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Genetic Diagnosis and Intellectual Property Rights: A Proposal To Amend “The Physician Immunity Statute”

Gregory P. Lekovic, M.D., J.D., Ph.D.*

It is difficult to overstate the extent of the revolution in medicine that is currently underway.¹ Across therapeutic areas, critical links between genes and disease are emerging and proving to be further-reaching than anticipated.² Researchers have realized that genetics can play a contributory role in the pathology of diseases long believed to be non-genetic, such as infectious disease.³ Improved understandings of the genetic bases of disease have raised prospects of novel therapies that have the potential to prevent or cure previously untreatable conditions.⁴ Arguably, this increased understanding of genetics has had its greatest impact in diagnostics where “molecular diagnostic tests . . . can provide . . . presymptomatic testing for late-onset disorders” and “can be used for population based screening to predict future genetic disease or assess the risk for complex conditions such as cancer, cardiovascular diseases, and

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* Resident, Division of Neurological Surgery, Barrow Neurological Institute, St. Joseph’s Hospital, Phoenix, Arizona. M.D, College of Medicine, University of Illinois at Chicago; Ph.D., Department of Anatomy and Cell Biology, University of Illinois at Chicago; J.D., Chicago-Kent College of Law, Illinois Institute of Technology. This work was supported by a Student Fellowship from the Chicago-Kent College of Law Institute of Science, Law, and Technology.

1. For a general genetics reference text, see EMERY AND RIMOIN’S PRINCIPLES AND PRACTICE OF MEDICAL GENETICS (David L. Rimoin et al. eds., 4th ed. 2002) [hereinafter PRINCIPLES AND PRACTICE].

2. One area in which “[m]olecular genetic testing is increasingly available [is] pediatric practice.” Comm. on Genetics, Am. Acad. of Pediatrics, Molecular Genetic Testing in Pediatric Practice: A Subject Review, 106 PEDIATRICS 1494, 1497 (2000) [hereinafter Am. Acad. of Pediatrics].

3. For example, the role of genetics in the progression of HIV to AIDS is a topic of current research. For an overview of the role of genetics in infectious disease, see Shelley Segal and Adrian V.S. Hill, Genetic Susceptibility to Infectious Disease, 11 Trends Microbiology 445 (2003).

neurodegenerative disorders in otherwise healthy people." Genetic diseases and syndromes such as Alpert’s Disease, Crouzon’s disease, Von Recklinghausen’s disease, hemophilia A, myotonic dystrophy, muscular dystrophy, hemochromatosis, and Canavan Disease can now all be diagnosed, even prenatally, with a high degree of accuracy, using molecular probes or polymerase chain reaction (PCR) technology. Pre-implantation diagnosis of embryos may in the future allow for the eradication of such diseases altogether. Although each of these diseases is very rare, in the aggregate they constitute a significant disease burden in the pediatric population; over five percent of all live born children will develop disease with a significant genetic contribution before the age twenty-five. Moreover, many of these diseases individually have a markedly increased incidence in select populations, such as Jews of Ashkenazi origin. For families afflicted with these rare conditions, the availability of

5. Am. Acad. of Pediatrics, supra note 2, at 1494, 1494.

6. In each of these cases, the gene responsible for the disease has been identified, and a test has been developed and brought to market that directly examines the patient’s DNA to determine if the suspected mutation is present. It is estimated that ten to twelve new molecular diagnostic tests become available each year. Am. Acad. of Pediatrics, supra note 2, at 1494. However, there are limits to the utility of genetic testing. Not all genetic diseases are best diagnosed by molecular tests: Cystic fibrosis, the most common genetic disease among Caucasians (one in twenty-five is a carrier), is not suited to molecular diagnosis because the number of mutations causing the disease is too high, making genetic screening currently impractical. Am. Acad. of Pediatrics, supra note 2, at 1495. For a complete list of genetic tests available, as well as a directory of laboratories offering testing, see http://www.genetests.org.

PCR stands for polymerase chain reaction and is the chemical reaction by which minute samples of DNA can be amplified into enough genetic material to be readily analyzed. Paul Rabinow, What Is PCR?, University of California, Berkeley, at http://sunsite.berkeley.edu/pcr/index.html (last visited May 1, 2004).

7. Pre-implantation genetic diagnosis is a technique that relies on genetic testing of embryos obtained through in vitro fertilization prior to ‘implanting’ the embryos back into the mother’s uterus. Thus, the likelihood that a child will be born with the disease can be greatly reduced by implanting only embryos that are free from disease. For an overview of the current status of the development of this technique, see Anuja Dokras, Pre-Implantation Genetic Diagnosis, at http://www.hygeia.org/poems5.htm (last visited Apr. 25, 2004).


9. Genetic diseases often have higher incidence in genetically isolated populations. For example, Ashkenazi Jews (Jews of Eastern European descent) are more likely to suffer from Tay-Sachs, Canavan’s disease, and several other disorders. Individuals of Ashkenazi Jewish heritage are advised to be screened for these diseases prior to having children. See
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genetic tests that can be used to determine whether adults are carriers of disease\textsuperscript{10} or to diagnose an unborn child may influence family planning decisions and therefore be of the utmost importance.

The cost of this rapid progress has been borne by both the public, via the National Institutes of Health, and by private enterprises, which have invested research dollars into developing quick, simple, and accurate means to diagnose genetic diseases. As an incentive (and reward) for efforts to discover the genes responsible for disease, the United States offers protected intellectual property rights. However, while the goal of the patent system is indisputably to promote the generation and dissemination of new knowledge and techniques, patents can paradoxically lead to a decrease in the availability of genetic-based tests.\textsuperscript{11} In Part I of this Article, I trace the major contours of the development of gene patenting in the United States and discuss the Physician Immunity Statute,\textsuperscript{12} a statute designed to ensure that the patenting of medical procedures does not impair the treatment of patients. As I argue below, the protections of the statute, in its current form, do not go far enough. In Part II, I illustrate the problems raised by the limitations of the Physician Immunity Statute by examining Canavan disease, the patent on the gene that encodes for it, and enforcement of that patent. Canavan disease is an incurable metabolic disorder, the gene for which was discovered in 1993 by Dr. Reuben Matalon.\textsuperscript{13} The gene was patented by Miami Children’s Hospital, which

\textsuperscript{10} For diseases caused by recessive genes, both copies of an individual’s gene must have the error that causes the disease. Individuals who have one gene with the error and one “normal” gene are called carriers. They do not themselves generally have the disease, but they can pass it onto their children. J. Cook, Mendelian Inheritance, in PRINCIPLES AND PRACTICE, supra note 1, at 104, 109. It is important to distinguish carriers of genetic diseases from carriers of infectious disease, who may transmit the disease simply through close contact with individuals.


\textsuperscript{12} 35 U.S.C. § 287(c) (2000).

\textsuperscript{13} What Is Canavan Disease?, Canavan Foundation, at http://www.canavanfoundation.org/canavan.php (last visited Apr. 25, 2004); see also Mary Kugler, Gene Patent: For Mankind’s Good, or For Profit?, About.com, at
subsequently enforced the patent, leading to a lawsuit filed by the families of Canavan-afflicted children. Canavan disease provides a particularly compelling example of the potential problems with gene patents for several reasons. The gene’s discovery involved research initiated by—and initially funded by—the afflicted families. Therefore, the Canavan story reflects an exception to the usual patent paradigm where a pharmaceutical company speculates on a technology by expending significant financial resources on research and development. In addition, since there is no treatment, let alone cure, for Canavan’s disease, genetic testing of the parents and/or prenatal screening represent the only options for parents who do not want to have a child with this devastating condition; these techniques allow parents either to avoid pregnancy or to terminate affected embryos.

