29 Biotechnology Law Report 609
Number 6, 2010

DOI: 10.1089/blr.2010.9911

Original Articles

Rethinking the Gene Patent

By ALAN J. MORRISON*

On May 12, 2009, the American Civil Liberties Union—acting on behalf of more than 20 plaintiffs—sued the U.S. Patent and Trademark Office and Myriad Genetics. The ACLU's goal was to invalidate Myriad's patent claims to isolated forms of the human breast cancer-related genes *BRCA1* and *BRCA2*.[1,2]

On March 30, 2010, District Court Judge Robert Sweet issued a decision invalidating Myriad's patent claims.[3] The decision is now on appeal to the U.S. Court of Appeals for the Federal Circuit (CAFC) and may ultimately reach the U.S. Supreme Court.

Myriad is remarkable in many ways. It is a gene patent case, yet gene patents do not fall within the realm of "civil liberties" as that term is generally understood. The Patent Office is named as a defendant, despite having no ownership rights in the patents at issue. Patent suits rarely involve more than a few plaintiffs, yet *Myriad* names a large and diverse array of plaintiffs, including research institutes, physicians, scientists, and patients. Moreover, the plaintiffs invoked the First and Fourteenth Amendments—an unorthodox approach for a patent suit.

Myriad's most important feature, however, is the question it answers: Is an isolated gene patentable subject matter?[4] The answer is of considerable importance to the biotechnology and pharmaceutical industries. Remarkably, neither the Supreme Court nor the CAFC has ever directly addressed this question.

For years, many in the legal field have presumed that isolated genes are patentable subject matter. This presumption has been based on statute, case law, and written Patent Office policies. It has also been based on the issuance of seemingly countless gene patents, some of which have survived invalidity challenges brought on other grounds. After *Myriad*, however, it is clear that this presumption of patentability is not shared by all.

Myriad has stirred debate in the legal and scientific communities over several issues: the ideal scope of patent-eligible subject matter generally; the wisdom of specifically excluding isolated genes (especially human genes) from patentable subject matter on legal or ethical grounds; and the potential effects of gene patents on scientific research and healthcare quality and accessibility.

Understandably, the general public has expressed discomfort with gene patents, given their potential effect on healthcare quality and accessibility. Thanks in part to the media's often inaccurate portrayal of gene patents,[5] the general public has also voiced concern over corporate "ownership" of their genes and the adverse practical and ethical effects of such ownership.

The *Myriad* decision is long. In it, Judge Sweet provides a robust discussion of the facts regarding DNA technology, the *BRCA1/2* genes, the diagnostic methods made possible by Myriad's patented inventions, and the various healthcare and research issues surrounding Myriad's patent position. Judge Sweet also provides an in-depth and essentially lucid review of the law of patent-eligible subject matter. His review emphasizes the chain of relevant Supreme Court cases on the matter, and also addresses lower court decisions that have traditionally been cited as supporting the patentability of isolated biomolecules.

Despite this lengthy treatment of the law of patent-eligible subject matter, and even assuming—for the sake of this article—that the court's understanding of this law is accurate, Judge Sweet's ruling in *Myriad* is

* Alan J. Morrison is a partner at the New York firm of Cohen Pontani Lieberman & Pavane LLP. This article solely reflects the views and considerations of the author, which should not be attributed to the firm or to any of its clients.

[1]"*BRCA1*" and "*BRCA2*" stand for human breast cancer susceptibility gene 1 and human breast cancer susceptibility gene 2, respectively, and are collectively referred to as "*BRCA1/2*."
[2]Myriad's patent claims to *BRCA1/2*-related methods were also challenged, as mentioned below.
[3]*Association of Molecular Pathology, et al. v. U.S. Patent and Trademark Office, et al.* (*Myriad*), No. 09 Civ. 4515, 2010 WL 1233416, *1 (S.D.N.Y. March 29, 2010). This decision is discussed in Biotechnology Law Report 29(3):303–9 and reprinted in Biotechnology Law Report 29(3):317–52.
[4]This article is solely devoted to the court's treatment of Myriad's composition claims (i.e., gene claims), and it does not address the court's treatment of Myriad's method claims.
[5]*See, e.g.*, Denise Caruso, Someone (other than you) may own your genes, *New York Times*, January 28, 2007.

disconcerting. It is the author's position that in holding Myriad's gene claims invalid, Judge Sweet did not properly apply the case law to the facts. Instead, and as addressed herein, he applied what appears to be his own doctrine, specifically excluding DNA from the family of naturally occurring biological compounds whose purified versions are patent-eligible.

