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Greed is Good, for Patients: How the Biotechnology Industry Saves Lives, One Gene Patent at a Time

By Nikki Buck*

¶1 A debate is raging over the constitutionality of gene patents and their effect on the availability of genetic diagnostics and therapies. Whether gene patents are in fact constitutional is for the courts to decide. Rather, this Comment will argue that patents for isolated human genes positively affect society as a whole, with particular emphasis on patients in need of genetic innovations. Gene patents elevate genetic engineering beyond the realm of basic science and spur important advances in therapeutic technology.

¶2 Part I(A) will introduce the history of the American patent system, with particular emphasis on patents in the field of biotechnology. Part I(B) will then discuss the basic science behind genes and the utility of isolated DNA. Part II will introduce the legal debate concerning the patentability of isolated DNA with an overview of the *Myriad* cases. Part III will discuss the economic advantages and disadvantages of gene patents and will introduce the arguments levied on both sides of the issue. Part IV will conclude the paper with a summary of this author's argument that gene patents act as integral incentives for biotechnological progress.

I. INTRODUCTION TO GENE PATENTS

¶3 To understand the debate over gene patents, it is necessary to first delve into the history of patent law and its connection to the current biotechnology industry.

A. Why Protect Science?

¶4 The authority of the United States government to grant temporary exclusionary rights[1] to inventors in order to promote science is deeply ingrained in American history. In 1788, the States ratified the U.S. Constitution, which included Article 1 § 8 cl. 8, giving Congress the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[2] The Constitution thus empowered Congress to set up a system that turned innovation into a property right, thereby allowing a market

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[1] Patents are often considered temporary monopolies over the patented invention. While monopolies prevent competition within a market, patents merely give the patent holder the right to exclude others from making, using, and selling his invention. Competitors may still make and sell their own inventions as long as they do not infringe on the patented invention. For a more thorough explanation of the differences between patents and monopolies, see Frank H. Easterbrook, *Intellectual Property is Still Property*, 13 HARV. J.L. & PUB. POL'Y 108, 108 (1990).

[2] U.S. CONST. art. I, § 8, cl. 8.

system to function.[3] The first Patent Act was enacted in 1790, setting forth the power of the Secretary of State, Secretary of the Department of War, and Attorney General to grant letters of patent to inventors of any "sufficiently useful and important" invention, art, or improvement thereof.[4]

¶5 The current Patent Act,[5] enacted in 1952, continues in the tradition of the First Congress. The lenient attitude toward the scope of patentable inventions was demonstrated in the legislative history of the Patent Act of 1952, which states that patents are available for "anything under the sun that is made by man."[6] The Patent Act sets forth eligible subject matter as "any new and useful process, machine, manufacture, composition of matter, or any new and useful improvement thereof. "[7]

¶6 Of course, controversies arose as science blurred the line between nature and invention. In 1980, the Supreme Court of the United States extended patent eligibility to living, man-made organisms, ushering in the age of biotechnology.[8] In *Diamond v. Chakrabarty*, Dr. Chakrabarty created an entirely new strain of bacteria capable of breaking down multiple components of crude oil. He did so by inserting non-native plasmids into the genome of a strain of naturally occurring bacteria that had been incapable of oil decomposition prior to the insertion of the plasmid.[9] In a parallel to the passage of the Plant Patent Act, the Court stated that "the relevant distinction was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions."[10] Then in 1982, the United States Patent and Trademark Office (USPTO) granted a patent to the University of California for the gene coding of insulin.[11] Since then, genetic engineering, which involves scientific manipulation of DNA to introduce desirable traits, has gained an important foothold in the pharmaceutical and biotechnology industries. In the late 1990s, the number of patents on genes worldwide increased rapidly: from around 1,175 granted between the years 1981 and 1995 to over 25,000 DNA-based patents by 2000.[12] Gene patents have been granted under the rationale that "isolated DNA is a discrete chemical compound and . . . cannot be found in a purified state in nature without meticulous human intervention."[13]

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[3] Kenneth W. Dam, *The Economic Underpinnings of Patent Law*, 23 J. LEGAL STUD. 247, 248 (1994).

[4] 1 Con. Ch. 7, April 10, 1790, 1 Stat. 190.

[5] The Leahy-Smith America Invents Act (AIA), signed into law in 2011, does not affect the issues presented in this article. For the full text of the AIA, see Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011).

[6] Committee Report accompanying 1952 Patent Act, S. Rep. No. 1979, 82d Cong., 22 Sess., 5 (1952); H.R. Rep. No. 1923, 82nd Cong., 2d Sess., 6 (1952). *See also* Diamond v. Chakrabarty, 447 U.S. 303 (1980) (citing the Patent Act of 1952 in the decision to allow Chakrabarty's patent over a live organism since its genome was man-made).

[7] 35 U.S.C.A. § 101 (2006).

[8] Diamond v. Chakrabarty, 447 U.S. 303 (1980).

[9] *Id.* at 305.

[10] *Id.* at 313 (referencing the "Plant Patent Act" 35 U.S.C. § 162 (1930)).

[11] Lamis G. Eli, Note, *When Myriad Genetics Prohibited a Myriad of Options:* Association for Molecular Pathology v. USPTO, 21 DEPAUL J. ART, TECH., & INTELL. PROP. L. 357, 360 (2011).

[12] Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing*, 10 HEALTH L.J. 123, 126 (2002) (citing T.A. Caulfield and E.R. Gold, "Whistling in the Wind: Patents on Genetic Research Are a Reality. It's Time to Reframe the Debate" (2000) Spring Forum for Applied Research and Public Policy 75; and Robert Mullan Cook-Deegan and Stephen J. McCormack, *Patents, Secrecy, and DNA*, 293 SCI. 217 (2001)).

[13] Stephen W. Chen et al., *Patent Protection in Medicine and Biotechnology: An Overview*, 4 J. HEALTH & LIFE SCI. L. 106, 127–28 (2011).

The next section will introduce the scientific principles and historical facts underlying the debate about patent eligibility for genes.

B. The Science Behind Gene Patents

1. Genes Within the Body

¶7 The human genome contains approximately 25,000 genes, each of which is coded by specific sequences of DNA.[14] Genes are the units of heredity in living organisms, responsible for the inheritance of discrete traits.[15] The information contained within the double-stranded DNA molecules that make up the human genome is encoded through a specific sequence of nucleotides.[16] These nucleotides consist of a base linked to a phosphorylated deoxyribose molecule. The DNA molecule resembles a twisting ladder, with a sugar "backbone" for the sides of the ladder and paired bases for the rungs.[17] Nucleotides link to other nucleotides within the DNA strand through the sugar backbone.[18] The four different DNA bases (adenine, thymine, guanine, and cytosine) pair with their complements on the opposite strand to create the double helix structure of DNA.[19] Adenine ("A") pairs with thymine ("T") and guanine ("G") pairs with cytosine ("C"). Three bases in sequence create a codon, which codes for a specific amino acid.[20] Amino acids are the building blocks of proteins, the basic functional units of the human body.[21] A sequence of DNA that codes for a protein is called a gene.

¶8 The process of creating proteins begins with a complete DNA molecule. A gene is transcribed into an intermediate nucleic acid called messenger RNA (mRNA).[22] The mRNA is then translated into the amino acid sequence of the protein.[23] Like DNA, RNA consists of bases attached to a sugar-phosphate backbone. However, RNA is only single-stranded and uracil replaces the thymine base present in DNA.[24] The mRNA sequence complements the DNA sequence from which it is transcribed.[25] For example, an original DNA sequence of AAAGTAGCA is transcribed into the mRNA sequence UUUCAUCGU.

