Gene patents at the Supreme Court: Association for Molecular Pathology v. Myriad Genetics

Ashish M. Bakshi*

Harvard Law School

*Corresponding author. E-mail: abakshi@jd15.law.harvard.edu

INTRODUCTION

In June 2013, the Supreme Court unanimously decided Assn. for Molecular Pathology v. Myriad Genetics Inc., ruling that isolated naturally occurring sequences of genomic DNA (gDNA) cannot be patented. The Court left open the possibility of patenting complementary DNA (cDNA)—synthetic DNA containing the same protein-coding information as a segment of natural DNA but omitting non-coding portions called introns—and novel methods of manipulating genes or applying the information contained therein.¹ Myriad is thus likely to trigger a series of follow-on suits to clarify the holding.

Myriad’s patents covered the precise location and sequence of two human genes, BRCA1 and BRCA2, mutations of which have been linked to breast² and ovarian³ cancer.⁴ Myriad began as a suit filed by medical researchers, cancer patients, advocacy groups, doctors, and the American Civil Liberties Union, aiming to invalidate Myriad’s patents on (1) BRCA1, BRCA2, and their associated cDNA, and (2) methods for testing drug efficacy and interpreting genetic test outputs by analyzing DNA sequences for BRCA mutations. Myriad held a patent-protected monopoly in U.S. screening tests targeting the genes.

¹ Ass’n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 186 L. Ed. 2d 124 (2013).
² American Cancer Association, Breast Cancer: Early Detection, http://www.cancer.org/cancer/breastcancer/moreinformation/breastcancerearlydetection/breast-cancer-early-detection-pdf (updated 24 October 2013).
³ American Cancer Association, Ovarian Cancer, http://www.cancer.org/cancer/ovariancancer/detailedguide/ovarian-cancer-pdf23 (updated 21 March 2013).
⁴ Myriad, 133 S. Ct., at 2110–1.
DNA SEQUENCE CLAIMS

The Federal District Court for the Southern District of New York granted the plaintiff's summary judgment, rejecting all of Myriad’s DNA sequence and method patents at issue.5 Judge Robert W. Sweet applied the ‘markedly different’ test from Diamond v. Chakrabarty, which determined the patentability of genetically modified organisms based on their degree of difference from organisms found in nature.6 The Court highlighted ‘the overriding importance of DNA’s nucleotide sequence to both its natural biological function as well as the utility associated with DNA in its isolated form’ and DNA’s ‘unique qualities as a physical embodiment of information’.7 This meant that while isolated genes may be chemically different from natural DNA, their encoded information covering a naturally occurring nucleotide sequence rendered them ‘unpatentable products of nature’8 under § 101 of the Patent Act, which defines patentable subject matter as a ‘process, machine, manufacture, or composition of matter.’9 The ‘laws of nature, physical phenomena, and abstract ideas have been held not patentable’ under § 101.10

The Court of Appeals for the Federal Circuit reversed.11 The three-judge panel ruled unanimously that cDNA was patentable12 and split 2–1 in favor of isolated gDNA patents. Former chemist Judge Alan Lourie’s lead opinion also applied the Chakrabarty ‘markedly different’ test, holding that since chemical bonds in natural DNA must be broken to isolate a gene, isolated gDNA does not exist in nature and is thus patentable.13 Judge Kimberly Moore, a former electrical engineer, agreed but on grounds that short isolated gDNA sequences had ‘new and distinct’ uses, and that the biotechnology industry had ‘settled expectations’ after decades of being issued gDNA patents by the U.S. Patent and Trademark Office (USPTO). Dissenting, Judge William Bryson agreed with the District Court, highlighting that genes’ function is to encode proteins, so isolation is an irrelevant distinction.14

The Supreme Court granted certiorari only on a single question: ‘Are human genes patentable?’15 In a short opinion written by Justice Thomas, the Court unanimously ruled that isolated gDNA does not constitute patentable subject matter under § 101, holding that ‘a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but that cDNA is patent eligible because it is not naturally occurring.’16 Myriad, the Court held, did not create or alter the

