harold Varmus. In February 1994, Varmus announced that the NIH was withdrawing its patent application on all ESTs (the number of ESTs in the application had since increased to 6869), saying that such patents are "not in the best interests of the public or science."[73] Varmus's decision was heavily influenced by advice from Rebecca Eisenberg, who served on an advisory panel.[74] David Galas, having moved from the DOE to become scientific director of a company called Darwin Molecular in Seattle, thought that the NIH was right to drop the application: "If [NIH officials] didn't think that the granting of the patents was in the public interest, then they were put in the position of pursuing with public funds something they hoped they'd lose."[75] The British MRC soon followed suit, withdrawing its own EST patent applications.[76]

* * *

The Ventner/NIH application, however, had let the genie out of the bottle, perhaps irreversibly. Several companies had followed the NIH's lead and filed their own patents on ESTs.

Venter initially claimed that neither his nonprofit research institute (TIGR) nor its associated company (HGS) would file patent applications for ESTs with unknown function.[77] A subsequent company prospectus for HGS, however, indicated that the company had filed patent applications for 9900 ESTs.[78] In addition, Incyte Pharmaceuticals, Inc., of Palo Alto, CA, filed for more than 40,000 ESTs.[79] Incyte planned to file applications for as many as 100,000 ESTs each year.[80] These applications were not affected by the change of heart at the NIH.

The genie was out on gene patenting as such, too. In 1995, Jeremy Rifkin's Foundation on Economic Trends formed an alliance with U.S. religious leaders opposed to human gene patents. On May 18, 1995, several religious leaders held a press conference in Washington, DC, in which they announced that a coalition of 180 religious leaders representing 80 denominations (plus Rifkin's group, which apparently organized this), had signed a Joint Appeal Against Human and Animal Patenting, which opposed the patenting of any human genes and any genetically altered animals. The group included Abdurahman Alamoundi, Executive Director of the American Muslim Council, Kenneth Carder and Jaydee Hanson of the United Methodist Church, Wesley Granberg-Michaelson, Secretary General of the Reformed Church in America, Richard Land, President of the Christian Life Commission of the Southern Baptist Convention, and Rabbi David Saperstein, Director of the Religious Action Center of Reform Judaism. Rifkin said: "By turning life into patented inventions, the government drains life of its intrinsic nature and sacred value." Land added, speaking to the *New York Times*, that "altering life forms, creating new life forms [is] a revolt against the sovereignty of God and an attempt to be God."[81]

Land and another leader of the Southern Baptist Convention's Christian Life Commission later added:

> "[T]he patenting of human genetic material attempts to wrest ownership from God and commodifies human biological materials and, potentially, human beings themselves. Admittedly, a single human gene or cell line is not a human being; but a human gene or cell line *is* undeniably human and warrants different treatment than all nonhuman genes or cell lines. The image of God pervades human life in all of its parts. Furthermore the right to own one part of a human

being is *ceteris paribus* the right to own all the parts of a human being. This right must not be transferred from the Creator to the creature."[82]

All the while, the biotechnology industry on both sides of the Atlantic had been paying close attention to the patentability of genes in Europe, and there by law ethical issues enjoyed a seat at the table of patent policymaking. According to article 53a of the in European patent convention, patents were inadmissible that violated "public order and morality." Since the late 1980s, the European Commission, the executive arm of the evolving European Community, had been seeking to promulgate a directive establishing he patentability of biotechnological inventions. It had been repeatedly blocked by the European Parliament, where advocates of ethical opposition — Green party members, for example — were strong. A new compromise draft directive from the Commission was before the Parliament in 1994 that allowed the patenting of human genes provided that "they cannot be linked to a specific individual."[83] Willy Rothley, of Germany, the head of the effort to find suitable language in the Parliament, considered the language a success: "The European Parliament has been able to impose an ethical dimension on patent rights and has been able to obtain most of the guarantees that it was asking for."[84]

However, Linda Bullard of the European Green Party, countered: "We feel that Parliament, having voted previously against patents on parts of the human body--including genes--under any circumstances, is morally obliged to reject this compromise. This is not a question of individual human dignity, but of collective human dignity."[85] Like William Noonan, in his Congressional testimony in 1992, researchers and biotech leaders, especially in the U.S., argued that morality had no place in the discussion about patenting DNA. George Poste, research director of SmithKline Beecham, argued typically: "Patent law is entirely unsuited to arbitrate on moral and ethical questions. A ban on genomic patents will not shield society from the evolution of genetic medicine or the need for vigilance against the misuse of genetic testing or the genetic modification of humans."[86]