A solution fashioned by the legislature that could ensure patients’ access to genetic testing information while recognizing the biotechnology companies’ financial interests in using gene patents to develop treatments and cures for genetic diseases would represent a crucial step forward in the genetic revolution. In Part III of the Article, I offer a proposal to amend the Physician Immunity Statute that would allow patients unfettered access to diagnostic testing for any known gene sequence, whether patented or not. Specifically, I argue that the provisions of the Physician Immunity Statute that prevent enforcement of patent infringement actions against physicians performing patented procedures or methods of diagnosis be applied to genetic diagnoses as well.

I. THE PATENT PROCESS

Congress is authorized by Article I, Section 8 of the United States Constitution to issue patents “[t]o promote the Progress of Science and Useful Arts.” The patent system has been described as a kind of bargain between the inventor and society, in which monopoly rights are granted to the inventor for a limited time in exchange for the disclosure of the invention. By disclosing the invention to the public, the inventor contributes knowledge to the arts and sciences and thereby spurs further


14. See infra Section II.B.
15. See id.
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innovation, including efforts to design around the patent. In order to allow competitors to engage in such innovation, however, the patent must give notice as to the scope of the invention through the use of specific and particular claims.

Current statutory requirements regarding patents were passed into law in the Patent Act of 1952.18 Five statutory requirements for patentability are that the invention be of patentable subject matter,19 that the invention be “non-obvious,”20 that it have utility,21 that it be adequately disclosed,22 and that it be precisely claimed.23 In exchange for disclosure, the patent holder gains the right to exclude others from making, selling, offering for sale, using, or importing the patented object in the United States.24 In order to enforce these rights, a patent holder can sue for infringement of the patent.25

A. Gene Patents

In 1980, the Supreme Court opened the door to gene patenting by clarifying that biological materials could fall within the purview of ordinary patent protection.26 Since then however, the practice of gene patenting has generated much controversy.27 Scholars have challenged the practice of

20. Id. § 103.
21. Id. § 101.
22. Id. § 112.
23. Id.
25. Infringement occurs when a patented invention is made, used, imported, offered for sale, or sold by someone other than the patent holder (or licensee). Infringement can be either literal, where the infringing product is exactly the same as the patented product, or by equivalence, where the differences between the patented invention and the infringing product are too minor to constitute successful “design around” the patent. See id. § 271 (2000).
26. Diamond v. Chakrabarty, 447 U.S. 303 (1980) (granting a patent for a genetically modified oil-dissolving microbe). The Court asserted in Diamond that “Congress intended statutory subject matter to include ‘anything under the sun that is made by man.’” Id. at 309 (quoting S. REP. NO. 82-1979, at 5 (1952); H.R. REP. NO. 82-1923, at 6 (1952)). The Court noted that the same language was used by P.J. Federico, “a principal draftsman of the 1952” legislation, in his testimony about the legislation before the House. Id. at 309 n.6. In Diamond, the bacteria in question had been modified and thus constituted a creation. Id.
27. See generally Barbara Looney, Should Genes be Patented? The Gene Patenting Controversy:
issuing patents on genes on policy grounds, and they have employed various moral, medical, ethical, and scientific arguments in opposition to the practice of issuing gene patents and to the withholding of data that might lead to those patents. Many argue against gene patents out of the fear that over-reaching DNA patents will enable patent holders to encroach on what is considered the "heritage of humanity," with consequent deleterious effects on patient care and privacy.

The United States Patent and Trademark Office (PTO) has responded to such concerns by assuring the public that "the concern that a person whose body 'includes' a patented gene could infringe the patent is misfounded. The body does not contain the patented, isolated and purified gene because genes in the body are not in the patented, isolated and purified form." Currently, the PTO sees little difference between DNA molecules and other chemical compounds. In 2001, the PTO issued "a revised version of guidelines to be used by Office personnel in their review of patent applications for compliance with the 'utility' requirement of 35 U.S.C. 101." Arguably, the patentability of Expressed Sequence Tags (ESTs), DNA fragments that can be used as "molecular probes," was "the most controversial issue addressed by the new guidelines." The 2001 guidelines make clear that ESTs are not categorically ineligible for patent protection,

30. Id.; see also Rebecca Eisenberg, Intellectual Property at the Public-Private Divide: The Case of Large Scale cDNA Sequencing, 3 U. CHI. L. SCH. ROUNDTABLE 557 (1996).
31. Out of over 2000 faculty researchers surveyed, a statistically significant higher proportion of genetic researchers (nearly one in six) refused to share research results with colleagues. David Blumenthal et al., Withholding Research Results in Academic Life Science, 277 JAMA 1224, 1224, 1227 (1997); see also Erin G. Campbell et al., Data Withholding in Academic Genetics: Evidence from a National Survey, 287 JAMA 473 (2002).
34. Id. at 1094.
35. Id. at 1092.
but also affirm that “[l]ike any descriptive property, a DNA sequence itself is not patentable. A purified DNA molecule isolated from its natural environment, on the other hand, is a chemical compound and is patentable if all of the statutory requirements are met.” In particular, the guidelines sought to operationalize the judiciary’s conception of the utility requirement by “require[ing] the disclosure of at least one specific, substantial, and credible utility.” Although it was not entirely clear how these criteria would apply to “a given EST,” the disclosure of a number of factors, such as “the sequence of the corresponding complete mRNA sequence, protein coding sequence or genomic sequence,” “the function of the protein encoded by the corresponding mRNA,” and “the phenotype of a mutation in the corresponding gene,” could all conceivably solidify a claim for patent protection of an EST.

Since patents are by definition exclusive, there is no positive burden on the patentee to use the invention; a patent simply grants the right to exclude others, including the right to restrict the licensing of the invention for non-economic reasons. Applied to diagnostics, the issuance of a patent practically creates a right to exclude patients from being diagnosed. Of particular importance in relation to diagnostic tests based on gene patents is the right of the patent holder to decrease access to prenatal screening, whether as a consequence of the patentee’s pecuniary interest or to further a non-economic objective.

Concerns that the patenting of genes would limit the availability of diagnostic testing are a relatively recent phenomenon. In fact, the first 150 years of patent jurisprudence in this country did not recognize the patentability of medical procedures, treatments, or methods of diagnosis. However, by the 1950s, the prohibition against the patenting of medical procedures began to erode, and by the early 1990s, the medical community began to become concerned about the potential impact such patents could have on the delivery of health care and research. While the

38. Id. cmt. 9.
39. Fate of Gene Patents, supra note 36.
41. Ex parte Scherer, 103 U.S.P.Q. 107 (BNA) (Pat. Off. Bd. App. 1954) (holding that claims for a medical treatment could be patented). The opposite trend was developing in the rest of the world. As of 1996, over eighty countries, as well as the European Union, exempt medical procedures from patent protection. Thus the Physician Immunity Statute can be seen as harmonizing U.S. law with that of other nations. Portman, supra note 40, at 92.
medical community secured some protection from Congress, the protections were not as great as they could have been or, as I will argue below, as great as they should have been. I turn to the history of these protections—and their limitations—in the next Section.

B. The Physician Immunity Statute

The rallying cry about the need for protections from patent infringement suits for the medical community came when Dr. Samuel Pallin sued Dr. Jack Singer for infringement of Pallin’s patented procedure for use in cataract surgery.42 Pallin v. Singer was the first case in which a physician sued another physician for infringement of a medical procedure patent; as a result, the medical community became concerned about the deleterious consequences such litigation would present should such patents become widespread.