5 Ass’n for Molecular Pathology v. U.S. Patent and Trademark Office, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) aff’d in part, rev’d in part, 653 F.3d 1329 (Fed. Cir. 2011) cert. granted, judgment vacated sub nom. Myriad, 132 S. Ct. 1794, 182 L. Ed. 2d 613 (U.S. 2012) and opinion vacated, appeal reinstated, 467 F. App’x 890 (Fed. Cir. 2012) and aff’d in part, rev’d in part, 689 F.3d 1303 (Fed. Cir. 2012) aff’d in part, rev’d in part sub nom. Myriad, supra note 1.
6 Diamond v. Chakrabarty, 447 U.S. 303, 100 S. Ct. 2204, 65 L. Ed. 2d 496 (1980).
7 Myriad, 702 F. Supp., at 229.
8 Id.
9 35 U.S.C.A. § 101.
10 Diamond v. Chakrabarty, supra note 6, at 309.
11 Ass’n for Molecular Pathology, 689 F.3d 1303 (Fed. Cir. 2012) cert. granted in part, 133 S. Ct. 694, 184 L. Ed. 2d 496 (U.S. 2012) and aff’d in part, rev’d in part sub nom. Myriad, supra note 1.
12 Id.
13 Id. at 1329.
14 Id. at 1341–4.
15 Myriad, 133 S. Ct. 694, 184 L. Ed. 2d 496 (2012).
16 Myriad, 133 S. Ct., at 2111.
information coded in BRCA1 or BRCA2, nor did it create or alter the DNA’s structure; it simply located and sequenced the genes.\footnote{Id. at 2116.} The Court stressed that Myriad had ‘found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention’.\footnote{Id. at 2117.}

The ruling thus invalidates every isolated gDNA patent crafted like Myriad’s gDNA claim: ‘an isolated DNA coding for [a particular protein]’.\footnote{Id. at 2113.} The Court held, however, that cDNA claims do meet the § 101 patentable subject matter threshold, because cDNA is not a ‘product of nature’.\footnote{Id. at 2119.}

**METHOD CLAIMS**

The Federal Circuit held that Myriad’s methods of analyzing sequences for mutations were not patentable, but its methods of screening potential cancer drugs were.\footnote{Ass’n for Molecular Pathology, 689 F.3d, at 1348–58.} In addressing only Myriad’s product patent claims, the Supreme Court let this decision stand. In 2012, the Court had decided *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, addressing the patentability of Prometheus’ biotherapeutic method claims under § 101.\footnote{Mayo Collaborative Services v. Prometheus Laboratories, Inc., 132 S. Ct. 1289, 182 L. Ed. 2d 321 (2012).} The Court held unanimously that claims to laws of nature fail under § 101, while claims to specific applications of laws of nature pass.\footnote{Id. at 1294.} The Federal Circuit’s method claim ruling in *Myriad* thus builds on *Prometheus*.\footnote{Ass’n for Molecular Pathology, 689 F.3d, at 1340.}

**IMPLICATIONS**

Myriad has downplayed the impact of the Supreme Court’s decision on its business, pointing out that most of its BRCA patents remain valid, including cDNA and many method patents. Further, several of the invalidated patents were to expire in 2014 in any case, and in announcing its expansion in Europe—where its patents had already been narrowed significantly\footnote{See, eg, Philippa Brice, *Myriad European BRCA1 Patent Upheld in Amended Form*, PHG Foundation (26 November 2008), http://www.phgfoundation.org/news/4412/ (last accessed 26 February 2014).} or compulsorily licensed\footnote{See E. Richard Gold & Julia Carbone, *Myriad Genetics: In the Eye of the Policy Storm*, 12 Genet. Med. S39 (April 2010).}—Myriad focused on the competitive advantage presented by its internal database of DNA sequences and associated patient outcomes developed over its two decades as the exclusive BRCA1/2 test provider.\footnote{Morningstar, *Myriad Genetics, Inc. Q2 2011 Earnings Call Transcript* (27 January 2011).} As a result, Myriad deemed just 3% of its test results ‘variants of unknown significance’ (VUS)—small mutations whose impact is uncertain—compared to competitors’ 20%.\footnote{Robert Cook-Deegan, John M. Conley, James P. Evans & Daniel Vorhaus, *The Next Controversy in Genetic Testing: Clinical Data as Trade Secrets?* 21 Eur. J. Hum. Genet. S85 (2013).}

