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The Supreme Court Identifies Categories of Patent-Eligible and Patent-Ineligible DNA Sequences



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Perhaps no other Supreme Court case involving patent law has attracted as much public attention as *Association for Molecular Pathology v. Myriad Genetics Inc*[1]. In a June 13, 2013, opinion authored by Justice Clarence Thomas, the Court unanimously held that

> a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but cDNA[2] is patent eligible because it is not naturally occurring.[3]

This seemingly straightforward bright-line rule establishes that, contrary to the past practices of the U.S. Patent and Trademark Office ("USPTO"), a gene is not a "chemical compound, albeit a complex one."[4] Instead, DNA is identified primarily by its *sequence*, and after *Myriad*, those DNA sequences that occur in nature may not enjoy patent protection.

This article first provides context and background information for the *Myriad* decision, and then, after analyzing the Court's opinion, considers some open questions and potential implications of the decision for various stakeholders interested in biotechnology and genetic medicine.

I. Litigation History and Legal Framework

Myriad Genetics Inc. ("Myriad") is a company that focuses on genetic testing and offers several products designed to determine whether a patient possesses variants of known DNA sequences. Myriad offers genetic tests relating to BRCA1 and BRCA2 (together, "BRCA"), two human genes in which known mutations are associated with an elevated risk of developing breast and ovarian cancers.

Myriad is the exclusive licensee of several patents protecting its BRCA tests. In 2009, a group of various plaintiffs represented by the American Civil Liberties Union ("ACLU") and the Public Patent Foundation sued Myriad and the USPTO in the U.S. District Court for the Southern District of New York.[5] Plaintiffs sought a declaration that composition and method claims in seven patents covering Myriad's BRCA tests were invalid because they covered or preempted the use

[1] 133 S.Ct. 2107 (2013).

[2] "cDNA" stands for complementary DNA, which the Court characterized as "synthetic DNA created from mRNA" containing only exon sequences of genes. Op. at 3; *see id.* at 2-3 (presenting an overview of genes, DNA transcription to create messenger RNA ("mRNA"), and mRNA's translation to create proteins).

[3] Slip Op. at 1.

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[4] *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991).

[5] *Ass'n for Molecular Pathology v. U.S. Patent and Trademark Office*, 702 F. Supp. 2d 181, 189 (S.D.N.Y. 2010) ("*Myriad I*").

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of naturally occurring BRCA genes. Plaintiffs argued that the Supreme Court excluded products existing in nature from patent eligibility in its past decisions interpreting 35 U.S.C. § 101. Section 101 states:

> Whoever 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.

In *Diamond v. Chakrabarty*, the Court concluded that Congress intended Section 101 to be broad, permitting patenting for ''anything under the sun that is made by man.''[6] The Court identified certain exceptions, including ''products of nature,'' that, unlike ''human-made inventions,'' may not be patented.[7] But the Court confirmed that human intervention may create patent-eligible products having ''markedly different characteristics from [those] found in nature'' that are ''not nature's handiwork.''[8]

The district court in *Myriad I* granted summary judgment in Plaintiffs' favor, holding all claims at issue invalid under Section 101.[9] On appeal, the Federal Circuit reversed the invalidity finding as to certain composition claims covering isolated genomic DNA—a DNA segment cut from a chromosome—and cDNA—DNA created from mRNA in the laboratory using a particular enzyme. Applying its ''machine-or-transformation'' test for patent eligibility, the Federal Circuit held that those ''transformed'' DNA molecules (isolated DNA and cDNA) could be patented under Section 101 because they ''exist in a distinctive chemical form—as distinctive chemical molecules—from DNAs in the human body, *i.e.*, native DNA.''[10]

After holding that the Federal Circuit improperly relied on the machine-or-transformation test as an exclusive arbiter of patent eligibility under Section 101 in *Mayo Collaborative Servs. v. Prometheus Labs. Inc.*,[11] the Supreme Court granted the Myriad plaintiffs' certiorari petition, vacated the Federal Circuit's decision, and remanded the case for further consideration.[12]

On remand, the Federal Circuit, in a fractured decision, renewed its holding that claims directed to isolated DNA and cDNA were patent-eligible, because covalent bonds in those molecules had been severed.[13] Judge Kimberly A. Moore joined Judge Alan D. Lourie's opinion that isolated human genomic DNA could be patented, though expressed additional reasons for reaching that conclusion.[14] Judge William C. Bryson dissented, contending that isolated human genomic DNA is not patent-eligible simply by virtue of its isolation.[15] All three judges agreed, however, that cDNA was ''especially distinctive from natural DNA'' and therefore patent-eligible under Section 101.[16]

Plaintiffs filed a second petition for certiorari, requesting review of three questions, one of which the Court granted: ''Are human genes patentable?''[17] In addition to briefing by the parties, the Court sought the views of the Solicitor General on the question.