The compromise directive, however, died in March 1995, when the European Parliament voted 240 to 188 against approval, with 23 abstentions. This signalled the end of the directive,

because under the terms of the Maastricht Treaty, the European Parliament has an effective veto over the process. The Greens and Jeremy Rifkin were celebratory. Rifkin said, "It is a great victory."[87]

In the States in May 1996, Rifkin spoke out on behalf of a group of women's rights leaders against patenting genes implicated in breast cancer. He claimed that efforts to patent these human genes represented an "assault on women" and "denies them control over the most intimate aspect of their being, their bodies' genetic blueprint."[88] He announced that a new coalition would file a petition with the PTO to challenge the patent claims filed by Myriad Genetics Inc. of Salt Lake City. Myriad was the company associated with Mark Skolnick of the University of Utah, who had isolated the breast cancer susceptibility genes, BRCA1 and BRCA2; Myriad had filed patent applications for both genes. Rifkin's statements were endorsed by members of women's health organizations in 69 countries, including author Betty Friedan, Gloria Steinem, the consulting editor of *Ms.* magazine, and Bella Abzug, the co-chair of the Women's Environment and Development Organization.[89] Abzug, who is also a former U.S. representative and a breast cancer survivor, said: "Human genes are not for sale or profit. Any attempt to patent human genetic materials by individuals, scientific corporations, or other entities is unacceptable."[90] Carolyn A. Marks, a breast cancer and ovarian cancer patient and a member of the National Ovarian Cancer Coalition, said it "boggles [her] mind" that someone would claim a patent on a human gene.[91] She added that it gives "a new definition to 'chutzpah,'" because Myriad is seeking a patent "for something that, in essence, was already there."[92] Rifkin said the new campaign is "the beginning of the genetic rights movement around the world."[93] Carl Feldbaum, president of the Biotechnology Industry Organization, said that last year Rifkin "wrapped the gene patenting issue in clerical garb. This year he came out [in] feminist garb."[94]

But Rifkin could expect to don many more garbs. The more numerous the number of genes for human disease that became known, the larger the number of interest groups whom the Rifkins might enlist in the anti-gene-patenting cause. To be sure, members of these interest groups might well take the position advanced by the biotechnology industry — that patents on human genes would encourage investment in treating the diseases they caused; and that no patents would leave the knowledge unexploited, much to the detriment of the people who

suffered.

Certainly the American biotechnology industry constitutes a formidable pressure group in both the United States and Europe against permitting the kind of ethical issues raised by Rifkin, the European Greens, and their allies to figure consequentially in the formation of patent policy for living organisms. The stakes for the biotechnology industry are high. It would obviously be costly to make what is patentable in the U.S. unpatentable in Europe. American biotechnologists also have a growing number of allies in Europe. Interpharma, an association representing Swiss pharmaceutical companies, supported patents on genes or gene fragments "in a form that does not occur in nature," arguing that "isolated genes do not occur naturally, nor do large quantities of purified proteins; they should, therefore, be patentable."[95] In Germany, biotechnology had been lagging. By 1996, the political winds had shifted and the federal government began offering financial incentives to encourage German biotechnology.[96] As Maria Leptin, head of the genetics faculty at the University of Cologne, put it: "if there's anything that's more important [to Germans] than saving the environment, it's saving jobs. As soon as people saw the [pharmaceutical] industry possibly disappearing, morality went out the window."[97]

The future of EST patenting in the United States and human gene as well as EST patenting in Europe remains open. Earlier this year, an official of the PTO surprised a meeting of the AAAS, in Seattle, by announcing that the PTO had decided that ESTs are patentable after all. He said that the PTO became convinced that ESTs would in fact be useful as genome probes, and that was apparently enough to change their minds. This summer, the European Parliament took up for reconsideration the question of the patenting of biological inventions. Whatever the outcome of these new developments, it is evident that human gene patenting has introduced a new dimension into the development of patent law, joining issues of ethics with the longstanding one of law itself and the political economy it expresses.