GENE PATENTS

Taken literally, the term "gene" suggests a segment of DNA containing a protein- or RNA-encoding sequence, one or more introns, and regulatory regions such as promoters and enhancers. In biotechnology patents, however, it is common to use the term "gene" more broadly to encompass DNA encoding a naturally occurring protein or RNA, whether or not this DNA occurs naturally, and whether or not this DNA includes introns or regulatory regions. Examples of such broadly defined genes include genomic DNA fragments and cDNAs. Thus, for the purposes of this article, a "gene patent" is a patent claiming an isolated gene as broadly defined in this way.

The Patent Office has issued gene patents for many years. Indeed, the Patent Office has a formal written policy that sanctions such patents.[6] According to the Utility Examination Guidelines, "an inventor's discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it."[7]

The validity of gene patent claims has been adjudicated on various grounds, such as non-obviousness and compliance with the written description requirement.[8] However, "the Supreme Court has never directly decided the patentability of natural DNA sequences."[9,10] In particular, the Supreme Court has never determined whether an isolated DNA, such as a human gene, constitutes patentable (i.e., patent-eligible) subject matter under §101 of the patent statute.[11] Moreover, the *Myriad* court cited no lower court decisions directly deciding the patent eligibility of isolated forms of natural DNA.

THE *BRCA1/2* GENES AND MYRIAD GENETICS

In the mid-1990s, scientists affiliated with Myriad and collaborating institutions sequenced *BRCA1*, and thereafter sequenced *BRCA2*.[12] *BRCA1/2* mutations correlate with increased risk of breast and ovarian cancer. As the *Myriad* court stated, "[t]he existence of *BRCA1/2* mutations is . . . an important consideration in the provision of clinical care for breast and/or ovarian cancer. A patient will not only learn of her risk for hereditary breast and ovarian cancer, but also can gain information that may be useful in determining prevention and treatment options."[13]

Based on this technology, Myriad developed and now offers several *BRCA1/2* tests to clinicians and patients. Each test costs more than $3,000. Patients typically rely on insurance to pay for these tests. However, some patients who need testing are either uninsured or do not carry insurance accepted by Myriad, and many of these patients cannot otherwise afford to be tested.[14]

MYRIAD'S PATENTS

Myriad involves 15 claims contained in seven patents.[15] The claims-in-suit are of two types—composition and method.[16]

As noted in *Myriad*, claim 1 of U.S. Patent No. 5,747,282 is representative of the composition claims.[17] This claim provides "[a]n isolated DNA coding for a *BRCA1* polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2." "SEQ ID NO:2" is the amino acid sequence of human BRCA1 polypeptide, and claim 1 encompasses all isolated DNAs coding for that polypeptide. Therefore, because of the degeneracy of the genetic code, claim 1

---

[6]Utility Examination Guidelines, 66 FR 1,092 (Jan. 5, 2001).
[7]*Id.* at 1093.
[8]*See, e.g., In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009)(relating to obviousness of claims to an isolated nucleic acid molecule encoding natural killer cell activation inducing ligand ("NAIL") or homologue thereof); *See, also, Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997)(relating to the written description requirement as applied to claims to cDNA encoding vertebrate insulin).
[9]Kaye Scholer, Pharmaceutical and Biotech Patent Law §7:6.2 (2008).
[10]In biotechnology patents, the term "sequence," when used in connection with DNA, typically has two meanings. The first is the sequence, or order, of individual nucleotide residues within the DNA. The second is the DNA itself. So, for example, the phrases "isolated sequence" and "isolated DNA" are often used synonymously in patents.
[11]35 U.S.C. §101.
[12]*Myriad*, 2010 WL at *17–9.
[13]*Id.* at *19.
[14]*Id.* at *20–1.
[15]Claims 1, 2, 5–7, and 20 of U.S. Patent No. 5,747,282; claims 1, 6, and 7 of U.S. Patent No. 5,837,492; claim 1 of U.S. Patent No. 5,693,473; claim 1 of U.S. Patent No. 5,709,999; claim 1 of U.S. Patent No. 5,710,001; claim 1 of U.S. Patent No. 5,753,441; and claims 1 and 2 of U.S. Patent No. 6,033,857.
[16]As stated above, this article focuses exclusively on the composition claims.
[17]*Myriad*, 2010 WL at *28.