Largely as a consequence of the Pallin litigation, the AMA adopted an ethical resolution in 1994 “vigorously condemning” the patenting of medical procedures and pledging to “work with Congress to outlaw” such patents.43 Soon after the AMA took this position, a coalition of medical and interest groups, the “Medical Procedure Patent Coalition,” was formed with the goal of persuading Congress to pass a legislative solution to the problem of procedure patents.44 Not surprisingly, the Coalition met with fierce resistance from the biotechnology and pharmaceutical lobbies. The biotechnology lobby, in particular, felt threatened by what it considered a “foolhardy” attempt to address the perceived problem through legislation, fearing that the legislation as initially proposed would adversely affect the industry’s ability to bring new therapeutic methods, such as Cephalon’s innovative use of the drug IGF-1, to market.45 Claiming that the legislation would “sever the critical lifeline” between the industry and the medical community,46 industry representatives were able to convince the Coalition to accept compromise legislation that specifically exempted

42. Pallin v. Singer, 36 U.S.P.Q.2d 1050 (BNA) (D. Vt. 1995). Dr. Pallin’s lawsuit was ultimately unsuccessful.
43. 1994 ANNUAL MEETING, AMA, Substitute Resolution 2.
44. See Portman, supra note 40.
46. Id. at 93.
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"biotechnology" patents from the legislation, 47 and the result 48 was adopted into law. 49 Thus, while the Physician Immunity Statute exempts “medical practitioner[s]” from liability for patent infringement for performing a qualified “medical activity,” the Statute specifies that a “medical activity” does not include the “practice of a process in violation of a biotechnology patent.” 50

The legislative history of the Physician Immunity Statute shows that the provisions which exclude the “patented use of a composition of matter in violation of such patent” 51 and “the practice of a process in violation of a biotechnology patent,” 52 respectively, are intended to protect “use patents.” 53 For purposes of this provision, the definition of a ‘biotechnology patent’ includes a patent on a ‘biotechnology process’ as defined in 35 U.S.C. §103(b), as well as a patent on a process of making or using biological materials. Thus, biotechnology patents are wholly exempt from the application of the Physician Immunity Statute. This result reflects the success of the biotechnology lobby’s aggressive efforts. 54

According to widely-held principles of bioethics, physicians should


51. Id. § 287(c)-(2)-(A) (ii). This provision is limited by the later § 287(c)-(2)-(F) to situations in which the use of the composition of matter is directly related to the objective of the procedure.

52. Id. § 287(c)-(2)-(A) (iii). This provision, unlike § 287 (c)-(2)-(ii), is not constrained by other subsections.

53. A use or utility patent is a patent obtained on an invented composition of matter (as opposed to a design patent, which is a patent on an ornamental design or appearance, or a plant patent, which is a patent on a novel plant). See BARRETT, supra note 17, at 111-371.

54. However, even the biotechnology industry is not without internal dissent. In testimony before the Federal Trade Commission and Department of Justice, Barbara Caulfield, general counsel for the biotechnology company Affymetrix stated that “there should be no patenting of gene sequences, period.” See Tom Abate, Do Gene Patents Wrap Research in Red Tape?, S.F. CHRON., March 25, 2002, at E1.
respect patients' abilities to make their own decisions about their healthcare; they also have a responsibility to avoid causing harm to patients or failing to prevent harm.\footnote{55} Under the principle of autonomy, a patient has the right to be free of interferences in making decisions regarding their own bodies and medical decisions.\footnote{56} Any interference in the ability to make such decisions compromises a patient's autonomy. Although there is no general right to diagnosis—there is no a priori absolute right to be diagnosed with a condition any more than an absolute right to health care—no one ought to have the absolute right to deny a patient means of being diagnosed, either. Under the principle of beneficence—the notion that physicians ought to prevent harm\footnote{57}—for a caregiver to deny a patient a means of diagnosis, where such a denial might cause the patient harm, would be unequivocally unethical. However, patents allow precisely this denial. Since the enactment of the Physician Immunity Statute, patented methods of diagnosis—except for biotechnology patents (i.e., gene tests)—are exempt from patent enforcement. Thus, the Physician Immunity Statute can be seen as supporting patient autonomy and physician beneficence by removing potential legal barriers to diagnosis.

However, as discussed at greater length below,\footnote{58} the exemption for biotechnology patents from the Physician Immunity Statute means that gene patents can limit the ability of doctors to diagnose and research genetic-based diseases. In Part II, I illustrate this danger by discussing the Canavan patent; and in Part III, I argue for an amendment to the Physician Immunity Statute that would limit the ability of patent holders to restrict the use of processes used in the gene-based diagnosis of diseases. The proposed amendment would extend support for the principles of patient autonomy and patient beneficence to genetically-based diagnoses.

II. THE CANAVAN DISEASE PATENT

As the Council of Scientific Affairs of the American Medical Association has recognized, the patent on the gene for Canavan disease

\footnote{56} Id. at 121.
\footnote{57} Id.
\footnote{58} See infra Subsections II.B.3-4 (discussing the limitations on screening and research caused by the Canavan gene patent).
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presents an excellent illustration of the problematic issues raised by the patenting of gene-based diagnostic tests.\textsuperscript{59} In its report announcing its position on gene patenting, the Council notes that the Canavan patent raises "serious issues of justice and fairness" and has resulted in the undesirable restriction of access to needed diagnostic testing and research.\textsuperscript{60} In this Part, I will take a closer look at the Canavan patent and the issues it raises as an example of the ability of "inventors" to restrict research and limit the availability of genetic testing using the patent system.

\textit{A. The Discovery of the Canavan Disease Gene}\textsuperscript{61}

Jonathan Greenberg was born in 1981. Although he seemed normal at birth, within a few months his parents became concerned about his development; six months later, he was diagnosed with Canavan disease, an inherited degenerative neurological disease. At the time, there were no screening tests available for parents, nor were there any means of prenatal diagnosis. The Greenbergs subsequently had another child, but their daughter Amy also began to develop the symptoms and signs of the disease.\textsuperscript{62}

In 1987, Jonathan’s father, Daniel Greenberg, approached Dr. Reuben Matalon, a physician then at the University of Illinois at Chicago, about initiating research with the goal of identifying the Canavan disease gene and ultimately developing a means to prevent or treat it. Daniel Greenberg had previously founded the Chicago chapter of the National Tay-Sachs and Allied Diseases Association (NTSAD); later, in conjunction with NTSAD, he had established a Canavan Registry, which compiled information about families who were carriers of the gene. Daniel Greenberg persuaded Matalon to undertake the research, and together with other families afflicted by Canavan disease, the Greenbergs supported Matalon’s research by supplying biological samples, including samples of Jonathan’s brain.


\textsuperscript{60} Id.

\textsuperscript{61} For background information on the Greenbergs and the efforts to find the gene responsible for Canavan disease, see generally Compl., Greenberg v. Miami Children’s Hosp. Research Inst., 208 F. Supp. 2d 918 (N.D. Ill. 2002) (No. 00C-6779); Eliot Marshall, Families Sue Hospital, Scientist for Control of Canavan Gene, 290 SCIENCE 1062 (2000).

\textsuperscript{62} See Compl. para. 4, Greenberg, 208 F. Supp. 2d 918.
after he died in 1992; family pedigree information; and financial support.  

Although Matalon had not previously engaged in Canavan research, he successfully isolated the Canavan disease gene in 1993. Identification of the gene made widespread, rapid, and accurate screening, as well as prenatal diagnosis, scientifically feasible—opening the door to the hope of an eventual treatment or cure using gene therapy.

Canavan disease is caused by a defect or absence of an enzyme called aspartoacylase. The disease is transmitted as an autosomal recessive trait and is “characterized by spongy degeneration of the white matter of the brain.” It is more prevalent in Ashkenazi Jews than in the general population, with the carrier rate among this demographic group as high as 1:36. The clinical manifestations vary, but the disease is uniformly fatal, usually within the first decade of life. The preferred means to diagnose Canavan disease is use of a biochemical assay that can detect the presence of N-acetylaspartic acid, the substrate of the aspartoacylase, in the urine or blood; carrier status can similarly be determined through the use of cultured fibroblasts.