Myriad’s patient database strategy highlights one potential effect of the Court’s invalidation of gDNA patents: genetic testing patent owners could turn to trade
secrets as an alternative to product patents. Myriad used to contribute VUS data to the National Human Genome Research Institute’s open-access Breast Cancer Information Core (BIC) mutation database, publicizing its contributions. Faced with patent challenges abroad and the specter of domestic competition, Myriad ceased contributing VUS data into BIC and peer-reviewed journals. This essentially ‘perpetuates Myriad’s exclusivity even after the expiration of its patent rights’ and has real clinical implications: ‘a woman might be able to receive BRCA testing from another laboratory in Malawi or Malta, where Myriad’s BRCA patent rights are not in force and testing is perfectly legal, but that laboratory will have no access to Myriad’s data and will thus be unable to interpret many VUS results’. While such asymmetry is common in health care, here it is based on the unavailability not of drugs or equipment but rather of ‘basic scientific and medical information’ that would be difficult to independently replicate without Myriad’s scale.

Critics of gene patents argue that exclusively licensed gene patents harm scientific research and patients’ interests. A March 2013 study found that the almost 40,000 U.S. patents on DNA sequences covered 41–100% (depending on type of analysis) of the human genome, including a single patent whose sequences matched at least 15 nucleotides of 91.5% of all known human genes. A report on gene patents by the Department of Health and Human Services Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) stated that disease-linked genes not under exclusive control attracted an ecosystem of laboratories innovating on quality and price; by contrast, sole providers—patent holders with exclusive license-enabled monopolies on testing, such as Myriad for BRCA—faced no competitive pressures and tended to limit availability of testing to patients. Beyond high pricing, the exclusive licensees did not accept specific payers, like state Medicaid, and preempted independent second-opinion testing. The report concluded that ‘the substantial number of existing patents on genes and methods of diagnosis also pose a threat to the development of multiplex testing, parallel sequencing, and whole-genome sequencing, the areas of genetic testing with the greatest potential future benefits’.

In the Leahy–Smith America Invents Act of 2011, Congress directed the USPTO to issue a report by June 2012 on gene

---

29 See Id.
30 See, eg, Rusconi E. William, Patenting and Licensing of the Breast Cancer Susceptibility Genes BRCA1 and BRCA2 (11 February 2005), http://www.genome.duke.edu/centers/cpg/case-histories/clinical-genetic-testing/documents/NAS%20Patents%20and%20BRCA%202-11-2005%20(2).pdf (last accessed 26 February 2014).
31 Cook-Deegan et al., supra note 28, at 586; Brief of Amici Curiae Christopher M. Holman and Robert Cook-Deegan in Support of Neither Party, at 27, Myriad, 2010 WL 4853323 (C.A.Fed.).
32 Cook-Deegan et al., supra note 28, at 586.
33 Id.
34 Jeffrey A. Rosenfeld & Christopher E. Mason, Pervasive Sequence Patents Cover the Entire Human Genome, Genome Med., Mar. 2013, at 3.
35 Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests, Report of the Secretary’s Advisory Committee on Genetics, Health, and Society, Apr. 2010.
36 Id.
37 Id. at 3.
38 Leahy–Smith America Invents Act, Pub. L. No. 112–29, 125 Stat. 284, 338 (2011).
diagnostic testing, independent second-opinion testing, exclusive licensing, and the impact of gene patents, but the USPTO has not yet delivered its report.\(^{39}\)

To the extent that *Myriad* enables other providers to enter the BRCA testing market, the decision could address some of the SACGHS report’s concerns. Immediately after the ruling, however, Ambry Genetics and Gene by Gene Ltd. launched cancer screening tests to compete with Myriad’s, and the original patent owners—led by Myriad—promptly sued both firms in early July 2013.\(^{40}\) Myriad alleged infringement of 10 other patents not at issue in the original suit, covering synthetic primes, probes, arrays, and methods of testing the BRCA1 and BRCA2 genes. Thus, exclusive licensees’ remaining cDNA and method patents mean that *Myriad* may not actually enable new entrants to offer genetic tests formerly covered by isolated gDNA patents.