¶9 Only small portions of the gene, called exons, functionally code for a protein. The excess sequences, called introns, are spliced out of the mRNA before a protein is created.[26] The resulting mRNA strand is about one-tenth the length of the gene that contains the coding sequence.[27] Codons of the mRNA are then translated into specific

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[14] Ass'n for Molecular Pathology v. USPTO (*Myriad II*), 653 F.3d 1329, 1335 (Fed. Cir. 2011).

[15] Ass'n for Molecular Pathology v. USPTO (*Myriad I*), 702 F. Supp. 2d 181, 194 (S.D.N.Y 2010).

[16] ALISON STEWART ET AL., GENETICS, HEALTH CARE AND PUBLIC POLICY: AN INTRODUCTION TO PUBLIC HEALTH GENETICS 24–25 (2007).

[17] K.K. JAIN, TEXTBOOK OF GENE THERAPY 5 (1998).

[18] *Id.*

[19] *Id.*

[20] *Id.* at 25.

[21] *Id.*; *see also Myriad I*, 702 F. Supp. 2d 181, 194 (S.D.N.Y 2010).

[22] STEWART ET AL., *supra* note 16, at 26.

[23] *Id.*

[24] *Id.*

[25] In RNA, adenine pairs with thymine, just as it does in DNA. However, since uracil takes the place of thymine in RNA, uracil pairs with adenine in RNA.

[26] JAIN, *supra* note 17, at 9.

[27] *Id.*

amino acids. For example, the previous mRNA sequence codes for the amino acid sequence Phenylalanine-Histidine-Arginine. Some amino acids are specified by multiple codons, and some codons specify stop sequences, which instruct the cellular machinery to stop the process of transcription and translation at that codon.[28] The amino acid sequence, called a polypeptide, folds into a functional three-dimensional structure: the protein.[29] Some proteins must be modified after translation in order to be functional within the cell.[30]

¶10 Genomic DNA is not found floating within the cell ready to be transcribed into mRNA. Rather, it is wound tightly around proteins called histones and packaged into twenty-three pairs of chromosomes.[31] The chromosomes are directly inherited from an individual's parents, twenty-three from the mother and twenty-three from the father.[32] When DNA is transcribed or replicated, only a small unit of the chromosome containing the gene of interest is unwound.[33]

¶11 Changes, or mutations, in the genetic sequence of a gene can result in alterations in the resulting proteins.[34] Mutations may be caused, for example, by environmental factors, errors in DNA processing, and inheritance (if the mutation occurs in a sex cell, also known as a germline mutation).[35] Point mutations consist of a single nucleotide base change that can result in translation of a different amino acid.[36] For instance, if the DNA sequence above began with a thymine instead of an adenine (TAAGTAGCA), the mRNA would become AUUCAUCGU. The resulting polypeptide chain would consist of Leucine-Histidine-Arginine instead of Phenylalanine-Histidine-Arginine. There will be little or no functional effect on the resulting protein when a point mutation occurs within a non-operative sequence of DNA (such as an intron), or when the sequence changes a codon that still encodes for the same or similar amino acid.[37] However, when the point mutation substitutes a very different amino acid or codes for a stop sequence, it may lead to a vastly different protein—or even no protein at all.[38] Larger scale changes in the DNA sequence include duplication, deletion, and rearrangement of large segments of DNA.[39] The effects of these mutations vary according to the size and location of the altered sequence.[40] Certain mutations are associated with particular diseases. DNA sequencing can be performed to test whether a person's DNA contains a certain mutation.[41]

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[28] STEWART ET AL., *supra* note 16, at 24.
[29] *Id*.
[30] *Id*. at 26–27.
[31] *Myriad II*, 653 F.3d 1329, 1338 (Fed. Cir. 2011).
[32] *Myriad I*, 702 F. Supp. 2d 181, 195 (S.D.N.Y 2010).
[33] JAIN, *supra* note 17, at 12. A single chromosome contains between 50–250 million base pairs, but only about 100,000 base pairs are unwound during replication or transcription.
[34] *Myriad II*, 653 F.3d at 1339.
[35] STEWART ET AL., *supra* note 16, at 31.
[36] *Id.*; *see also Myriad II*, 653 F.3d at 1338.
[37] STEWART ET AL., *supra* note 16, at 31.
[38] *Id*.
[39] *Myriad II*, 653 F.3d at 1338.
[40] STEWART ET AL., *supra* note 16, at 32.
[41] *Myriad II*, 653 F.3d at 1338.

2. Isolated DNA: Process and Utility

¶12 In 1990, the United States National Institutes of Health (NIH) launched the Human Genome Project, a $3 billion effort to create a detailed genetic and physical map of the entire human genome.[42] This effort worked with national genome programs in several other countries to create a draft sequence of the entire human genome,[43] which was published in *Nature* in 2001.[44] Celera, a private company that had been simultaneously analyzing the human genome using different methods, published its own draft of the genome within the same week as the Human Genome Project.[45] Since the Human Genome Project created the "reference sequence,"[46] focus has turned to using the sequence to identify and characterize genes, their functional sequences, and the products of the genome.[47]

¶13 An important step in the process of genetic sequencing involves extracting and purifying DNA from its cellular environment.[48] Several well-established laboratory techniques exist for DNA extraction.[49] Often, specific DNA segments are cut from the chromosomal DNA through the use of restriction enzymes.[50] Sections of DNA can then be separated by size using gel electrophoresis.[51] DNA that has been extracted from the non-DNA materials in the cell is legally termed "extracted DNA."[52] "Purified DNA" refers to DNA that has been further refined to separate a particular segment of DNA, such as a specific gene.[53] Scientists can also synthesize, or create, DNA molecules in the laboratory if the sequence is known.[54] This artificial DNA is termed "synthesized DNA."[55] "Isolated DNA," consists of a "free-standing portion of a native DNA molecule, frequently a single gene."[56] It may be extracted and purified from native DNA or synthesized using a known sequence.[57]

¶14 Purified and synthesized DNA may be used as laboratory tools in applications for which native DNA may not be used.[58] For example, laboratory applications often require

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[42] JAIN, *supra* note 17, at 11.

[43] IAN D. YOUNG, MEDICAL GENETICS 5 (2005).

[44] Int'l Human Genome Sequencing Consortium, *Initial Sequence and Analysis of the Human Genome*, 409 NATURE 860 (2001).

[45] J. Craig Venter et al., *The Sequence of the Human Genome*, 291 SCI. 1304 (2001). Considerable controversy exists concerning Celera's ability to sequence the human genome without the use of publicly available maps and sequence data from the Human Genome Project. See STEWART, *supra* note 16, at 55 for an analysis of Celera's methods.

[46] The reference sequence does not represent a single human individual, but was assembled from the DNA sequences of multiple volunteers.

[47] STEWART ET AL., *supra* note 16, at 57.

[48] *Myriad I*, 702 F. Supp. 2d 181, 196 (S.D.N.Y 2010). *See also* STEWART ET AL., *supra* note 16, at 48 (giving a more technical explanation of recombinant DNA technology).

[49] *Myriad II*, 653 F.3d 1329, 1338 (Fed. Cir. 2011).

[50] STEWART ET AL., *supra* note 16, at 48.

[51] *Id*.

[52] *Myriad I*, 702 F. Supp. 2d at 196.

[53] *Id*.

[54] *Id*.

[55] *Id*.

[56] *Myriad II*, 653 F.3d 1329, 1351 (Fed. Cir. 2011).