encompasses the isolated *BRCA1* gene as well as any other isolated DNA (such as a cDNA[18]) that happens to code for human *BRCA1*.

Claim 1 of U.S. Patent No. 5,837,492 functions in the same manner regarding *BRCA2*.

THE LAW OF PATENTABLE SUBJECT MATTER

The *Myriad* court provides a detailed review of the law of patentable subject matter. Following a discussion of the language of §101, the court reviews case law from the 19th century onward that interprets this statute and articulates what subject matter falls within its scope. The *Myriad* court pays particular attention, as it must, to Supreme Court precedent. It also focuses on key lower court decisions that address the question of whether isolated forms of naturally occurring products are patentable subject matter. In its discussion of the case law, the court carefully points out which of those cases actually adjudicate such issues and which merely address them through dicta.

Provided below is a brief discussion of the patent statute, 35 U.S.C. §101, and the most germane cases on which the *Myriad* court relied in forming its understanding of the relevant law. For the sake of accuracy, the court's language is liberally quoted wherever appropriate.

The patent statute

Section 101 provides that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."[19]

Applicable case law

As the Supreme Court has acknowledged, statutory subject matter "includes anything under the sun that is made by man."[20] However, "[t]he laws of nature, physical phenomena, and abstract ideas have been held not patentable."[21]

In *American Fruit Growers v. Brogdex*,[22] the Supreme Court held that fruit whose skin was treated with borax to make it mold-resistant was not patentable subject matter. "Acknowledging that the 'complete article is not found in nature,' and 'treatment, labor and manipulation' went into producing the fruit, the [Supreme] Court nonetheless held that the fruit did not become an 'article of manufacture' unless it 'possesses a new or distinctive form, quality or property' compared to the naturally occurring article."[23] That is, "[t]here must be transformation; a new and different article must emerge having a distinctive name, character, or use."[24] In *American Fruit Growers*, the Supreme Court determined that there was "no change in the name, appearance, or general character of the fruit. It remains a fresh orange, fit only for the same beneficial uses as theretofore."[25]

In *Funk Brothers v. Kalo*,[26] the Supreme Court held that a non-synergistic mixture of several naturally occurring bacterial cultures was not patentable subject matter. The invention was based on the discovery that these particular cultures could be combined without any of the cultures in the mixture inhibiting the function of the other cultures. In support of its decision, the Court deemed the bacterial mixture a manifestation of laws of nature, and stated that such "manifestations . . . [are] free to all men and reserved exclusively to none."[27]

Diamond v. Chakrabarty involved a patent application claiming a *Pseudomonas* bacterium genetically engineered to break down elements of crude oil, and hence useful in cleaning up oil spills. Specifically, the *Pseudomonas* bacterium had plasmids (i.e., circular, gene-carrying molecules of DNA found naturally in some bacteria) introduced into it from other bacteria. These plasmids, which are not naturally found in *Pseudomonas*, confer oil degradation abilities on the engineered bacterium. The Supreme Court held that this genetically modified organism is patent-eligible subject matter, in that the invention is "a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use.' "[28]

American Fruit Growers, Funk Brothers, and *Chakrabarty* are relied on in *Myriad* to establish the general standard for patent eligibility. None of these cases, however, addresses the question of whether a naturally occurring compound, once isolated, is patentable subject matter.