Matalon wrote the entry on Canavan disease in the current edition of

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63. See id. para. 11, 17, 19.
65. Previously, prenatal diagnosis was not possible because there is insufficient aspartoacylase activity in chorionic villi and amniotic cells to render enzyme-based assays of amniotic fluid or chorionic villus samples satisfactory. R. Matalon et al., Prenatal Diagnosis of Canavan Disease, 15 J. INHERITED METABOLIC DISEASE 392 (1992). However, researchers continue to make progress toward a genetic test for Canavan disease. See C. Janson et al., Clinical Protocol: Gene Therapy of Canavan Disease: AAV-2 Vector for Neurosurgical Delivery of Aspartoacylase Gene (ASPA) to the Human Brain, 13 HUM. GENE THERAPY, 1391 (2002).
66. This means that it can skip generations and that if a child’s mother and father are both carriers of the gene, the child has a twenty-five percent chance of inheriting the disorder.
69. Fibroblasts are a connective tissue cell type that can easily be cultured from skin. Id. It is not altogether clear why biochemical tests are still the preferred means of testing. There are, however, at least two probable explanations: (1) Phenotypic expression (i.e. diminished aspartoacylase activity) is the definition of the disease and, therefore, the “gold standard” of determining whether one clinically suffers from Canavan disease; and 2) Because of the possibility of novel spontaneous mutations, current genetic tests are most likely not one hundred percent sensitive.
the Nelson Textbook of Pediatrics, the most widely used general pediatrics textbook. Under the heading “Treatment and Prevention,” Matalon explained, “No specific treatment is available. . . . Genetic counseling, carrier testing, and prenatal diagnosis are the only methods of prevention.” Even when a pediatric patient, as opposed to a fetus, is diagnosed using the biochemical assay, Matalon writes that it is “important to obtain a molecular diagnosis.” Characterizing the patient’s DNA mutation makes possible the prenatal diagnosis of fetuses with that mutation.

The discovery of the Canavan gene represented a rapid advance in scientific knowledge and the potential (at least from a technological perspective) to prevent a devastating disease. Had this discovery led to widespread, easily accessible testing and research, it could have immediately been considered a modern medical miracle. However, the Miami Children’s Hospital Research Institute (MCHRI), the hospital for which Matalon worked when the gene was discovered and the patent assignee, obtained a patent on the Canavan gene. Instead of maximizing the possibility of preventing the disease by allowing the unlimited use of Matalon’s invention, MCHRI opted to maximize the licensing revenue it could derive from the discovery. By threatening independent laboratories and universities with infringement actions, MCHRI forced such centers to refrain from offering testing, thus limiting research and the availability of testing. Although the Canavan disease case, in which the parents of a child afflicted with the disease sued MCHRI over the enforcement of the patent, settled in 2003 on terms not available to the public, the facts of the case illustrate the issues at question in the controversy over gene patents.

B. The Canavan Patent

On October 21, 1997, the U.S. PTO issued patent 5,679,635, entitled “Aspartoacylase gene, protein, and methods of screening for mutations associated with canavan [sic] disease” (the “Canavan patent”). The patent specification discloses the cDNA sequence of the wild-type aspartoacylase
gene, along with the predominant mutations of the gene that cause Canavan disease. Additionally, the patent teaches methods to screen individuals for the presence of the gene. In exchange for this disclosure, the patentees were granted claims not only on the gene and mutations that they disclosed, but also on all human variants of the gene as they exist in nature, whether or not yet discovered or disclosed in the application; any fragment of the gene greater than or equal to 1.1% (sixteen base pairs) of the disclosed sequence; any methods to test for the presence or absence of the gene, or any variant of the gene, in a patient; and any probe which might be useful in detecting or researching the disease. The patentees were also granted claims on basic tools of research, including any and all recombinant vectors, host cells, and methods of producing recombinant protein—i.e., tools absolutely necessary to develop a treatment or cure for the disease.

1. DNA Sequence Claims

The claims of the Canavan patent are disproportionate to what the specification discloses. The heart of the invention in the Canavan patent is the sequence for the aspartoacylase gene, together with the discovery that defective functioning of the gene product leads to the disease. The patent discloses the wild-type sequence of the gene, as well as several mutations of the gene that have been shown to be causative of Canavan disease.

complementary to the messenger RNA transcript of the genomic DNA (gDNA). Practically, cDNA differs from gDNA in that the sequence of the cDNA has been edited by the cellular machinery to remove any introns (i.e., DNA which does not encode proteins) or other intervening sequences that exist in the genomic sequence. See G. Barsh et al., Genome Structure and Gene Expression, in PRINCIPLES AND PRACTICE, supra note 1, at 60, 66, 68, 78.

76. A wild-type gene is "[t]he form of an organism that occurs most frequently in nature." For this and other definitions, see Human Genome Information Project, Genome Glossary, at http://www.ornl.gov/sci/techresources/Human_Genome/glossary/ (last visited July 9, 2004).

77. "Teaches" is a term of art for the information which the patent discloses in its specification.


79. Id. claims 1c, 38.

80. Id. claims 25-37, 40-44.

81. Id. claims 8-11.

82. Id. claims 14-15.

83. Id. claims 16-17.

84. Id. claims 18-24, 39.

85. Id. at General Discussion.
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Specifically, using the pedigree data from seventeen non-related Jewish families, the disclosure teaches that eighty-five percent of Canavan patients of Ashkenazi Jewish descent share a point mutation—i.e., a change in a single DNA base out of the 1435 bases that code for the aspartoacylase protein.\textsuperscript{86} The causative mutation in another 14.8 percent of patients is another point mutation that causes the premature arrest of the transcription of the gene.\textsuperscript{87} The patent additionally discloses various other mutations.\textsuperscript{88}

However, in addition to claiming the disclosed sequences—the wild-type gene and specific mutations identified—the Canavan patent broadly claims any and all forms of the gene and/or mutations thereof: Claim 1 of the Canavan patent asserts the generic claim to a human aspartoacylase gene,\textsuperscript{89} and in claim 3, the patent goes on to explicitly claim any aspartoacylase gene that "differs by at least one nucleotide from the nucleotide sequence of [the wild-type gene], and is a naturally-occurring allele of human aspartoacylase having an altered biological activity."\textsuperscript{90} Thus, the Canavan disease patent bars the characterization of a patient's DNA regardless of whether or not the patient has the disease, and even if the patient has a mutation that is not specifically disclosed in the Canavan patent. This is the case because the patent discloses only the most common disease-causing alleles, but claims "allelic variants" in addition to those mutations disclosed.\textsuperscript{91} In effect, the patent obtained is on the Canavan locus.\textsuperscript{92} In other words, the patentees have extended their disclosure of a handful of mutations known to cause Canavan disease into claims on any and all possible mutations, as well as any different aspartoacylase genes that might exist in humans anywhere, regardless of their effect on the function of the gene—or the fact that they have yet to be discovered. As the specification asserts, "[i]t will be understood by those of skill in the art that allelic or other sequence variations in the DNA . . . sequence[] of the

\begin{itemize}
  \item \textsuperscript{86} \textit{Id.}
  \item \textsuperscript{87} \textit{Id.} at General Discussion, Example 12.
  \item \textsuperscript{88} \textit{Id.} at General Discussion.
  \item \textsuperscript{89} The claim reads in full: "An isolated nucleic acid molecule comprising: (a) a nucleic acid sequence encoding a human aspartoacylase polypeptide; (b) a nucleic acid sequence fully complementary to nucleic acid sequence (a); or (c) a nucleic acid sequence at least 16 nucleotides in length capable of hybridizing specifically with one of said nucleic acid molecules (a) or (b)." \textit{Id.} claim 1.
  \item \textsuperscript{90} \textit{Id.} claim 3.
  \item \textsuperscript{91} \textit{Id.}
  \item \textsuperscript{92} For further discussion of the basic difference between an allele and a locus, see Am. Acad. of Pediatrics, \textit{supra} note 2, at 1494.
\end{itemize}
[aspartoacylase] gene . . . are included in the present invention."