[57] *Id*.

[58] *Myriad I*, 702 F. Supp. 2d at 196.

large amounts of the sequence of interest.[59] There are two main methods of copying and amplifying (i.e. making multiple copies of) DNA.[60] The first method, molecular cloning, harnesses the replication properties of a host organism, often a single-celled organism.[61] The target DNA is inserted into the host genome through the use of a vector, which includes all the necessary sequence information to make the host copy the target DNA when it multiplies.[62] The second method of DNA amplification is called polymerase chain reaction (PCR).[63] PCR amplifies DNA exponentially and does not require a living organism to do so.[64] The drawback, however, is that PCR requires a DNA primer, a short piece of complement DNA that binds to each end of the replicating strand.[65] This means that DNA may only be amplified using PCR when at least a portion of the sequence is known.

¶15 Aside from their use in PCR amplification, DNA primers may also be used to determine the sequence of nucleotides in a DNA molecule in the first place.[66] Short sequences of nucleotides labeled with fluorescent tags can also be used as "probes," which are diagnostic tools often used in conjunction with DNA microarrays to detect thousands of genes within a single sample.[67] Probes bind with complementary sequences in a sample of DNA within a microarray and tag the specific sequence so it may be detected by laboratory hardware.[68] Overall, the utility of a purified gene or sequence of interest depends upon its ability to selectively bind to a complementary DNA sequence.[69]

II. THE MYRIAD CASES

A. Introduction to the Debate: BRCA1/2

¶16 Even before the Human Genome Project mapped the genome, researchers have been associating diseases with particular genes and genetic mutations. For instance, researchers at Myriad Genetics, Inc. and the University of Utah Research Foundation (collectively known as "Myriad") identified the basis by which genetic mutations of the BRCA1 and BRCA2 genes correlate with an increased risk of breast and ovarian cancer.[70] About 5% of all breast cancer cases involve germline mutations of either the BRCA1 or BRCA2 (BRCA1/2) genes.[71] If an individual tests positive for mutations on

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[59] STEWART ET AL., *supra* note 16, at 50.
[60] *Id.*
[61] *Id.*
[62] *Id.*
[63] *Id.*
[64] *Id.* at 51. *See also Myriad I*, 702 F. Supp. 2d 181, 197 (S.D.N.Y 2010)..
[65] STEWART ET AL., *supra* note 16, at 51.
[66] *Myriad I*, 702 F. Supp. 2d at 196.
[67] *See* STEWART ET AL., *supra* note 16, at 51 (explaining the use of probes in microarrays); *see also Myriad I*, 702 F. Supp. 2d at 196–97 (referencing the use of short DNA sequences as probes to be used as diagnostic tools).
[68] STEWART ET AL., *supra* note 16, at 51.
[69] *Myriad I*, 702 F. Supp. 2d at 197.
[70] *Myriad II*, 653 F.3d 1329, 1339 (Fed. Cir. 2011). *See also* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012), *opinion vacated, appeal reinstated*, 467 F. App'x 890 (Fed. Cir. 2012); *cf.* JAIN, *supra* note 17, at 155 (stating that mutations in the BRCA1 gene are present in 5% of ovarian cancer cases of women diagnosed before the age of 70).
[71] YOUNG, *supra* note 43, at 200.

either BRCA gene, she[72] has about a 60-80% risk of developing breast cancer within her lifetime.[73]

¶17 Myriad used known scientific processes to identify, isolate, and sequence the BRCA1/2 genes.[74] The researchers then developed diagnostic tools to test individuals for mutations in the BRCA1/2 genes.[75] Myriad filed a patent application covering the isolated and purified DNA containing the BRCA1 gene as well as the diagnostic methods in 1994, followed by an application covering the BRCA2 DNA and diagnostics in 1995.[76] The first BRCA1 patent was issued to Myriad in 1997, and the first BRCA2 patent was issued in 1998.[77] Other clinical BRCA1/2 testing services became available while Myriad was in the process of using and patenting the BRCA1/2 genes.[78] In early 1998, Myriad sent one such institution, the University of Pennsylvania's Genetic Diagnostic Laboratory ("GDL"), a letter informing it of Myriad's patents over the BRCA1 gene and diagnostics, and proposing a collaborative license agreement.[79] The proposed license would have limited GDL's testing services.[80] Later in the year, GDL received a letter from a law firm that represented Myriad, giving GDL two choices: (1) agree to a licensing arrangement with the company, or (2) "cease all infringing testing activity."[81] In the letter, Myriad told GDL that it could continue using BRCA testing "for the purpose of furthering non-commercial research programs."[82] This would have allowed GDL to perform BRCA testing as long as patients were not informed of the outcome and GDL received no payment.[83] During this time, Myriad also sent cease-and-desist letters and initiated several patent infringement suits against providers of clinical BRCA diagnostic testing.[84] Since 1999, Myriad has continued to be the only provider of clinical genetic testing for BRCA1/2 mutations in the United States.[85] The plaintiffs in *Association for Molecular Pathology v. United States Patent and Trademark Office (Myriad I)* filed a suit challenging the validity of Myriad's patents over BRCA1/2 genes and diagnostic methods in 2009.[86]

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[72] Male carriers of BRCA1/2 mutations are predisposed to prostate and colon cancer, Kenneth P. Tercyak et al., *Parental Communication of BRCA1/2 Genetic Testing Results to Children*, 42 PATIENT EDUC. & COUNSELING 213, 213 (2001), though this predisposition is less severe than the female equivalent. Males also have about a 5% chance of developing breast cancer within their lifetimes if they have a germline mutation of the BRCA2 gene. YOUNG, *supra* note 43, at 200.

[73] *Myriad II*, 653 F.3d at 1339.

[74] *Id*. The genetic basis for familial breast and ovarian cancer was identified through a process known as positional cloning. *Id.* Researchers identified families with inherited breast and ovarian cancers, gathered large sets of DNA, and compared the occurrence of cancer with certain markers on the DNA sequences. *Id.*

[75] *Id*.

[76] *Id*.

[77] *Id*.

[78] *Id*.

[79] *Id*. at 1339–40.

[80] *Id.* at 1340.

[81] *Id*.

[82] *Id*. (quoting the letter received by Dr. Kazazian, the co-director of GDL).

[83] *Id*.

[84] Ass'n for Molecular Pathology v. USPTO (*Myriad I*), 702 F. Supp. 2d 181, 205–06 (S.D.N.Y 2010), *rev'd in part and aff'd in part*, 653 F.3d 1329 (Fed. Cir. 2011), *cert. granted, judgment vacated sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012), *opinion vacated, appeal reinstated*, 467 F. App'x 890 (Fed. Cir. 2012).

[85] *Myriad II*, 653 F.3d at 1340.

[86] *Myriad I*, 702 F. Supp. 2d at 186.