NOTES

1. Christopher Anderson, "US patent application stirs up gene hunters," Nature, 353 (Oct. 10, 1991), pp. 485-486.

2. Mark D. Adams, Jenny M. Kelley, Jeannine D. Gocayne, Mark Dubnick, Mihael H. Polymeropoulos, Hong Xiao, Carl R. Merril, Andrew Wu, Bjorn Olde, Ruben F. Moreno, Anthony R. Kerlavage, W. Richard McCombie, and J. Craig Venter, "Complementary DNA sequencing: expressed sequence tags and Human Genome Project," Science, 252 (June 21, 1991), pp. 1651-1656.

3. Mark D. Adams, Jenny M. Kelley, Jeannine D. Gocayne, Mark Dubnick, Mihael H. Polymeropoulos, Hong Xiao, Carl R. Merril, Andrew Wu, Bjorn Olde, Ruben F. Moreno, Anthony R. Kerlavage, W. Richard McCombie, and J. Craig Venter, "Complementary DNA sequencing: expressed sequence tags and Human Genome Project," Science, 252 (June 21, 1991), pp. 1651-1656.

4. Leslie Roberts, "Genome patent fight erupts," Science, 254 (Oct. 11, 1991), pp. 184-186.

5. Karen Young Kreeger, "Genome investigator Craig Venter reflects on turbulent past and future ambitions," The Scientist, 9 (July 24, 1995), p. 1.

6. Federal Technology Transfer Act of 1986, Public Law 99-502 (Oct. 20, 1986).

7. Leslie Roberts, "Genome patent fight erupts," Science, 254 (Oct. 11, 1991), pp. 184-186.

8. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

9. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

10. The Human Genome Organization, "HUGO statement on the patenting of DNA sequences," January 1995.

11. Leslie Roberts, "Genome patent fight erupts," Science, 254 (Oct. 11, 1991), pp. 184-186.

12. Leslie Roberts, "Genome patent fight erupts," Science, 254 (Oct. 11, 1991), pp. 184-186.

13. Christopher Anderson, "US patent application stirs up gene hunters," Nature, 353 (Oct. 10, 1991), pp. 485-486.

14. Anna Maria Gillis, "The patent question of the year," BioScience, 42 (May 1992), pp. 336-339.

15. Andy Coghlan, "US gene plan 'makes a mockery of patents'," New Scientist, 133 (Feb. 22, 1992), p. 10.

16. Leslie Roberts, "NIH gene patents, round two," Science, 255 (Feb. 21, 1992), pp. 912-913.

17. Anna Maria Gillis, "The patent question of the year," BioScience, 42 (May 1992), pp. 336-339.

18. Rebecca S. Eisenberg, "Genes, patents, and product development," Science, 257 (Aug. 14, 1992), pp. 903-908.

19. Christopher Anderson, "US patent application stirs up gene hunters," Nature, 353 (Oct. 10, 1991), pp. 485-486.

20. Leslie Roberts, "Genome patent fight erupts," Science, 254 (Oct. 11, 1991), pp. 184-186.

21. Leslie Roberts, "Genome patent fight erupts," Science, 254 (Oct. 11, 1991), pp. 184-186.

22. Leslie Roberts, "Genome patent fight erupts," Science, 254 (Oct. 11, 1991), pp. 184-186.

23. Leslie Roberts, "Genome patent fight erupts," Science, 254 (Oct. 11, 1991), pp. 184-186.

24. Anna Maria Gillis, "The patent question of the year," BioScience, 42 (May 1992), pp. 336-339.

25. Christopher Anderson, "US patent application stirs up gene hunters," Nature, 353 (Oct. 10, 1991), pp. 485-486.

26. D'Arcy Jenish, "A patent on life: scientists seek legal rights to genes," Maclean's, 105 (Aug. 31, 1992), pp. 38-39.

27. Reid G. Adler, "Genome research: fulfulling the public's expectations for knowledge and commercialization," Science, 257 (Aug. 14, 1992), pp. 908-914.

28. Rebecca S. Eisenberg, "Genes, patents, and product development," Science, 257 (Aug. 14, 1992), pp. 903-908.

29. Reid G. Adler, "Genome research: fulfulling the public's expectations for knowledge and commercialization," Science, 257 (Aug. 14, 1992), pp. 908-914.