---

[18]cDNA encoding *BRCA1/2* does not exist in nature, unlike genomic DNA encoding *BRCA1/2*, which does.

[19]35 U.S.C. §101.

[20]*Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980)(quoting S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952); H.R. Rep. No. 1979, 82d Cong., 2d Sess., 6 (1952)).

[21]*Id.* at 309.

[22]*Am. Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1 (1931).

[23]*Myriad*, 2010 WL at *36 (quoting *Am. Fruit Growers*, 283 U.S. at 11).

[24]*Am. Fruit Growers*, 283 U.S. at 12-13 (quoting *Anheuser-Busch Brewing Ass'n v. United States*, 207 U.S. 556, 562 (1908)(internal citation and quotation marks omitted)).

[25]*Id.* at 12.

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

[27]*Id.* at 130.

[28]*Chakrabarty*, 447 U.S. at 309-10 (quoting *Hartranft v. Wiegermann*, 121 U.S. 609, 615 (1887)).

Myriad cited *Parke-Davis v. Mulford*[29] to support its position that isolating a naturally occurring compound renders it patent-eligible. This decision, by Judge Learned Hand, relates to the patenting of an isolated form of adrenaline, a naturally occurring biological compound. However, as the *Myriad* court correctly pointed out, the question adjudicated in *Parke-Davis* was one of novelty, not patentable subject matter. The language in *Parke-Davis* relating to patentable subject matter, and relied on by Myriad, is therefore dicta.

Myriad also discussed the lower court decision *Merck v. Olin Mathieson*,[30] whose facts closely parallel those of *Myriad*:

> In *Merck*, the Fourth Circuit considered the validity of a patent claiming a Vitamin B_{12} composition useful for treating pernicious anemia. *Id.* at 157. Although naturally occurring Vitamin B_{12} produced in cows had known therapeutic properties and was commercially available, the court found the purified B_{12} composition, which was obtained from a microorganism, patentable. In upholding the validity of the patent, the court held [that . . . 'Each] slight step in purification does not produce a new product. What is gained may be the old product, but with a greater degree of purity. . . .'[31]

However, the *Merck* court went on to state that "[t]he fact . . . that a new and useful product is the result of processes of extraction, concentration and purification of natural materials does *not* defeat its patentability."[32] (emphasis added).

According to the *Myriad* court, "*Merck* . . . is entirely consistent with the principle set forth in *Funk Brothers* and *American Fruit Growers* that something derived from a product of nature must 'possess a new or distinctive form, quality, or property' in order to become patentable subject matter."[33]

> Because the court concluded that the purified B_{12} was more than a "mere advance in the degree of purity of a known product," it determined that the claimed invention was entitled to patent protection.[34] "[M]ere purification of known materials does not result in a patentable product," unless "the product obtained in such a case had properties and characteristics which were different in kind from those of the known product rather than in degree."[35]

The *Myriad* court neatly summed up its understanding of the law of patentable subject matter as follows: "the clear line of Supreme Court precedent and accompanying lower court authorities . . . establishes that purification of a product of nature, *without more*, cannot transform it into patentable subject matter. Rather, the purified product must possess '*markedly different characteristics*' in order to satisfy the requirements of § 101."[36] (emphasis added).

THE *MYRIAD* COURT'S ANALYSIS

As Judge Sweet's own synopsis of the law makes clear, a purified product of nature *can indeed* satisfy the requirements of §101, provided it possesses characteristics markedly different than those of the non-purified product.[37]

The *Myriad* court therefore addressed the question of whether the isolated *BRCA1/2* genes possess characteristics markedly different than those of the genes in their non-isolated state, and held that they do not.[38] For the reasons that follow, it is the author's position that in reaching this conclusion, the *Myriad* court did not properly apply existing law. Instead, the court invoked a new and troubling doctrine of exclusion unique to DNA.

The court did not properly apply existing law

"[T]he Federal Circuit has expressly held that '[i]n the final analysis under §101, the claimed invention, *as a whole*, must be evaluated for what it is' "[39] (emphasis added).