B. Myriad I*: United States District Court for the Southern District of New York*

1. Opponents of Gene Patents

¶18 The Plaintiffs in *Myriad I* roughly broke down into two groups: (1) those who were actually injured by Myriad's patent rights over the BRCA1/2 genes and diagnostics, and (2) those who represent others with concrete interests in the availability of BRCA1/2 testing sites. The first group included several patients who could not afford Myriad's testing as well as Dr. Kazazian, who received a cease-and-desist letter from Myriad and ceased BRCA1/2 testing as a result.[87] The latter group included patients' rights groups such as Breast Cancer Action and medical societies such as the College of American Pathologists.[88] Several amicus briefs were filed on behalf of the plaintiffs, arguing that Myriad's patents were directed at unpatentable subject matter and violated medical ethics, among other arguments.[89]

2. Proponents of Gene Patents

¶19 The case was brought against three different defendants. Defendant Myriad Genetics, Inc., a for-profit biotechnology company, is the exclusive licensee of the patents-in-suit.[90] It is the only institution currently providing commercial BRCA1/2 testing in the United States.[91] Defendant University of Utah Research Foundation took part in the research that led to the BRCA1/2 patents and is the owner and co-owner of some of the patents-in-suit.[92] Defendant United States Patent and Trademark Office, a government agency within the U.S. Department of Commerce,[93] granted the patents-in-suit to Myriad in 1998 and 1999.[94] Amici curiae for defendants include non-profit trade associations, a health advocacy organization, for-profit corporations, and a public university.[95] The amici contend that the patents-in-suit fall within the requirements of 35 U.S.C. § 101 and also add that a ban on isolated DNA patents is an undesirable public policy because patents promote innovation.[96]

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[87] *Id.* at 187–89.

[88] *Id.* at 186–88.

[89] *Id.* at 190. The amicus briefs submitted by several non-profit public health organizations including the National Women's Health Network contends that patents over isolated DNA "stifl[e] innovation and interfer[e] with patient access to medical testing and treatment." *Id.* Another amicus brief submitted by two non-profit organizations dedicated to protecting indigenous people argued that gene patents violate the public trust doctrine and patients' rights to informed consent. *Id.*

[90] *Id.* at 189.

[91] *Id.* at 189.

[92] *Id.* at 189–90; *see also* Ass'n for Molecular Pathology v. USPTO (*Myriad II*), 653 F.3d 1329, 1333 (Fed. Cir. 2011), *cert. granted, judgment vacated sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012), *opinion vacated, appeal reinstated*, 467 F. App'x 890 (Fed. Cir. 2012).

[93] *Myriad I*, 702 F. Supp. 2d at 189.

[94] *See Myriad II*, 653 F.3d at 1339.

[95] *Myriad I*, 702 F. Supp. 2d at 190-92. Amici curiae also include a law professor and a patent attorney.

[96] *Id.* Amici also contend that the claims-in-suit are sufficiently limited to avoid claiming products of nature.

3. Court Opinion

¶20 After discussing factual issues, the court considered the issue of law that is of greatest importance to this article: whether the composition claims over the isolated BRCA1/2 DNA were valid under 35 U.S.C. § 101.[97] The court first considered whether there was an issue of law or fact upon which to test the merits of the plaintiffs' claims (in other words, whether summary judgment should be granted to defendants).[98] Defendants argued that patents are afforded a presumption of validity[99] and cited the USPTO's own prior consideration of the validity of gene patents.[100] The court rejected the proposed "rule of judicial deference to the USPTO's practices," noting that 40% of patents challenged in courts are found to be invalid and 74% of patents challenged through reexamination are either canceled or changed by the USPTO itself.[101]

¶21 Myriad also argued that constitutional property rights apply to its patents. It argued that "invalidating the patents-in-suit would constitute an unconstitutional taking in violation of the Fifth Amendment . . . or a violation of the United States' obligations under the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)."[102] The court rejected the arguments as "unpersuasive," stating that Myriad's takings argument was novel and runs counter to the history of patent claim invalidation by the courts.[103] The court also stated that TRIPS allows governments to consider public health concerns in the development of its intellectual property law.[104]

¶22 Next, the court considered whether the matter covered by the patents was "markedly different" from a product of nature and decided that isolated DNA is not "markedly different" from native DNA.[105] The "markedly different" terminology was taken from *Chakrabarty*, in which the Court stated that "the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility."[106] The court in *Myriad I* explained that for the purposes of § 101, "markedly different characteristics" are those that have "a new or distinctive form, quality, or property."[107]

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[97] The court also considered the validity of several other patent claims, including two methods claims over the analysis and comparison of DNA and comparison of the growth rate of cells—which the court invalidated as unpatentable abstract mental processes and the application of the scientific method itself. *Id.* at 232–37. The court dismissed the constitutional claim brought against the USPTO, following the doctrine of constitutional avoidance. The court stated that it was unnecessary to reach the constitutional question because the patents issued by the USPTO were invalidated. *Id*. at 237–38.

[98] *Id*. at 220.

[99] *See* 35 U.S.C. § 282 (2006).

[100] *Myriad I*, 702 F. Supp. 2d at 220–21. *See also* Utility Examination Guidelines, 66 Fed. Reg. 1092, 1092–99 (Jan. 5, 2001); J.E.M. Ag Supply v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124 (2001) (finding the USPTO's policy of granting utility patents for plants that pass the *Chakrabarty* "man-made" test establishes that the plants in question could be patented).

[101] *Myriad I*, 702 F. Supp. 2d at 221.

[102] *Id.* at 221.

[103] *Id*. at 221–22.

[104] *Id*. at 222. It is interesting to note that the court rejected the consideration of public health concerns and other policy as factual disputes outside the context of the motions, *id.* at 211, and yet cites an allowance in the treaty to consider such concerns to exclude diagnostic methods from patentability, *id*. at 222.

[105] *Id*. at 222, 227–28, 232. For a discussion of the scientific differences between "isolated and purified" DNA and naturally occurring DNA, see *supra* Part I(B).

[106] Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980).

[107] *Myriad I*, 702 F. Supp. 2d at 223 (quoting Am. Fruit Growers v. Brogdex Co., 283 U.S. 11 (1931), in

¶23 The court rejected Myriad's argument that the process of isolation and purification changed the chemical nature of the DNA in question in such a way as to create patentable subject matter.[108] The court contrasted DNA with other chemical compounds eligible for patent protection, stating that the unique informational quality of DNA makes it the "physical embodiment of laws of nature."[109] The unique qualities of all DNA, the court asserted, rendered the structural and functional differences between Myriad's isolated BRCA1/2 genes and naturally occurring DNA inadequate to make the patented genes markedly different from their natural counterparts.[110] The court then rejected the structural differences between natural DNA and isolated DNA as merely differences in purity, which cannot establish patent eligibility.[111]

¶24 The court further rejected Myriad's argument that native DNA contains introns, while the patents-in-suit cover purified DNA containing only exons.[112] To do so, the court looked to the language of the patent claims, several of which cover DNA "coding for a BRCA1[/2] polypeptide," which inherently includes DNA with introns, as well as solely exons.[113] The court stated that the functional, coding portions of the DNA sequences are identical between the claimed DNA and naturally occurring chromosomal DNA.[114] Overall, the court decided that DNA's inherent utility in therapeutics and diagnostics arises from its ability to bind selectively with antiparallel DNA segments.[115] Since this utility is unchanged by the isolation and purification of genetic DNA in a laboratory, the function of isolated DNA is not markedly different from that of native DNA.[116] The court, therefore, held that isolated DNA is not considered patentable subject matter.[117]

C. Myriad II*: U.S. Court of Appeals for the Federal Circuit*

¶25 In a plurality opinion issued in July of 2011, the Court of Appeals for the Federal Circuit reversed the lower court's decision that isolated and purified BRCA1/2 genes were not patentable subject matter.[118]

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which the Supreme Court rejected patent claims over fruit whose outer surface was treated with an anti-mold composition. The Court stated that although production of the fruit required "treatment, labor, and manipulation," the fruit did not become an "article of manufacture" without possessing a "new or distinctive form, quality, or property" that the natural article lacks.).

[108] *Myriad I*, 702 F. Supp. 2d at 224, 227.

[109] *Id.* at 228.