30. Rebecca S. Eisenberg, "Genes, patents, and product development," Science, 257 (Aug. 14, 1992), pp. 903-908.

31. Roger S. Johnson, "NIH files for second patent on expressed sequence tags," Genetic Engineering News, March 1, 1992, p. 17.

32. Rebecca S. Eisenberg, "Genes, patents, and product development," Science, 257 (Aug. 14, 1992), pp. 903-908.

33. D'Arcy Jenish, "A patent on life: scientists seek legal rights to genes," Maclean's, 105 (Aug. 31, 1992), pp. 38-39.

34. Reid G. Adler, "Genome research: fulfulling the public's expectations for knowledge and commercialization," Science, 257 (Aug. 14, 1992), pp. 908-914.

35. Rebecca S. Eisenberg, "Genes, patents, and product development," Science, 257 (Aug. 14, 1992), pp. 903-908.

36. Reid G. Adler, "Genome research: fulfulling the public's expectations for knowledge and commercialization," Science, 257 (Aug. 14, 1992), pp. 908-914.

37. Norton D. Zinder, "Patenting cDNA 1993: efforts and happenings," Gene, 135 (Dec. 15, 1993), pp. 295-298.

38. Academy of Sciences, Paris, The Patentability of the Genome, Academy of Sciences, Paris Bilingual Report No. 32, Lavoisier:Paris, 1995.

39. Anna Maria Gillis, "The patent question of the year," BioScience, 42 (May 1992), pp. 336-339.

40. Alan Howarth, "Patenting complementary DNA," Science, 256 (April 3, 1992), p. 11.

41. Andy Coghlan, "Truce declared in gene patent war," New Scientist, 140 (Nov. 6, 1993), p. 10; Christopher Anderson, "NIH drops bid for gene patents," Science, 263 (Feb. 18, 1994), pp. 909-910.

42. Andy Coghlan, "Truce declared in gene patent war," New Scientist, 140 (Nov. 6, 1993), p. 10.

43. Michael Waldholz and Hilary Stout, "A new debate rages over the patenting of gene discoveries," The Wall Street Journal, April 17, 1992, p. 1.

44. Jerry E. Bishop, "At center of Human Genome Project, Nobel laureate and businessman clash," The Wall Street Journal, April 13, 1992, p. B6.

45. Christopher Anderson, "US to seek gene patents in Europe," Nature, 357 (June 18, 1992), p. 525.

46. Federal Technology Transfer Act of 1986, Public Law 99-502 (Oct. 20, 1986).

47. D'Arcy Jenish, "A patent on life: scientists seek legal rights to genes," Maclean's, 105 (Aug. 31, 1992), pp. 38-39.

48. Christopher Anderson, "Controversial NIH genome researcher leaves for new $70-million institute," Nature, 358 (July 9, 1992), p. 95.

49. D'Arcy Jenish, "A patent on life: scientists seek legal rights to genes," Maclean's, 105 (Aug. 31, 1992), pp. 38-39.

50. Christopher Anderson, "Controversial NIH genome researcher leaves for new $70-million institute," Nature, 358 (July 9, 1992), p. 95.

51. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

52. Leslie Roberts, "NIH gene patents, round two," Science, 255 (Feb. 21, 1992), pp. 912-913.

53. Norton D. Zinder, "Patenting cDNA 1993: efforts and happenings," Gene, 135 (Dec. 15, 1993), pp. 295-298.

54. Christopher Anderson, "NIH cDNA patent rejected; backers want to amend law," Nature, 359 (Sept. 24, 1992), p. 263.

55. Christopher Anderson, "NIH cDNA patent rejected; backers want to amend law," Nature, 359 (Sept. 24, 1992), p. 263; The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

56. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

57. Christopher Anderson, "NIH cDNA patent rejected; backers want to amend law," Nature, 359 (Sept. 24, 1992), p. 263.

58. Anna Maria Gillis, "Ethics muddle NIH's genome patent application," BioScience, 42 (Dec. 1992), p. 874.

59. Christopher Anderson, "NIH cDNA patent rejected; backers want to amend law," Nature, 359 (Sept. 24, 1992), p. 263.

60. Roger S. Johnson, "Gene patents," Genetic Engineering News, June 15, 1992, pp. 3, 20.

61. Anna Maria Gillis, "Ethics muddle NIH's genome patent application," BioScience, 42 (Dec. 1992), p. 874; The genome project:the ethical issues of gene patenting, Hearing before the

Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

62. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

63. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

64. Anna Maria Gillis, "Ethics muddle NIH's genome patent application," BioScience, 42 (Dec. 1992), p. 874.

65. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

66. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

67. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

68. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

69. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

70. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

71. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993).