Myriad's claimed invention is an *isolated* DNA coding for *BRCA1* or *BRCA2*. This invention, *as a whole*,

---

[29] *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95 (S.D.N.Y. 1911), *aff'd*, 196 F. 496 (2d Cir. 1912).

[30] *Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958).

[31] *Myriad*, 2010 WL at *40-1 (quoting *Merck*, 253 F.2d at 163).

[32] *Merck*, 253 F.2d at 164.

[33] *Myriad*, 2010 WL at *40 (quoting *Am. Fruit Growers*, 283 U.S. at 11).

[34] *Id.* at *41 (citing *Merck*, 253 F.2d at 164).

[35] *Id.* at *37 (quoting *In re Merz*, 97 F.2d 599, 601 (C.C.P.A. 1935)).

[36] *Id.* at *41.

[37] To quote again from Judge Sweet's summary, "the purified product must possess 'markedly different characteristics' in order to satisfy the requirements of §101." This "markedly different" threshold has been phrased in different ways by different courts (e.g., "new or distinctive form, quality, or property" (*American Fruit Growers*, 283 U.S. at 11) and "properties and characteristics which [are] different in kind" (*Merz*, 97 F.2d at 601)).

[38] In this article, the author's remarks concerning the court's analysis based on the "markedly different characteristics" standard would be equally appropriate under the more permissive "distinctive name, character or use" standard articulated in *Chakrabarty*.

[39] *Myriad*, 2010 WL at *42 (quoting *In re Grams*, 888 F.2d 835, 839 (Fed. Cir. 1989)(quoting *In re Abele*, 684 F.2d 902, 907 (C.C.P.A. 1982))).

functions in ways not possible for *BRCA1/2*-coding DNA when that DNA is in its natural state—i.e., as part of a chromosome. For example, Myriad's DNA can function as "molecular diagnostic tests (e.g., as probes, primers, templates for sequencing reactions), in biotechnological processes (e.g., production of pure *BRCA1* and *BRCA2* protein), and even in medical treatments (e.g., gene therapy)."[40] The claimed DNA—by virtue of its isolated form—plays a vital role in medicine. The *BRCA1/2* genes, in their non-isolated form, can do no such thing despite having nucleotide sequences in common with the claimed DNA. As a result, the claimed DNA differs from its non-isolated counterpart not only in its purity, but also in its considerable value as a diagnostic tool.

As already noted, the facts of *Myriad* parallel those of *Merck*, wherein a purified B_{12} composition having therapeutically superior properties was held to be patentable subject matter. The *Myriad* court deemed *Merck* "entirely consistent with the principle set forth in *Funk Brothers* and *American Fruit Growers*" regarding the threshold for patentable subject matter as applied to "something derived from a product of nature."[41]

Despite this parallel, the *Myriad* court rejected the notion that Myriad's isolated DNA is patent-eligible. The court did so abruptly and without rigorously applying existing case law. As the *Myriad* court stated,

> [t]he central premise of Myriad's argument that the claimed DNA is "markedly different" from DNA found in nature is the assertion that "[i]solated DNA molecules should be treated no differently than other chemical compounds for patent eligibility," Myriad Br. at 26, and that the alleged "differences in the structural and functional properties of isolated DNA" render the claimed DNA patentable subject matter, Myriad Br. at 31. . . . Myriad's focus on the chemical nature of DNA, however, fails to acknowledge the *unique characteristics* of DNA that differentiate it from other chemical compounds.[42] (emphasis added).

The court created a new doctrine of exclusion unique to DNA

Integral to the *Myriad* court's ruling is its understanding of DNA's unique physical properties and its view that these properties somehow mandate special treatment of Myriad's invention under §101. The following excerpts from Judge Sweet's opinion convey the essence of the court's reasoning on this point.