[110] *Id.* at 229. The court also rejects Myriad's contention that § 101 inquiries should focus on the differences between native and isolated DNA, rather than their similarities as overly broad and untenable. *Id.*

[111] *Id.* at 229–30.

[112] *Id.* at 230.

[113] *Id.*

[114] *Id.* This argument ignores the functions of introns which, while largely unknown, include sequences that may be involved with inhibition or over-expression of certain genes. *See* A.B. ROSE, *Intron-Mediated Regulation of Gene Expression*, *in* CURRENT TOPICS ON MICROBIOLOGY AND IMMUNOLOGY 277 (2008).

[115] *Myriad I*, 702 F. Supp. 2d at 231.

[116] *Id.*

[117] *Id.* at 232.

[118] Ass'n for Molecular Pathology v. USPTO (*Myriad II*), 653 F.3d 1329 (Fed. Cir. 2011), *cert. granted, judgment vacated sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012), *opinion vacated, appeal reinstated,* 467 F. App'x 890 (Fed. Cir. 2012).

1. The Opinion of the Court

¶26 After considering the issue of standing, the Court turned to the issue at hand: whether the composition claims covered patentable subject matter under 35 U.S.C. § 101. The majority wrote that the Supreme Court's construction of § 101 is broad, but not unlimited.[119] Based on the decisions in *Chakrabarty* and *Funk Brothers Seed Co. v. Kalo*, the majority stated that the distinction between man-made invention and products of nature "turns on a change in the claimed composition's identity compared with what exists in nature."[120] These changes must be "markedly different" or "distinctive."[121]

¶27 Unlike the lower court, the majority in *Myriad II* decided that the chemical manipulation of the BRCA1/2 genes that removed it from the genome and created isolated BRCA1/2 DNA changed the DNA from a natural material to a distinct chemical entity.[122] The majority rejected the lower court's method of basing the distinctiveness of isolated DNA on the single similarity it shares with its naturally occurring antecedent: the information contained within the nucleotide sequence.[123] The Court rejected the creation of a categorical rule preventing patent eligibility for isolated genes, stating that the Supreme Court has cautioned courts against adding limitations to patent laws that were not expressed by the legislature.[124] Finally, unlike the lower court in *Myriad I*, the majority also gave deference to the "longstanding" USPTO practice that allowed for the patentability of isolated DNA molecules.[125]

2. Judge Moore's Partial Concurrence

¶28 Judge Moore's partial concurrence agreed with the majority as to the issue of standing, but disagreed with the majority's reasoning for the allowance of isolated DNA as patent-eligible subject matter.[126] Through a scientific explanation of DNA as a simple polymer, Judge Moore emphasized the functional differences between fragments of DNA molecules and the entire genomic structure found in nature.[127] The concurrence challenged the lower court's contention that isolation of genes is akin to separating out impurities from a naturally occurring mineral.[128] The analysis emphasized the chemical

[119] *Id*. at 1348 (quoting *Bilski v. Kappos*, 130 S.Ct. 3218, 3225 (2010) (relying upon *Chakrabarty* for the notion that Congress intended patent laws to be given wide scope)).

[120] *Id*. at 1351 (building upon the rules in *Chakrabarty* and Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948) (invalidating a patent covering a mixture of certain strains of bacteria that do not naturally cohabitate)).

[121] *Id*. at 1351.

[122] *Id*.

[123] *Id*. at 1353 (stating that "the patent eligibility of an isolated DNA is not negated because it has similar informational properties to a different, more complex natural material that embodies it").

[124] *Id*. *See also Bilski*, 130 S.Ct. at 3226, 561 U.S. __.

[125] *See Myriad II*, 653 F.3d at 1354.

[126] *Id*. at 1358. The concurrence also agreed with the majority's opinion with regard to the affirmation of the lower court's rejection of the method claims, as well as the majority's conclusion that the cDNA sequences are patentable. With regard to the composition claims on isolated DNA, the concurrence agreed with the judgment, but not the reasoning. *Id.*

[127] *Id*. at 1361–62.

[128] *Id*. at 1363.

and structural differences between excised (or synthesized) DNA fragments and those connected to a chromosome.[129]

¶29 The concurrence, however, did not rely solely on the marked difference in chemical structure to deem isolated DNA patentable.[130] Rather, the concurrence focused upon the utility gained by the difference in structure.[131] Judge Moore gave weight to the possible uses of shorter sequences of isolated DNA as primers and probes.[132] The concurrence did not go so far as to conclude that isolated DNA sequences that include an entire gene are eligible for patents based on structural and utility concerns alone.[133] Instead, Judge Moore, like the majority, gave deference to the policies of the USPTO to allow patents for isolated natural products.[134] Unlike the majority opinion, the concurrence also expressed deference for the expectations of the biotechnology industry and the thousands of isolated DNA patents already issued by the USPTO.[135] Finally, the concurrence argued that the court is ill-suited to determine whether or not isolated DNA claims promote or inhibit science, and therefore leaves the question to the constitutional authority of Congress.[136]

3. Judge Bryson's Partial Concurrence and Partial Dissent

¶30 Judge Bryson's partial concurrence disagreed with both the majority and Judge Moore's concurrence with regard to the patentability of isolated DNA sequences. Judge Bryson simplified the issue down to one question: Are human genes patentable?[137] In a comparison with isolation of native minerals, Judge Bryson's opinion stated that "merely isolating the products of nature by extracting them from their natural location and making those alterations attendant to their extraction does not give the extractor the right to patent the product themselves."[138] In the end, Judge Bryson formulated the rule that "the extraction of a product in a manner that retains the character and function of the product as found in nature does not result in the creation of a human invention."[139] In a move that seems to follow the argument of the lower court, Judge Bryson focused upon the similarity in function between the isolated BRCA1/2 genes and the genes within chromosomal DNA.[140] The partial concurrence limited the patentability of isolated DNA to applications of gene sequences, and not of the gene sequences themselves.[141]

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[129] *Id.*

[130] *Id.* at 1365–68

[131] *Id.*

[132] *Id.* at 1365. *See also supra* Part I(B) for a discussion of DNA fragments as primers and probes.

[133] *Id.* at 1366. (In fact, Moore states that if she were to make the patentability decision based on a blank canvas, she might conclude that such a DNA sequence would not be patentable.)

[134] *Id.* at 1367 (relying on 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001), which states that the USPTO's policy that "[a]n isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because . . . that DNA molecule does not occur in that isolated form in nature").

[135] *Id.* at 1368.

[136] *Id.* at 1372.

[137] *Id.* at 1373.

[138] *Id.* at 1375. The dissent further argues against the majority's fundamental conclusion that cleavage of the bonds between DNA and the histone proteins to isolate DNA chemically alters the identity of the DNA. Rather, the dissent likens chemical bonds between atoms to weaker interatomic forces. *Id.*

[139] *Id.* at 1377.

[140] *Id.* at 1376–77.