The breadth of this claim runs counter to the principle that for DNA patents enough of the sequence must be disclosed to justify the breadth of the claim sought. MCHRI’s attempt to broadly claim all aspartoacylase sequences is reminiscent of Amgen v. Chugai, where a patent was found invalid because the biotechnology firm Amgen claimed all possible sequences coding for the gene for erythropoietin, but only disclosed the wild-type sequence and a few analogs. However, although MCHRI’s patent may be overbroad, the validity of the patent has not been challenged directly. The full breadth of the patent, as issued, would cover any genetic mutation causing Canavan disease, whether or not discovered by Dr. Matalon or other researchers at MCHRI.

2. Methods for Screening for Canavan Mutations

The Canavan patent employs two overlapping strategies for obtaining coverage of all means of diagnosing the presence of the Canavan disease gene: Claims 25-37 are “method” or “process” claims, and claims 8-11 cover the DNA molecule probes that are essential to amplifying a patient’s DNA in order to utilize those methods or processes. Claim 25 broadly claims a generic method for screening a person for the gene:

A method of screening a subject to determine if said subject is a Canavan carrier or a Canavan patient, comprising (a) providing a biological sample of the subject to be screened; and (b) submitting the sample to an assay for detecting in the biological sample the presence of a wild-type aspartoacylase gene, a mutant aspartoacylase gene or a mixture thereof, wherein said gene has a DNA sequence of claim 1, and wherein detection of a mutant as [sic] aspartoacylase gene indicates that the subject is a Canavan carrier or a Canavan patient.

The patent goes on to specifically claim different methods well known in the art which could be used to test for the presence of the mutant gene, whether by hybridization assay, labeled nucleotide probes, DNA

95. Id. at 1214.
97. Id. claims 8-11.
98. Id. claim 25.
99. Id. claim 26. Hybridization assays, whether using radionucleotide probes (i.e.,
hybridization assay, RFLP, heteroduplex analysis, or kits for performing these procedures. The result of these expansive claims is that any attempt to test a person’s genetic material for the mutant gene using conventional molecular genetic tools found in any molecular biology laboratory will infringe on the Canavan patent.

3. Decreased Availability of Screening

In testimony before Congress, the College of American Pathologists complained of the deleterious effect of patent enforcement on the availability of diagnostic tests generally, stating that forty-eight percent of seventy-four university-based clinical laboratories surveyed had ceased performing or developing a test for either clinical or research purposes because of patent restrictions. That patent enforcement leads to diminished availability for genetic testing has also been shown for another genetic disorder, hereditary haemochromatosis.

In light of these facts, it is not surprising that the enforcement of the Canavan patent also led to diminished availability of testing. Citing negotiations with “major pharmaceutical companies” seeking licensing to offer Canavan tests, MCHRI in November of 1998 began to assert its patent

radioactively labeled DNA) or other DNA sequence fragments, rely on the double-stranded nature of DNA. They work because single strands of DNA will automatically bind complementary sequences. Thus, labeled DNA fragments can be used to bind larger DNA fragments (i.e., those isolated from a patient). Human Genome Information Project, supra note 76.

100. U.S. Patent No. 5,679,635, supra note 64, claim 27.
101. Id. claim 30.
102. Id. claim 31. Restriction fragment length polymorphisms (RFLPs) rely on bacterial enzymes that cut DNA strands at known sequences. When a mutation changes the sequence, the bacterial enzyme no longer can cleave the DNA. Human Genome Information Project, supra note 76.
103. U.S. Patent No. 5,679,635, supra note 64, claim 32.
104. Id. claims 33-37, 42, 44.
106. Jon F. Merz et al., Diagnostic Testing Fails the Test, 415 NATURE 577, 577 (2002). Merz and his colleagues conducted a survey of clinical labs and examined whether the existence of patents on the gene causing haemochromatosis, a blood disorder causing excessive red blood cell production, affected the offering of genetic tests for the disease. They concluded that enforcement of hemochromatosis gene patents caused laboratories to cease offering testing for the gene. Id. at 578-79.
rights by sending cease-and-desist letters to centers offering testing without a license; the letters advised the centers of MCHRI’s intention to “enforce vigorously our intellectual property rights relating to carrier, pregnancy, and patient DNA tests for Canavan Disease mutations.”\textsuperscript{107} As a result, community organizations and academic centers previously offering testing were forced to stop doing so or risk liability for patent infringement. Referring specifically to the availability of Canavan disease testing, the AMA concluded in December 2000 that “[t]he ultimate impact [of patent enforcement] is that the test is currently not available to many of those who desire it.”\textsuperscript{108}

Because prior art biochemical assays remain the preferred means of diagnosing Canavan disease in patients once they are born, the most significant effect of the Canavan patent is on prenatal testing, which cannot be done using the prior art methods.\textsuperscript{109} Thus, the restriction of testing due to exclusive licensing is most acutely felt where it is currently needed most—in disease prevention.

4. Canavan Patent Restricts Research

While the lack of availability of genetic testing is an undeniably important problem for families who may be carriers of these diseases, another concern raised by the award of gene patents is their potentially chilling effect on innovative attempts to treat or cure genetic disease.\textsuperscript{110} Because Canavan disease is caused by an inborn error of metabolism, gene therapy provides the only hope for developing treatment or a cure. Unfortunately, MCHRI was granted claims on the very basic tools of molecular research—the vectors,\textsuperscript{111} host cells,\textsuperscript{112} and recombinant genes\textsuperscript{113}

\begin{itemize}
\item \textsuperscript{108} COUNCIL ON SCI. AFFAIRS, supra note 59. For information about the current availability of Canavan disease testing, see Screening & Testing Centers, Canavan Foundation, at http://www.canavanfoundation.org/screening.php (last visited May 17, 2004). Availability remains limited, id., nearly one year after the Greenberg case was settled, infra text accompanying note 118.
\item \textsuperscript{109} See supra note 65.
\item \textsuperscript{110} It is difficult to determine definitively the inhibitory effect of the Canavan patent on research as there is no way to know what projects might have been undertaken were it not for the patent. Under the terms of the settlement agreement, researchers may now use the Canavan disease gene without fear of litigation.
\item \textsuperscript{111} U.S. Patent No. 5,679,635, supra note 64, claims 14-15.
\item \textsuperscript{112} Id. claims 16-17.
\end{itemize}
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absolutely essential to researching a treatment or cure. The patent uses this combination of claims to cover the basic methodologies of genetic research, making it impossible for a worker skilled in the art to research Canavan disease without infringing on the patent. Unlike many other industrialized nations, the United States's recognition of an "experimental use" exception to patent infringement is extremely narrow. Researchers hoping to cure Canavan disease through gene therapy would not be protected from a patent infringement suit, since such research could be viewed as a "commercialization" of the Canavan patent.

In the case of Canavan disease, the families who motivated the Canavan disease research and supplied the biological materials that were necessary for the discovery of the gene filed a complaint alleging breach of fiduciary duty, lack of informed consent, and unjust enrichment. Although there was no remedy for them under U.S. patent law, the families and MCHRI reached a settlement on August 6, 2003, ensuring the free use of the Canavan gene in research to cure the disease. MCHRI will, however, continue to collect royalties on the screening test. It is important to

113. Id. at 18-24.

114. For a comparative review of nations' experimental use exception to patents, see Natalie M. Dzerko, A Local and Comparative Analysis of the Experimental Use Exception—Is Harmonization Appropriate?, 44 IDEA 1, 28-70 (2003).