72. Christopher Anderson, "NIH to appeal patent decision," Science, 259 (Jan. 15, 1993), p. 302.

73. Christopher Anderson, "NIH drops bid for gene patents," Science, 263 (Feb. 18, 1994), pp. 909-910.

74. Christopher Anderson, "NIH drops bid for gene patents," Science, 263 (Feb. 18, 1994), pp. 909-910.

75. Christopher Anderson, "NIH drops bid for gene patents," Science, 263 (Feb. 18, 1994), pp. 909-910.

76. Christopher Anderson, "NIH drops bid for gene patents," Science, 263 (Feb. 18, 1994), pp. 909-910.

77. The genome project:the ethical issues of gene patenting, Hearing before the Subcommittee on Patents, Copyrights and Trademarks of the Committee on the Judiciary, U.S. Senate, 2:S. Hrg. 102-1134, Sept. 22, 1992 (U.S. Govt. Printing Office, 1993); Christopher Anderson, "NIH to appeal patent decision," Science, 259 (Jan. 15, 1993), p. 302.

78. Christopher Anderson, "NIH drops bid for gene patents," Science, 263 (Feb. 18, 1994), pp. 909-910.

79. Christopher Anderson, "NIH drops bid for gene patents," Science, 263 (Feb. 18, 1994), pp. 909-910.

80. Christopher Anderson, "NIH to appeal patent decision," Science, 259 (Jan. 15, 1993), p. 302.

81. Ted Peters, "Patenting life: Yes," First things: a monthly journal of religion and public life, 63 (May 1996), pp. 18-20.

82. Richard D. Land and C. Ben Mitchell, "Patenting life: No," First Things, 63 (May 1996), pp. 20-22.

83. David Dickson, "British MPs 'likely to oppose gene patents,'" Nature, 373 (Feb. 16, 1995), p. 550.

84. David Dickson, "British MPs 'likely to oppose gene patents,'" Nature, 373 (Feb. 16, 1995), p. 550.

85. David Dickson, "British MPs 'likely to oppose gene patents,'" Nature, 373 (Feb. 16, 1995), p. 550.

86. George Poste, "The case for genomic patenting," Nature, 378 (Dec. 7, 1995), pp. 534-536.

87. David Dickson, "European parliament rejects bid to stem confusion over gene patents," Nature, 374 (March 9, 1995), p. 103.

88. "US coalition counters breast gene patents," Nature, 381 (May 23, 1996), p. 265.

89. Eliot Marshall, "Rifkin's latest target: genetic testing," Science, 272 (May 24, 1996), p. 1094; "US coalition counters breast gene patents," Nature, 381 (May 23, 1996), p. 265.

90. Eliot Marshall, "Rifkin's latest target: genetic testing," Science, 272 (May 24, 1996), p. 1094.

91. Eliot Marshall, "Rifkin's latest target: genetic testing," Science, 272 (May 24, 1996), p. 1094.

92. Adam Marcus, "Owning a gene: patent pending," Nature Medicine, 2 (July 1996), pp. 728-729.

93. Eliot Marshall, "Rifkin's latest target: genetic testing," Science, 272 (May 24, 1996), p. 1094.

94. Adam Marcus, "Owning a gene: patent pending," Nature Medicine, 2 (July 1996), pp. 728-729.

95. David Dickson, "European patent directive in critical test over genes," Nature, 372 (Nov. 24, 1994), p. 310.

96. Steven Dickman, "Germany joins the biotech race," Science, 274 (Nov. 29, 1996), pp. 1454-1455.

97. Steven Dickman, "Germany joins the biotech race," Science, 274 (Nov. 29, 1996), pp. 1454-1455.

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