*Myriad* enables scientists to work freely with isolated gDNA, but the prospect of patent infringement may not have universally been an issue of great concern among scientists or physicians in any case. By Myriad’s count, some 18,000 researchers published 8000 papers from BRCA1/2-related studies conducted after Myriad’s gDNA patents were issued.\(^{41}\) In March 2013, months before *Myriad*, the American College of Medical Genetics and Genomics issued a much-awaited report, republished in its official journal in July 2013.\(^{42}\) The report recommends that all genetic analysis laboratories should at minimum always test 57 specified genes, including BRCA1 and BRCA2, regardless of what test the patient ordered.\(^{43}\) In advising its members, the leading body of geneticists’ only mention of the patent infringement risk reads, ‘We also did not address issues of patents in making these recommendations’.\(^{44}\) Many of the *Myriad* plaintiffs, though, were researchers sued or otherwise compelled by Myriad to stop testing for BRCA genes.

**LEGAL IMPLICATIONS**

While *Myriad*’s impact in expanding access to gene testing may be blunted by remaining cDNA and method claims under \(\S\) 101, a 2009 Federal Circuit decision, *In re Kubin*, may have the opposite effect.\(^{45}\) Beyond the \(\S\) 101 test at issue in *Myriad*, any DNA claims still have to meet the other patentability requirements: novelty (\(\S\) 102),\(^{46}\) nonobviousness (\(\S\) 103),\(^{47}\) and sufficiently explicit description (\(\S\) 112).\(^{48}\) In *Kubin*, the Court set a stricter standard for the \(\S\) 103 requirement, holding that significant existing knowledge about the (1) protein coded by a gene and (2) techniques necessary for isolating and sequencing the gene makes the gene itself unpatentably obvious.\(^{49}\) Under the

---

\(^{39}\) U.S. Patent and Trademark Office, AIA Studies and Reports, http://www.uspto.gov/aia’implementation/aia’studies’reports.jsp (accessed 25 February 2014).

\(^{40}\) Myriad Genetics, Inc. et al. v. Ambry Genetics Corporation, No. 2:13-CV-00640 RJS (D. Utah filed 9 July 2013); Myriad Genetics, Inc. et al. v. Gene by Gene Ltd., No. 2:13-CV-00643-EJF (D. Utah filed 10 July 2013).

\(^{41}\) Brief for Respondents, at 10, Myriad, 2013 WL 860315 (U.S.).

\(^{42}\) R. C. Green et al., ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing (Mar. 2013), reprinted in 15 Genet. Med. 565 (2013).

\(^{43}\) Id. at 570–71.

\(^{44}\) Id. at 569.

\(^{45}\) In re Kubin, 561 F.3d 1351 (Fed. Cir. 2009).

\(^{46}\) 35 U.S.C.A. \(\S\) 102.

\(^{47}\) 35 U.S.C.A. \(\S\) 103.

\(^{48}\) 35 U.S.C.A. \(\S\) 112.

\(^{49}\) Id.
Kubin standard, many of the isolated single-gene gDNA patents struck down by Myriad might have already been invalid. Even claims allowed under § 101 by Myriad (eg cDNA) may be more difficult to gain post-Kubin. Looking forward, ‘next-generation’ whole-genome sequencing technologies do not target single isolated genes and thus may entirely sidestep the isolated gDNA patents at issue in Myriad.

The Court noted that its decision in Myriad did not address method claims, ‘new applications of knowledge’ about genes, or ‘the patentability of DNA in which the order of naturally occurring nucleotides has been altered’. Still, Myriad’s logic could have effects outside the Court’s intended scope; lower courts, for instance, could apply Myriad to product patents for isolated biological materials like cell lines and proteins. Indeed, at a recent hearing, a Federal Circuit panel indicated that the Court ‘made it clear in Myriad [that] genetic identicality is off the table’, meaning that not only are cloned animals likely unpatentable, as at issue there, but also potentially stem cell lines, as argued by plaintiffs in another pending Federal Circuit case.

A NEED FOR JUDICIAL SPECIALIZATION?

Beyond its merits, Myriad showcases Judge Learned Hand’s comments on American patent law in Parke-Davis, ‘calling attention to the extraordinary condition of the law which makes it possible for a man without any knowledge of even the rudiments of chemistry to pass upon such questions as these. The inordinate expense of time is the least of the resulting evils.' The Supreme Court Justices deciding Myriad lacked scientific experience, could rely on no fact-finding hearings, and in oral argument struggled to analogize gene isolation to everyday objects, yet were tasked with setting the future path for an extremely broad set of biomedical advances. Justice Scalia issued a concurrence underscoring his inability to understand on ‘[his] own knowledge or even [his] own belief’, the ‘fine details of molecular biology’ at hand. Unsurprisingly, one commentator likened the first part of the Myriad decision, describing basic genetics, to ‘an earnest seventh grader’s book report’.