[141] *Id.* at 1373. The dissent also delves into the perceived danger of broad patent protection over genetic

D. *Subsequent History of* Myriad

¶31 In 2012, the Supreme Court took on the issue of patents attempting to claim laws of nature in *Mayo Collaborative Services v. Prometheus Laboratories, Inc*.[142] The Court invalidated method claims that optimized dosage of a drug for the treatment of certain autoimmune diseases.[143] Justice Breyer asserted that merely stating a law of nature and writing "apply it" in the patent application does not satisfy the requirement that a process based upon a natural law must also contain an "inventive concept" that amounts to significantly more than a patent over the natural law itself.[144] Just six days after the Supreme Court decided *Mayo v. Prometheus*, it vacated the opinion in *Myriad II* and remanded the case back to the Federal Circuit for consideration in light of *Mayo*. [145]

¶32 The Federal Circuit's second review of *Myriad* resulted in a restatement of *Myriad II's* findings for the composition claims.[146] As before, the majority found that the composition claims directed to the "isolated" DNA and to cDNA cover patent eligible subject matter.[147] Judge Lourie again emphasized the fact that the "isolated" DNA covered by the patent does not exist in its isolated form in nature. Importantly, Judge Lourie addressed the Supreme Court's decision in *Mayo* by stating that *Mayo* does not control the subject matter eligibility of composition claims.[148] Therefore, *Mayo* did not affect the Federal Circuit's decision in regards to the patent eligibility of "isolated" DNA and cDNA sequences.

III. THE ECONOMICS OF GENE PATENTS

A. Open-Source Science and Opponents of Gene Patents

¶33 In 1948, the Supreme Court of the United States declared "manifestations of . . . nature, [are] free to all men and reserved exclusively to none."[149] Though this doctrine has changed throughout the years, the sentiment that unchanged products of nature are unpatentable under 35 U.S.C. § 101 persists.[150] Opponents of gene patents argue that isolated DNA, although chemically altered by the isolation process, is still a natural substance with the same utility as its native counterpart and therefore is ineligible for patent protection.[151] Beyond the legal arguments described in the *Myriad* cases,

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material as a hindrance to future genetic innovation. This argument, the threat of the anti-commons, is further discussed in Part III, *infra*.

[142] 132 S. Ct. 1289 (2012).

[143] *Id*.

[144] *Id*. at 1294. In *Mayo v. Prometheus*, the patent at issue covered the application of a known correlation between a levels of certain metabolites in a patient's blood and the efficacy of the drug thiopurine. *Id.*

[145] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012) (mem.) (granting cert and vacating opinion below allowing the patenting of extracted DNA and remanding for analysis in line with *Mayo*).

[146] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303 (Fed. Cir. 2012).

[147] *Id*. at 1309.

[148] *Id*. at *15.

[149] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

[150] *See, e.g., Myriad II*, 653 F.3d 1329; *see also* Diamond v. Chakrabarty, 447 U.S. 303 (1980).

[151] *See, e.g., Myriad II*, 653 F.3d 1329 at 1378 (Bryson, J., dissenting); *see generally* Jonah D. Jackson, Note, *Something Like the Sun: Why Even "Isolated and Purified" Genes are Still Products of Nature*, 89

opponents present policy arguments against the patentability of genes. These include the notion of the "tragedy of the anticommons" and an overall ethical question about the justification of incentives to the biotechnology industry.

1. The "Tragedy of the Anticommons"

¶34 In 1998, Michael Heller and Rebecca Eisenberg published a highly influential article applying the notion of the "tragedy of the anticommons" to the patentability of biomedical research.[152] The authors argue that patents on upstream technology—such as gene sequences—have the unintended consequence of stifling downstream innovation by imposing burdensome transaction costs.[153] These transaction costs arise from the need to collect all the necessary licenses to use the upstream technologies.[154]

¶35 Heller and Eisenberg allow that intellectual property protection in biomedical research incentivizes researchers to undertake risky research projects and could even help equitably distribute profits across the various stages of research and development.[155] On the other hand, the authors argue that privatization limits future research when too many entities hold rights to discoveries that serve as obstacles to further research.[156] Heller and Eisenberg predicted that patents on gene fragments would cause researchers developing therapeutic proteins and diagnostic tests to bundle licenses together before they could effectively develop the downstream technologies.[157] This clearly relates to the *Myriad* cases, in which the exclusive licensee of the BRCA1/2 genes imposed high transaction costs on entities hoping to license the BRCA1/2 genes and perform their own diagnostic tests.[158] Though the article suggests the possibility of the biomedical research community correcting its own anticommons problems in ways similar to the actions of the music industry, the authors identify several impediments to such a concerted action.[159] These include the greater relative importance of patents to the biotechnology and pharmaceutical industries, the heterogeneity of interests of upstream rights holders, and even a cognitive bias on the part of patent holders to believe that their patents hold

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TEX. L. REV. 1453 (2011).

[152] *See* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698 (1998). Heller introduced the "tragedy of the anticommons" theory in broader application earlier that year in an article in the Harvard Law Review. *See* Heller, Michael, *The Tragedy of the Anticommons: Property in the Transition from Marx to Markets*, 111 HARV. L. REV. 3, 621–88 (1998).

[153] *Id*. at 698. The theory relates to Garrett Hardin's metaphor in property law of the "tragedy of the commons," which has been used to explain such phenomena as overpopulation, species distinction, and air pollution. *See* Garrett Hardin, *The Tragedy of the Commons*, 162 SCI. 1243 (1968).

[154] Rebecca S. Eisenberg, Symposium, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 HOUS. L. REV. 1059, 1060 (2008).

[155] Heller & Eisenberg, *supra* note 152, at 698. *See also* Thomas A. Hemphill, *Gene Patents, The Anticommons, and the Biotechnology Industry*, RES. TECH. MGMT., Sept.-Oct. 2010, at 11.

[156] Heller & Eisenberg, *supra* note 152, at 698.

[157] *Id*. at 699. When licenses are bundled together, researchers have the ability to pay one fee in order to use all the patented technologies within the bundle. While this has the ability to speed up the process and lower the cost of licensing, it may also cause researchers to pay for licenses within the bundle that they would not have needed if the licenses had been obtained separately. Also, bundles create a hold out problem when one patent holder refuses to license his or her technology to others.

[158] *See supra* Part II(B) for a discussion of the facts in *Myriad*. Ass'n for Molecular Pathology v. USPTO (Myriad II), 653 F.3d 1329 (Fed. Cir. 2011).

[159] Heller & Eisenberg, *supra* note 152.

the "key" to downstream production, leading these patent holders to hold out for high licensing fees.[160] The "tragedy of the anticommons" ultimately results in abandonment of research projects that have been deemed too costly from an IP licensing standpoint.[161]

2. Ethics of Gene Patents

¶36 Opponents of gene patents also present several ethical arguments, including consent issues involved in personalized medicine, and open source arguments for the dissemination of information. Patients' groups contend that certain gene patents violate individual human rights by bypassing patients' informed consent.[162] For instance, in 2010, members of the Havasupai Native American tribe claimed that Arizona State University used their DNA samples in ways other than those agreed upon, and won $700,000 in an out-of-court settlement.[163] One court treated DNA donors as "tissue sources" with no rights to be informed about the possible commercialization of the tissues to be donated.[164]

¶37 Unlike in the United States, informed consent is governed by the European medical community through a directive of the European Union's Parliament and Council states that persons from whose bodies biological material is being taken for biotechnological discovery "must have . . . an opportunity of expressing free and informed consent thereto."[165] Gene patent consent issues also sometimes involve religious beliefs and fears about genetic discrimination.[166] Reproductive liberty issues also attach to the discussion of gene sequencing and patenting.[167] An in-depth discussion of such ethical issues is outside the scope of this article.

¶38 Opponents of patents also argue that the commercial incentives of patents will slow the process of technology by undermining the open-science research norm.[168] Since the passage of the Bayh-Dole Act in 1980, universities and small businesses have had the ability to claim IP protection over federally funded discoveries.[169] Patent opponents argue that this has led universities away from the historical ideal of open access to basic research.[170] Traditionally, researchers were incentivized to keep science within the

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[160] *Id*. at 700–01.