> As Myriad's expert . . . observed: "Genes are of [a] double nature: On the one hand, they are chemical substances or molecules. On the other hand, they are physical carriers of information; i.e., where the actual biological function of this information is coding for proteins . . ." . . . This informational quality is unique among the chemical compounds found in our bodies, and it would be erroneous to view DNA as "no different[]" than other chemicals previously the subject of patents.[43]
>
> . . .
>
> DNA, and in particular the ordering of its nucleotides, . . . serves as the physical embodiment of laws of nature—those that define the construction of the human body. Any "information" that may be embodied by adrenaline [in reference to the invention in *Parke v. Davis*] and similar molecules serves no comparable function . . . Consequently, the use of simple analogies comparing DNA with chemical compounds previously the subject of patents cannot replace consideration of the distinctive characteristics of DNA.[44]
>
> . . .
>
> In light of DNA's unique qualities as a physical embodiment of information, none of the structural and functional differences cited by Myriad between native *BRCA1/2* DNA and the isolated *BRCA1/2* DNA claimed in the patents-in-suit render the claimed DNA "markedly different." . . . The preservation of this defining characteristic of DNA in its native and isolated forms mandates the conclusion that the challenged composition claims are directed to unpatentable products of nature.[45]

In essence, the *Myriad* court makes two related points. First, DNA has "unique characteristics" that differentiate it from other compounds, in that DNA is both a molecule *and* a physical carrier of information. Second, and in that regard, DNA is a "physical embodiment of laws of nature,"[46] and thus, in the court's opinion, the purity and medical advantages of the claimed DNA somehow fail to qualify as markedly different characteristics.

---

[40] *Id.* at *44 (citing Myriad Reply at 9).
[41] *Id.* at *40.
[42] *Id.* at *41.
[43] *Id.*
[44] *Id.* at *42.
[45] *Id.*
[46] The *Myriad* court also refers to DNA as a "physical embodiment of information."

Importantly, the *Myriad* court cites no basis in statute or case law for relying on DNA's unique features to reach its holding of invalidity. Instead of adhering to the Supreme Court decisions and other case law it so thoroughly explores, the *Myriad* court appears to fashion a new doctrine that neatly exempts isolated DNA from patentable subject matter. It is unclear to the author how this doctrine is justified.

DNA's "unique" role as a carrier of information is *in addition to*—and *not instead of*—its status as a molecule. As a molecule, it can be extracted from its native chromosomal environment and isolated. Moreover, the resulting isolated DNA has vital uses that the native DNA does not—and cannot—have because of its placement within a chromosome. The fact that DNA serves as a carrier of information does not negate its properties as a molecule that can be isolated—like vitamin B_{12}—and thereby rendered medically useful. That is, the fact that both isolated and native DNA function according to their nucleotide sequences does not negate DNA's status as an isolatable molecule falling within the scope of §101. The *Myriad* court does not explain how, in view of the case law, isolated DNA's "informational" role mandates treating it as something other than a patent-eligible molecule.

As for the court's point that DNA is a physical embodiment of the laws of nature, it is unclear how this distinction is limited to DNA, as opposed to any other biomolecule. Every isolated naturally occurring biomolecule such as a protein, a carbohydrate, a vitamin, or an organic compound such as taxol[47] can properly be thought of as a physical embodiment of the laws of nature.

Regardless, it is unclear how isolated DNA, by being a "physical embodiment of the laws of nature," loses its status as a patent-eligible molecule. As a corollary, it is unclear why DNA and vitamin B_{12}—which are *both* naturally occurring biomolecules and physical embodiments of the laws of nature—should be treated differently once isolated.

Unfortunately, the *Myriad* court does not explain how an isolated DNA's role as a carrier of information and a "physical embodiment of the laws of nature" trumps its status as a molecule that can be isolated and made medically useful. Absent such explanation, it is unclear how removing isolated DNA from patent eligibility is appropriate.

CONCLUSION

The court in *Myriad* held that isolated *BRCA1/2* genes are not patentable subject matter, regardless of their clinical value. Accordingly, the court held Myriad's gene claims invalid for failing to satisfy §101 of the patent statute. It is the author's position that in doing so, the court did not properly apply existing law. Instead, it relied on what appears to be a new and problematic doctrine excluding isolated DNA from the realm of patent-eligible subject matter.

---

[47]Taxol (known generically as paclitaxel) is a naturally occurring and widely used anti-cancer drug sold under the trademark TAXOL®.