115. Madey v. Duke Univ., 307 F.3d 1351, 1362 (Fed. Cir. 2002) (noting that "the experimental use defense is very narrow and strictly limited").


An experimental use exception has met with little success in the United States... . The U.S. Court of Appeals for the Federal Circuit has grudgingly recognized the existence of a common law experimental use defense, but characterizes it as 'truly narrow' and applicable only to trifling 'dilettante affairs.' Banished from the experimental use defense is any activity viewed as 'commercialization' or otherwise grounded on profit motive. The current narrow interpretation of the doctrine virtually assures that it cannot be relied on by the rapidly growing number of university and industry collaborations whose research and development efforts are ultimately targeted at the commercialization of new biomedical products.

Id. at 5 (internal citations omitted).


recognize that this settlement was made possible, in large part, by the particular facts of the Canavan gene discovery, which was funded initially by Canavan families, who then challenged the ownership of the patent on grounds outside the arena of ordinary patent law. Because of the complaint brought by the Greenberg family, all patients suffering from Canavan disease, as well as their families, enjoy the hope that they might benefit from the free use of the gene for research toward a cure. Unfortunately, these facts would apply to few, if any, patients suffering from other genetic diseases; these patients, therefore, will not have the same opportunity to ensure access to research.

Importantly, the effects on scientific research may be more insidious than simply the ability of the patentee to deny a competitor the right to do research. The AMA Council on Scientific Affairs warns of the corrupting influence that licensing agreements, which are beyond the purview of the Patent Office, may have on clinical research. The Council has noted that nothing would prevent a patentee from restricting a license such that the licensee would be “‘gagged’ regarding findings that question the validity and quality of data.”

Whether continued enforcement of the Canavan gene patent would have resulted in less research, less critical examination of the research that did occur, less prenatal screening, or all of the above, the future for potential victims of Canavan disease would have been similarly bleak: Under any of these scenarios, the enforcement of the Canavan patent undoubtedly would result in more children being born with this devastating neurological condition than would be the case if diagnostic testing were freely and widely available. Although the specter of intellectual property rights impeding the discovery of treatments and cures is today counterfactual in the Canavan case, this troubling prospect, along with the more immediately palpable problem of decreased access to screening technologies, is of general concern in the era of gene patents.

III. AMENDING THE “PHYSICIAN IMMUNITY STATUTE”

At its 2000 interim meeting, the American Medical Association (AMA) House of Delegates adopted a resolution declaring that the AMA “supports equitable access to licenses or sublicenses of gene patents for diagnostic genetic tests to any Clinical Laboratory Improvement Act (CLIA)-certified laboratory at a reasonable royalty.” Unfortunately, given the practice of

119. COUNCIL ON SCI. AFFAIRS, supra note 59.
120. COUNCIL ON SCI. AFFAIRS, AMA, REPORT NO. 5, GENE PATENTING: UTILITY

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patentees negotiating exclusive licensing agreements, the lack of controls to ensure widespread licensing, and the legal difficulties that would be incurred by attempts to institute controls such as mandatory licensing, the AMA's proposal for widespread access to diagnostic tests for a "reasonable royalty" is inadequate to remedy the problems posed by patents for gene-based diagnostic tests. The Canavan patent does not exist in a vacuum, nor is its enforcement just a case of moral bankruptcy on the part of one particular hospital. Rather it is a systemic problem that requires an adjustment to the law to cure.

Specifically, the Physician Immunity Statute should be amended so that the exemption for "medical activ[ies]" includes the identification of a patient's genes for purposes of diagnosis or prenatal screening. Such an amendment would define the limits of a patent holder's right to exclude, thereby allowing patients' greater access to the diagnostic tests that play such an important role in the diagnosis and prevention of genetic-based diseases. This proposal brings the scope of patent protection for genetic testing into accord with that of other diagnostic procedures already encompassed by the Physician Immunity Statute.

A. Amending the Statute

As I argued earlier, the legislative history of the Physician Immunity Statute shows that the exclusion of "biotechnology patent[s]" from the Act's protections was the result of aggressive lobbying on the part of the biotechnology lobby, and the exclusion is broadly defined: A

122. For an illustration of how exclusive licensing can have adverse effects, see Peter Mikhail, Hopkins v. CellPro: An Illustration That Patenting and Exclusive Licensing of Fundamental Science Is Not Always in the Public Interest, 13 HARV. J.L. & TECH. 375 (2000).
123. See generally Janice M. Mueller, Patent Misuse Through the Capture of Industry Standards, 17 BERKELEY TECH. L.J. 623, 664-69 (2002) (discussing the use of mandatory licensing as a sanction for failing to disclose patent rights). Although Mueller argues for compulsory licenses of patented technology that becomes an "industry standard," id. at 664, this article provides an overview of the historical objections to mandatory licensing schemes.
125. See Portman, supra note 40. A use or utility patent is a patent obtained on an

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"biotechnology patent" includes a "biotechnology process," as defined in 35 U.S.C. §103(b), as well as a patent on a process of making or using biological materials.

Thus, included under this exemption are claims, like those in the Canavan patent, premised on standard molecular techniques, such as restriction fragment length polymerase (RFLP) testing, used in the gene-based diagnosis of diseases. This result reflects the success of the biotechnology lobby's aggressive efforts. In order to roll back this exemption and ensure greater access to genetic diagnostic tests, I propose the following amendment to 287(c)(2):

Recognizing that the human genome is the common heritage of all humanity, and that genetic diagnostic testing is playing an increasingly important role in the prevention of disease, Section 287(c) of Title 35, United States Code, is amended by replacing § 287(c)(2)(A)(iii) with the following revised subsection: "(iii) the practice of a process in violation of a biotechnology patent, other than for purposes of diagnosis."

In March 2002, Representative Lynn Rivers sponsored legislation similar to that proposed here. The "Genomic Research and Diagnostic Accessibility Act of 2002" included provisions allowing gene sequences to be used for research and diagnosis, and it required the disclosure of DNA sequences at the time an individual applied for a patent. Unfortunately,

invented composition of matter (as opposed to a design patent, which is a patent on an ornamental design or appearance, or a plant patent, which is a patent on a novel plant). See BARRETT, supra note 17, at 111-371.

126. However, even the biotechnology industry is not without internal dissent. In testimony before the Federal Trade Commission and Department of Justice, Barbara Caulfield, general counsel for the biotechnology company Affymetrix stated that "there should be no patenting of gene sequences, period." See Tom Abate, Do Gene Patents Wrap Research in Red Tape?, S.F. CHRON., March 25, 2002, at E1.

127. Genomic Research and Diagnostic Accessibility Act of 2002, H.R. 3967, 107th Cong. (2002), was introduced in the House of Representatives in March of 2002. Section 3 of the bill provided that "the term 'medical activity' means the performance of a genetic diagnostic, prognostic, or predictive test or a medical or surgical procedure." It further defined those terms as follows:

[T]he term "genetic diagnostic, prognostic, or predictive test" means any test, designed to detect disease, to predict the potential for a medical disorder, or to predict the effectiveness of therapeutics, which uses either an ordered listing of nucleotides comprising a portion of a human or human pathogen genetic code or the proteins encoded by such nucleotides.

Id.
the legislation died when Representative Rivers lost her Congressional seat to fellow incumbent Representative John Dingell following redistricting. Nevertheless, there is an increasing awareness of the continued need for a legislative remedy for the growing conflict between patent jurisprudence and the needs of medical researchers and patients.  