[161] *See* Jacob D. Moore, Note, *The Forgotten Victim in the Human Gene Patenting Debate: Pharmaceutical Companies*, 63 FLA. L. REV. 1277, 1291 (2011); *see also* Heller & Eisenberg, *supra* note 152, at 700.

[162] Lori B. Andrews & Jordan Paradise, *Gene Patents: The Need for Bioethics Scrutiny and Legal Change*, 5 YALE J. HEALTH POL'Y L. & ETHICS 403, 408 (2005).

[163] Arthur Piper, *Who Owns Human Nature?*, 65 No. 2 IBA GLOBAL INSIGHT, April 2011, at 47, 49.

[164] Andrews & Paradise, *supra* note 162, at 410 (referring to Greenberg v. Miami Children's Hosp., 264 F. Supp. 2d 1064 (S.D. Fla. 2003)).

[165] *Id.* (citing Council and Parliament Directive 98/44/EC of 6 July 1998 on the Legal Protection of Biotechnological Inventions, 1998 O.J. (L 213) 14, recital 26, http://europa.eu.int/eurlex/pri/en/oj/dat/1998/1_213/1_21319980730en001130021.pdf).

[166] *Id.*; *see also* Piper, *supra* note 163, at 49 (discussing the taboo nature of schizophrenia research, which angered the Havasupai people).

[167] Andrews & Paradise, *supra* note 162, at 410.

[168] Timothy Caulfield et al., *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 NATURE BIOTECHNOLOGY 1091, 1091 (2006).

[169] STEPHEN A. MERRILL ET AL., REAPING THE BENEFITS OF GENOMIC AND PROTEOMIC RESEARCH: INTELLECTUAL PROPERTY RIGHTS, INNOVATION, AND PUBLIC HEALTH 20, 24 (2006).

[170] Richard R. Nelson, *The Market Economy, and the Scientific Commons*, 33 RES. POL'Y 455, 469 (2004).

public domain because rewards to scientists were tied to acclaim within the community following the publication of peer-reviewed articles.[171] More recently, many universities (and their researchers) are aiming to "maximize[] expected revenues from intellectual property."[172] This new incentive to patent takes away from the traditional open research incentives, leading to an increase in the secretive nature of academic research, delays in publication of findings, and resistance to sharing data and research materials.[173]

B. Counter-Arguments to Opponents of Gene Patents

1. The "Tragedy of the Anticommons" Is Not So Tragic

¶39 Ten years after the publication of the *Science* article that catapulted the "tragedy of the anticommons" into the discussion of biotechnological patent policy, Rebecca Eisenberg admitted that "intellectual property has presented fewer impediments to research than policymakers may have projected on the basis of early salient controversies."[174] In an empirical study of the impact of patents on biomedical research in United States universities, a research team lead by John Walsh concluded that patents have had little detrimental impact upon academic researchers.[175] Several other empirical studies reported similar findings.[176] A study performed by the American Association for the Advancement of Science (AAAS), which included both academic and private researchers, found that only 1% of survey respondents in the U.S. abandoned a research project as a result of the need to obtain patent licenses.[177] Although approximately 20% of all human genes are covered by at least one patent, anticommons problems have been shown to be "relatively uncommon."[178] Eisenberg attributes the lack of obstacles demonstrated in the studies, in part, to the fact that such empirical studies tend to measure upstream rather than downstream innovation, but admits that the data demonstrate that the effects of the "tragedy of the anticommons" are far less serious than predicted.[179]

¶40 Walsh then focused his research on the anticommons effect of patents covering upstream research tools upon downstream innovation. He found that the patenting of upstream research tools has an insignificant effect on downstream diagnostic and therapeutic discovery. Although there has been an increase in the number of patents on research tools in the last thirty years, those patents have not impeded biomedical

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[171] *Id.* at 455.

[172] *Id.* at 469.

[173] Caulfield, *supra* note 168, at 1091. Most writing on the topic of open source science concerns basic science research and draws a definitive line between "basic" and "therapeutic" or "technology-based" science. See Nelson, *supra* note 170, for an analysis of the open science opinion focusing solely on basic research. See also Paul A. David, *Can "Open Science" Be Protected from the Evolving Regime of IPR Protections* 1-27 (Stanford Inst. Econ. Policy Research, Policy Paper No. 02-042, 2003)), for a call to action to halt the privatization of public domain information.

[174] Eisenberg, *supra* note 154, at 1061.

[175] John P. Walsh et al., *Working Through the Patent Problem*, 299 SCI. 1021 (2003).

[176] Eisenberg, *supra* note 154.

[177] AM. ASS'N FOR THE ADVANCEMENT OF SCI., INTERNATIONAL INTELLECTUAL PROPERTY EXPERIENCES: A REPORT OF FOUR COUNTRIES 6–8 (2007), *available at* http://sippi.aaas.org/Pubs/SIPPI_Four_Country_Report.pdf.

[178] Caulfield, *supra* note 168, at 1091.

[179] Eisenberg, *supra* note 154, at 1075.

innovation.[180] Several factors led to the rise in patents on research tools, including increased patenting by the biotech industry generally, the allowance of patents over university research following the Bayh-Dole Act, and the rise of defensive patenting by biotech companies.[181]

¶41 The increase in the complexity of the patent landscape would lead believers in the anticommons problem to expect a resulting decrease in innovation. Yet, the Walsh study found no such evidence. In fact, of fifty-five researchers surveyed, only one reported an instance during which a breakdown in the negotiations for rights to a research tool resulted in the termination of a project.[182] Also, though the number of licenses obtained by researchers has increased in recent years, the number appears to remain relatively small and the fees did not cause researchers to abandon projects.[183] In fact, researchers reported "the productivity gains conferred by the licensed research tools were thought to be worth the price."[184] This shows that researchers are willing to bear the costs of licensing upstream research tools because they increase the productivity of downstream innovations.

C. Benefits of Patents in the Realm of Biotechnological Innovation

¶42 The private United States biotechnology ("biotech") and pharmaceutical industry spent approximately $49 billion on biomedical research in 2006, accounting for 41% of national biomedical research spending.[185] Private biotech and pharmaceutical companies "must invest hundreds of millions of dollars in research and development over many years to bring their products to market."[186] Estimates place the cost of developing and testing a new pharmaceutical entity in the 1980s and 1990s above $800 million.[187] Furthermore, this cost "has increased and seems destined to continue increasing," causing

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[180] *See* John P. Walsh, et. al., *Effects of Research Tool Patents and Licensing on Biomedical Innovation*, *in* PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285 (Wesley M. Cohen & Stephen A. Merrill eds., 2003) (assessing the empirical evidence regarding effect of patents on research tools, or inputs to drug discovery, between the years 1986 and 2003). Gene sequence patents, like the patent at issue in the *Myriad* cases, can be considered patents on research tools because genetic sequences serve as starting points for further diagnostic and therapeutic research.

[181] *Id.* at 294–95. *See also* Caulfield, *supra* note 168 (explaining the rise of patenting by universities following the Bayh-Dole Act). The term "defensive patenting" refers to the practice of patenting often used in the telecommunications industry in which each small part of an invention is patented separately in order to protect a company from a possible future infringement suit. See Walsh, *supra* note 180, at 295, for an example of defensive patenting.

[182] Walsh, *supra* note 180, at 295.

[183] *Id.* at 294–95, 300. Researchers reported that while the number of patents that are initially considered for licensing is high—sometimes on the order of hundreds—the number of licenses that are necessary to obtain is "substantially smaller"—often closer to 3 to 6.