---

50 See eg, Joanne Kwan, A Nail in the Coffin for Gene Patents, 25 Berkeley Tech. L. J. 9 (2014); James B. Monroe & Lawrence L. Ilag, Obviousness of DNA Fragments in the Post-Kubin Era, LIFE SCIENCES INTELLECTUAL PROPERTY REVIEW, 30 April 2013.
51 See W. Nicholson Price II, Unblocked Future: Why Gene Patents Won’t Hinder Whole Genome Sequencing and Personalized Medicine, 33 Cardozo L. Rev. 1601 (2012); Christopher M. Holman, Will Gene Patents Derail the Next-Generation of Genetic Technologies?: A Reassessment of the Evidence Suggests Not, 80 UMKC L. Rev. 563 (2012).
52 Myriad, 133 S. Ct., at 2119–20.
53 Michael A. Swit, Two Federal Appeals Court Proceedings May Impact Patent and Regulatory Strategies for Developers of Stem Cell Technologies, Lexology, 11 February 2014.
54 Id.
55 Hank Greely, Myriad Decision Invoked in Appeal of Suit to Invalidate Embryonic Stem Cell Patent Claims, Stanford Law and Biosciences Blog (4 July 2013), http://blogs.law.stanford.edu/lawandbiosciences/2013/07/04/myriad-decision-invoked-in-appeal-of-suit-to-invalidate-embryonic-stem-cell-patent-claims/(last accessed 26 February 2014).
56 Parke-Davis & Co. v. H. K. Mulford Co., 189 F. 95, 115 (C.C.S.D.N.Y. 1911) aff’d in part, rev’d in part sub nom. Parke-Davis & Co., 196 F. 496 (2d Cir. 1912).
57 John Golden & William Sage, A Cure for Patent Pathology? The Supreme Court Reviews the Patentability of Human Genes, Health Affairs (7 December 2012).
58 Myriad, 133 S. Ct., at 2120.
59 Noam Prywes, The Supreme Court Has a Disturbingly Sketchy Understanding of Molecular Biology, SLATE, 14 June 2013.
Even at the semi-specialized Federal Circuit, which handles patent appeals from all U.S. jurisdictions, the three-judge panel lacked specific domain expertise, with some speculation that the judges’ experience in other scientific fields might have tilted their thinking. Yet over a century ago, Judge Hand had proposed ‘technical judges … who can intelligently pass upon the issues without blindly groping among testimony upon matters wholly out of their ken. How long … shall [we] continue to blunder along without the aid of unpartisan and authoritative scientific assistance in the administration of justice?’

While not much has changed in the century after Judge Hand’s suggestions with regard to judicial specialization, Myriad lays the groundwork for what has already become a dizzying array of lawsuits struggling to clarify the law on genetic product and method patents.

ACKNOWLEDGEMENTS

The JLB Editors-in-Chief wish to acknowledge Holly Lynch, JD, M. Bioethics, who coordinated the new development pieces in this issue. She considered proposals from Harvard Law School students, selected authors, provided feedback on outlines and drafts, and liaised with JLB.

60 Golden & Sage, supra note 57.
61 Parke-Davis & Co., 189 F., at 115.
62 At press time, Myriad itself is involved in at least six follow-on federal suits concerning BRCA1/2 alone; see e.g. Myriad Genetics, Inc. et al. v. Ambry Genetics Corporation, No. 2:13-CV-00640 RJS (D. Utah filed 9 July 2013); Myriad Genetics, Inc. et al. v. Gene by Gene Ltd., No. 2:13-CV-00643-EJF (D. Utah filed 10 July 2013); Quest Diagnostics, Inc. v. Myriad Genetics, Inc., No. 13-1587 (U.S. Dist. Ct., C.D. Cal., filed 10 October 2013); Myriad Genetics, Inc. et al. v. GeneDX, Inc., No. 2:13-CV-00954 TS (D. Utah filed 16 October 2013); Myriad Genetics, Inc. et al. v. Quest Diagnostics, Inc., No. 2:13-CV-00967 BSJ (D. Utah filed 22 October 2013); Myriad Genetics, Inc. et al. v. Invitae Corporation, No. 2:13-CV-01049-EFJ (D. Utah filed 25 November 2013).