The simpler proposal offered here more narrowly addresses the specific issue of ensuring physician immunity from patent infringement in the diagnosis of genetic disorders. Such a remedy allows patients at risk of genetic disorders to have unfettered access to diagnostic testing, without being encumbered by the broader issues of the effect of gene patents on research and industry disclosure raised by Representative Rivers's proposal. Although the effect of gene patents on research remains a significant concern, I have deliberately chosen to adopt a more modest approach in my proposal. Indeed, a broader approach, such as the one attempted by Representative Rivers, would be more likely to mobilize the biotechnology lobby and impede the likelihood of the amendment's success.

Moreover, extending the protection from infringement to academic or industrial researchers (or others not engaged directly in patient care) is unnecessary to redress the problem of the negative effect of patents on genetic testing. Rather, the potential for commercial gain from applications other than testing, such as would be obtained though commercial research, would be all the more critical after passage of this proposed amendment eliminating such gains from diagnostic applications. Experience in the pharmaceutical and medical device industries is persuasive that patent protection or, more specifically, the economic incentives associated with such protection are critical to the development of novel therapies. Therefore it is the express intention of this proposal

128. See John Barton, Patents, Genomics, Research and Diagnostics, 77 Acad. Med. 1339 (2002). Professor Barton advocates for a narrow legislative exemption aimed at protecting medical research from patents on ESTs and SNPs, as well as legislative and/or judicial challenges to the Court of Appeals for the Federal Circuit's recent extensions of patentable subject matter.

129. It is widely believed that the pharmaceutical industry would not engage in the costly research and development process required for new therapies, if not for the monopoly rights guaranteed by patent protection. While other public policies—including tax incentives and grants of public monies—may also encourage technical innovation, patents continue to be viewed as the essential element. See Org. for Econ. Cooperation & Dev't, Patents and Innovation: Trends and Policy Challenges 9 (2004), http://www.oecd.org/dataoecd/48/12/24508541.pdf; Wesley M. Cohen, Patents: Their Effectiveness and Role, Presentation to the FTC/DOJ Hearings on Competition and Intellectual Property Law in the Knowledge-Based Economy (Feb. 20, 2002),
to maintain the traditional patent incentives in such cases. However, whereas biotechnology patents may well be necessary to ensure the commercial viability of the development of gene therapies (in analogy to pharmaceuticals), molecular diagnostics are more easily developed, and genetic diagnosis is easily performed once a gene has been sequenced.

By limiting the biotechnology patent exemption of § 287(c), the restrictions on diagnostic testing, as in the case of Canavan disease, would be loosened to the benefit of patients. The precise extent of this loosening would have to be worked out in the political process. For example, a Congressional majority might want to impose stricter restrictions on parents’ access to fetal genetic information than it would on individuals’ access to their own “personal” genetic information. Even if the legislative process, subject to judicial review, were to maintain relatively tight restrictions on access to genetic testing, it is better that those restrictions be controlled by the policy choices of publicly accountable representatives, rather than the individual actions of private parties.

This modification would result in more widely available tests and, consequently, increased prevention of genetic disease. In addition, the proposal would alleviate concerns about the potential gagging effect of licenses, since physicians would be free to perform the diagnostic tests and report their efficacy in journals without the fear of data being subjected to oversight by the licensing company. The potential for licenses to gag

http://www.ftc.gov/opp/intellect/cohen.pdf. There is considerable debate about how to most efficiently achieve costly drug innovation and whether current patent terms are ideal. See, e.g., OXFAM, IMPLAUSIBLE DENIAL: WHY THE DRUG GIANTS’ ARGUMENTS ON PATENTS DON’T STAKE UP (2001), at http://www.oxfam.org.uk/what_we_do/issues/health/implausible_denial.htm (last visited May 17, 2004); see also Heller & Eisenberg, supra note 11. However, there is little question that the costs of developing diagnostics are less than for developing therapeutics, see infra note 130 and accompanying text; one can hypothesize that the incentives required are also reduced.

130. The timeline for scientific development and regulatory approval of diagnostics is shorter than for therapeutics and the process, overall, is less expensive. However, the revenue potential is smaller for diagnostics than for therapeutics for several reasons, including greater price sensitivity. See, e.g., Robert S. Schifreen, Molecular Diagnostics: The Challenge for the Future, IVD TECH., Nov. 2003, at 27.

131. For example, one study found that many laboratories offered testing for genes based on published sequence data, before any commercial kits were made available (and not coincidentally before the patents were enforced). Mildred K. Cho, Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services, 5 J. MOLECULAR DIAGNOSTICS 3 (2003).
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physicians is based on a contractual relationship between the physician and the patent holder; thus, in the absence of such an agreement, a physician would be able to publish based on his or her own clinical experience with the test. This would in turn benefit patients, since the doctor-physician relationship requires that patients be able to trust their physicians, and is undermined by third party influences on physician decision making.

B. Policy Cost-Benefit Analysis

The biotechnology lobby, in its attack on the original incarnation of the Physician Immunity Statute, argued that gene patents protect companies’ investments and therefore have a net effect of increasing research and development, resulting in more diagnostic tests, drugs, and novel therapies. While it is likely that patent protection, generally speaking, does stimulate research and development, several coinciding factors dilute the value of the patent “incentive” not just for gene patents on methods of diagnosis, but for gene patents in general. In the early days of biotechnology, the effort required to clone a gene or elucidate its sequence was staggering. Courts were cajoled into recognizing the substantial amount of labor that scientists put into these “inventions” in order to provide the nascent biotechnology industry with an incentive to continue such tedious work. However, they could not have anticipated that what in the 1980s required Herculean labor would, by the mid-1990s, easily be achieved in a day. The increase in the speed and ease of sequencing has meant that the “innovation” required to patent a gene is not now what it was when Dr. Chakrabarty successfully defended his groundbreaking patent on a genetically-modified oyster before the Supreme Court. With each passing day, as technology becomes more advanced, it requires less and less “innovation” to patent a gene.

132. Hearings on H.R. 1127, supra note 45, at 92, 94-98 (prepared testimony of Frank Baldino, Jr., President and CEO of Cephalon, Inc.).
133. At its inception around 1990, it was estimated that the Human Genome Project would take 30,000 person-years to complete, based on the then maximum rate of sequencing of 100,000 base pairs per person per year. PRINCIPLES AND PRACTICE, supra note 1, at 291. With the advent of automated high-output sequencing, analysis of the human genome can proceed at a much faster pace now than it could just a few years ago. See Mark Adams et al., Complementary DNA Sequencing: Expressed Sequence Tags and Human Genome Project, 252 SCIENCE 1651, 1651 (1991). Perhaps even more important is the diminution in the costs of sequencing that comes with automation. Id. at 1651.
A second consideration is the "gold rush" aspect of gene patenting. The human genome is finite—more so than was at first appreciated—and researchers have already completed sequencing the human genome. University scientists "and at least one major pharmaceutical company" have reacted to the attempt by genome companies to appropriate the human genome by dedicating sequence data to the public, creating prior art hurdles for many gene patents. Between the sequences dedicated to the public, and those already "invented," the window for inventors to "invent" human genes is closing. In fact, before the PTO imposed the utility requirements on EST patent claims, many companies had been filing for patent applications on DNA molecules for which no function is known, simply speculating on the possibility that their patented sequence will turn out to be an important one. At least in the initial stage of the genetic revolution, a "gold rush" mentality dominated. Despite the PTO's heightened emphasis on the utility criterion, individuals and enterprises who were attracted to this "patent bonanza" atmosphere might continue to file for intellectual property protection not to further knowledge, but rather to stake a claim to a patch of DNA that the "inventor" hopes will one day yield a mother lode.