[184] *Id.* at 301.

[185] Elias A. Zerhouni, Special Communication, Nat'l Inst. Health, *U.S. Biomedical Research: Basic, Translational, And Clinical Sciences*, 294 J. AM. MED. ASS'N 1352 (2006).

[186] MERRILL ET AL., *supra* note 169, at 20.

[187] Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH & ECON. 151–85 (2003) (estimating the cost for new chemical entities to be $820 million in year 2000 dollars based on studies of pharmaceuticals developed between the years 1983 and 1994). *See also* Michael Dickson & Jean Paul Gagnon, *Key Factors in the Rising Cost of New Drug Discovery and Development*, 3 NATURE REVIEWS 417, 424–26 (2004)(placing the cost of development of new pharmaceuticals as high as $897 million in year 2000 dollars).

pharmaceutical innovation to be more expensive today.[188] Biotechnological innovation may in fact be more expensive than traditional pharmaceutical discovery.[189] The increase in expense stems from the riskiness of the drug development process, higher research and development costs, and highly specialized manufacturing and distribution processes when compared with those for traditional chemical entities.[190] More recent estimates place the cost of development of biopharmaceuticals—therapies based on mechanisms within the human body rather than strictly chemical compounds—above $1.2 billion.[191]

¶43 The high cost of pharmaceutical innovation makes intellectual property protection "essential" to the industry.[192] Studies demonstrate that the incentive effect of patents is more pronounced in the pharmaceutical industry than in other realms of science.[193] One study demonstrated that biotech firms expect to earn between 45–79% more on patented inventions than they would earn on those inventions if they had not been patented.[194] Patents are especially important—even critical—to start-up companies, which require significant investment from outside sources.[195] The surge in new entrants into the biotech industry in the last twenty years is widely attributed to the availability of patents in biotechnological innovation.[196]

¶44 The increased expense of biotechnological innovation further emphasizes the need for patent protection. Without patents, innovation would be hindered by the "appropriability problem."[197] This doctrine states that if an entity is unable to recover the costs of research and development because the resulting information would be available to the general public, then there would be a suboptimal level of innovation.[198] To contend with this problem without abandoning innovation, genetic researchers often turn to trade secrecy to protect the value of their discoveries.[199] The use of trade secrets to protect DNA sequences limits the free flow of information within the research community. The scientific community's traditional emphasis on disclosure and information sharing would fall by the wayside if trade secret became the main method of intellectual property protection.

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[188] Dickson, *supra* note 187, at 419.

[189] Bill Edelman, *Explaining the Cost of Biotech Therapies*, BIOTECHNOLOGY HEALTHCARE 37, 38 (2004) (stating that "it is a reasonable bet that most biologics would be of higher than average cost" when compared with traditional pharmaceutical entities).

[190] *Id.*

[191] Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 469 (2007).

[192] MERRILL, *supra* note 169, at 20.

[193] James Bessen & Michael J. Meurer, *Lessons for Patent Policy from Empirical Research on Patent Litigation* 10 (Boston Univ. Sch. of Law, Working Paper Series, Law & Econ., Working Paper No. 05–22, 2005).

[194] Ashish Arora et al., *R&D and the Patent Premium* 30, 47 (Nat'l Bureau of Econ. Research, Working Paper No. 9431, 2003). According to Arora, the patent premium for the biotech industry was higher than that of any other industry, including traditional pharmaceuticals.

[195] Walsh, *supra* note 180, at 287 (quoting the licensing director of a large pharmaceutical firm as saying, "Patents are critical to start-ups. Without patents, we won't even talk to a start-up about licensing.").

[196] *Id.*

[197] Dam, *supra* note 3, at 247.

[198] *Id.*

[199] Robert Mullan Cook-Deegan & Stephen J. McCormack, *Patents, Secrecy, and DNA*, 293 Sci. 217, 217 (2001) (stating that trade secrets are the primary intellectual property regime for the most valuable DNA sequence data).

¶45 Patents simultaneously incentivize investment in innovation and disseminate information to the scientific community, solving both portions of the "appropriability problem."[200] In fact, most patents filed in the United States are published after eighteen months, establishing a limitation for the time period of secrecy for researchers who choose to patent their innovations by requiring that the invention is disclosed.[201] In the case of patents covering DNA sequences, this publication rule restores the informational value contained within the DNA sequence.[202] Some researchers even argue that patents facilitate the exchange of technological information "by forcing would-be copyists to invent around and or to pursue alternative avenues of research. . . ."[203] For instance, a patent on a gene sequence claims only uses of the sequence itself, not the protein or smaller expressed sequence tags (ESTs) of cDNA. Researchers are encouraged to discover the use of the protein without dealing directly with the gene sequence.[204] The existence of patents may actually spur superior scientific advances by forcing researchers to develop new technology that works around existing patents.

IV. CONCLUSION

¶46 In the case of isolated genes, patent eligibility acts as a critical incentive for scientific research. The costs of research and development of research therapies act as a barrier-to-entry that may only be overcome through the influx of capital supplied by investors looking to make a return on their investment. As the costs of research, development, and testing have soared within the biotech industry, patents have become crucial to start-up companies and established companies alike. Thus, useful, often life-changing, technologies would never be available to patients if not for the USPTO's decades-long practice of granting gene patents.

¶47 Opponents of gene patents argue that the allowance of exclusive rights over upstream research technology will have a deleterious effect on downstream innovation.[205] Researchers termed this theory the "tragedy of the anticommons."[206] Empirical studies have shown that the "tragedy of the anticommons" does not exist within the realm of biotechnology.[207] Though patents on upstream research tools have increased throughout the years, downstream technology has not been hindered.[208]

¶48 In the words of the U.S. Constitution, patents "promote the progress of science and useful arts"[209] by incentivizing both discovery and disclosure. Gene patents provide

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[200] Dam, *supra* note 3, at 247.

[201] Cook-Deegan & McCormack, *supra* note 199, at 218.

[202] *Id.* at 219.

[203] Edward T. Lentz, *Are Real Business People So Easily Thwarted?*, *in* PERSPECTIVES ON PROPERTIES OF THE HUMAN GENOME PROJECT 441, 442 (F. Scott Kieff ed., 2003).

[204] *See* Walsh, *supra* note 180, at 299 (referring to Dennis Henner's testimony before Congress about the nature of EST patents and their inability to block patents over whole genes and proteins because each discovery is a separate invention, *Oversight Hearing on "Gene Patents and Other Genomic Inventions" Before the Subcomm. on Courts & Intellectual Prop. of the H. Comm. on the Judiciary*, 106th Cong. 74–75 (2000) (statement of Dennis Henner, Senior Vice President of Research, Genentech)).

[205] *See, e.g.*, Heller & Eisenberg, *supra* note 149.

[206] *Id*.

[207] *See* Walsh, *supra* note 180; *see also* Caulfield, *supra* note 168; Eisenberg, *supra* note 154 at 1060.

[208] Walsh, *supra* note 180.

[209] U.S. CONST. art. I, § 8, cl. 8.

important monetary incentives for companies developing downstream technology without violating the traditional open information norm of the scientific community. Empirical data has shown the "tragedy of the anticommons" to have an insignificant practical effect upon biomedical innovation, while gene patents themselves spur innovation by providing for an influx of capital for corporations performing important biotechnological research. Without gene patents, researchers lose out on a large source of potential funding and may turn to trade secrets to protect discoveries. Overall, gene patents lead to important medical discoveries by incentivizing research, providing for monetary capital, and allowing the free flow of scientific information.