Moreover, while the relatively small number of genes being dedicated to the public increases, the number of overlapping, or stacked, patents on genes is likely to increase. Since many "stacked" patents on the same disease gene will increase the licensing costs of the diagnostic test, it is possible, if not likely, that gene-based diagnostic tests will be kept out of the market not by scientific obstacles, but rather by commercial ones. The liberal issuance of "Expressed Sequence Tag" (EST) patents

139. This is what Michael Heller and Rebecca Eisenberg have referred to as the "tragedy of the anticommons . . . in biomedical research." Heller & Eisenberg, supra note 11, at 701. "A proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream." Id. at 698.
140. An EST is a cDNA corresponding to randomly selected messenger RNA isolated from a cell. Because messenger RNA is the transcript of genomic DNA on its way to being "expressed" as protein, the sequences are limited to expressed sequences. It is further called a 'tag' because the procedure generated only a fragment of the cDNA transcript.
threatened to inordinately dilute the value of a patent on a gene for purposes of diagnosis because ESTs are by definition non-functional fragments of a gene; their main potential commercial utility is to aid in diagnosis. 141 Although patents for bare sequences can no longer be used to claim the underlying gene and protein if their functions are unknown,142 there remains the problem of overlapping or stacked patents due to polymorphisms or mutations of the same gene. There are literally hundred of mutations of the breast cancer gene, each one potentially patentable.143 Theoretically, even a handful of disease-causing alleles could each be subject to several patents, so that the number of cross-licenses needed to market a diagnostic test would be unworkable.144

Moreover, in addition to these trends, it is too simplistic to argue that private capital provided by biotechnology investors, enticed by the prospect of licensing fees, is absolutely necessary for the discovery of genes and the development of diagnostic tests. The Medical Procedure Patent Coalition argues that the patent “incentive” is unnecessary in medical practice, as “the development of new medical procedures often occurs during the normal course of medical practice and generally does not require significant capital investment.”145 Even if genetic tests are not

141. See, e.g., AM. SOC’Y OF HUMAN GENETICS, PATENTING OF EXPRESSED SEQUENCE TAGS (1991), http://genetics.faseb.org/genetics/ashg/policy/pol08.htm (recognizing the potential commercial application in the realm of diagnostics but noting that “the utility of ESTs can be seriously questioned. Scientific experience suggests that an EST itself is unlikely to have commercial utility. The [principal] anticipated utility of an EST is simply as a research tool to identify the remainder of the coding region of the gene.”).

142. “If a patent discloses only nucleic acid structure for a newly discovered gene, and no utility for the claimed isolated gene, the claimed invention is not patentable. . . . ESTS which meet the criteria for utility, novelty, and nonobviousness are eligible for patenting when the application teaches those of skill in the art how to make and use the invention.” Utility Examination Guidelines, supra note 33, at 1093-94 (Jan. 5, 2001); see also Tom Hollon, Gene Patent Revisions To Remove Some Controversies, 6 NATURE MED. 362, 362 (April 2000).

143. There are approximately 460 known, distinct sequence variants of BRCA1 (one of two known breast and ovarian cancer genes). Therese Serlie et al., Mutation Screening of BRCA1 Using PTT and LOH Analysis at 17q21 in Breast Carcinomas from Familial and Non-familial Cases, 48 BREAST CANCER RES. TREAT. 259, 259 (1998).

144. Cf. Heller & Eisenberg, supra note 11, at 699 (discussing the analogous problem of “concurrent fragments” in pharmaceutical screening).

generally developed "during the normal course of medical practice," these
tests may well require less investment of time, money, and talent to develop
than other inventions, such as pharmaceuticals. Moreover, as with other
medical procedures, researchers may be draw substantial motivation from
non-monetary incentives, such as a desire to improve their professional
stature or reputation. In addition, in the case of many rare diseases, it is
patients, patient support groups, and their doctors who raise money and
awareness of the disease seeking a treatment, diagnostic test, or cure.
Canavan disease is a formidable example of research driven by patients,
not industry. Exempting physicians from patent infringement would have
had little, if any, effect on Matalon's discovery of the gene, although it
might have spared "Canavan families" the burden of pursuing their lawsuit.

The societal benefit of these private research dollars is further reduced
by a corresponding increase in costs associated with gene patenting, which
effectively retards research. These costs range from the systemic effects of
gene patenting that create commercial incentives that skew academic
research away from free disclosure of information to the diminution in
research caused by inhibiting basic academic research secondary to
increased research costs.¹⁴⁶ The Canavan patent, for example, covers any
and all uses of the gene or even fragments of the gene, making research on
the Canavan disease gene without a license impossible. In addition, the
specter of stacked patents on ESTs may exacerbate these negative
tendencies exponentially. Imagine the same facts surrounding the
Canavan patent, but where the testing centers were issued cease-and-desist
letters from a dozen different genome corporations with claims to parts of
the Canavan sequence, or prominent mutations. Given these negative
factors, it is not at all clear that the net effect on innovation attributable to
gene patents is positive.

There are other costs associated with patents on genetic diagnostic
tests. In fact, there are human costs. There can be no question that the
enforcement of the Canavan patent claims on diagnostic tests results in
more children being born with this preventable genetic disease which
causes incredible suffering and hardship on families and which is
ultimately uniformly lethal.

Finally, the patent right may be subject to abuse. The fundamental
right a patent provides is the right to exclude others from making or using
the disclosed invention. Thus, for example, a religious group that fears

¹⁴⁶ David Blumenthal, Academic-Industrial Relationships in the Life Sciences, 349 NEW ENG.
J. MED. 2452, 2455 (2003); see also Blumenthal, supra note 31.
¹⁴⁷ See generally Heller & Eisenberg, supra note 11, at 700.
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that diagnostic tests will result in more prenatal diagnosis and abortion could purchase patents on childhood diseases to prevent the development of such tests. Alternatively, a company could patent a gene, but then not have the financial resources to exploit its invention and allow the patent to languish. 148

While patent protection currently leads to monopoly control over a gene, conversely, stacked patents, which each necessitate cross-licensing, potentially dilute the value of any individual patent. The amendment to the Physician Immunity Statute which I propose would obviate entirely the issue of whether one is infringing on one exclusive licensee or two hundred potential licensees by allowing unfettered access to genetic diagnosis. Similarly, should a patent-holder not have the means to develop or market kits to make diagnosis practically feasible, independent labs would be free to do so. Finally, the provision would prevent the patent system from being used as a vehicle for restricting licenses out of non-economic concerns, such as to prevent pre-implantation diagnosis or family planning.

IV. CONCLUSION

There is no doubt that society benefits from medical advances in its ability to diagnose and treat human ailments in which genetic predisposition is a causal or contributing factor. Society can also benefit from the patenting of genes that can be exploited to develop novel medicines such as Epogen, Amgen's recombinant erythropoietin product, or incorporated into gene therapies. These are examples of beneficent applications of gene patents; so, too, are patents for pharmaceuticals that encourage innovation and research into new drug treatments. The proposed legislation would have no effect on the biotechnology industry's ability to continue to bring such ground-breaking and important inventions to market. For example, gene therapy—attempts to correct the genetic defect through the use of recombinant technology—would not be affected by the proposed legislation. As far as diagnostics are concerned, though, patent protection is not in the public interest. This Article proposes a narrowly tailored approach that would alleviate the problems caused by patents such as the Canavan patent without affecting the ability

148. For an overview of the history of suppressed patents (where a company withholds development of a patent for strategic reasons), as well as for a proposal for compulsory licensing of non-used patents, see Kurt Saunders, Patent Nonuse and the Role of Public Interest as a Deterrent to Technology Suppression, 15 HARV. J.L. & TECH. 389 (2002).
of—or incentives for—biotechnology or pharmaceutical companies to develop novel, and patentable, drugs or other therapies.