II. The Court's Decision—Isolated DNA: No; cDNA: Yes (Usually)

After announcing its holding regarding isolated DNA and cDNA, the Court's opinion provides some background scientific information related to the decision, including the structure and function of DNA and its organization into genes.[18] The Court's scientific discussion focuses almost exclusively on the narrow function of DNA corresponding to protein production.[19] This is interesting because, as discussed below, the Court's holding is not so limited.

Justice Antonin Scalia wrote separately without signing on to the Court's discussion of the ''fine details of molecular biology'' in the Court's opinion.[20] Justice Scalia instead affirmed ''that the portion of DNA isolated from its natural state sought to be patented is identical to that portion of the DNA in its natural state; and that complementary DNA (cDNA) is a synthetic creation not normally present in nature.''[21]

The opinion continues by discussing the various discoveries that led to the patents-in-suit and the claims before the Court relating to isolated DNA and cDNA sequences corresponding to the polypeptide coding region of BRCA genes, including genes with common mutations.[22] The Court observed that the claims at issue gave Myriad ''the exclusive right to isolate an individual's BRCA1 and BRCA2 genes (or any strand of 15 or more nucleotides within the genes)'' or to ''synthetically create BRCA cDNA.''[23] Noting that ''isolation is necessary to conduct genetic testing,'' the Court went on to summarize Myriad's enforcement activities that established it as the sole provider of BRCA testing, activities that precipitated this lawsuit.[24]

As for the application of Section 101, the Court reiterated its longstanding exception that ''naturally occurring things'' such as ''laws of nature, natural phenomena, and abstract ideas are not patentable.''[25] The Court explained that:

> without this exception, there would be considerable danger that the grant of patents would tie up the use of such tools and thereby inhibit future innovation premised upon them.[26]

Because ''all inventions at some level embody, use, reflect, rest upon, or apply'' these fundamental natural

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[6] 447 U.S. 303, 309 (1980) (internal citations and quotation marks omitted).
[7] *Id.* at 313.
[8] *Id.* at 310.
[9] *Myriad I*, 702 F. Supp. 2d at 221, 232.
[10] *Ass'n for Molecular Pathology v. U.S. Patent and Trademark Office*, 653 F.3d 1329, 1351 (Fed. Cir. 2011) (''*Myriad II*'').
[11] 566 U.S. ___, 132 S.Ct. 1289 (2012).
[12] *Ass'n for Molecular Pathology v. U.S. Patent and Trademark Office*, 566 U.S. ___, 132 S.Ct. 1794 (2012).
[13] *Ass'n for Molecular Pathology v. U.S. Patent and Trademark Office*, 689 F.3d 1303, 1328 (Fed. Cir. 2012) (''*Myriad III*'').
[14] *Id.* at 1337, 1341-43.
[15] *Id.* at 1348, 1354.
[16] *Id.* at 1329, 1333, 1337, 1348.
[17] *Ass'n for Molecular Pathology v. Myriad Genetics Inc.*, 568 U.S. ___, 133 S.Ct. 694 (2012).
[18] Slip Op. at 2-4.
[19] *Id.*
[20] Scalia, J., concurrence at 1.
[21] *Id.*
[22] Slip Op. at 4-6.
[23] Slip Op. at 6.
[24] *Id.*
[25] Slip Op. at 11 (citations omitted).
[26] *Id.* (citation and internal quotation marks omitted).

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principles, the Court analyzed Myriad's claims with an eye towards maintaining a:

> delicate balance between creating incentives that lead to creation, invention and discovery and impeding the flow of information that might permit, indeed spur, invention.[27]

Myriad's principal argument before the Court was that, under *Chakrabarty*, the human intervention of isolating the BRCA gene sequences from their native chromosomes could form the basis for a patent-eligible invention. The Court disagreed. Noting that the invention in *Chakrabarty* created a new bacterium ''with markedly different characteristics from any found in nature,'' the Court flatly declared that ''Myriad did not create anything.''[28] While Myriad may have identified ''an important and useful gene,'' simply ''separating that gene from its surrounding genetic material is not an act of invention.''[29] The Court held the isolated DNA sequence of Myriad's claims to be ''squarely within the law of nature exception'' to patent eligibility, and could not be ''new . . . composition of matter'' under Section 101.[30] In reaching this conclusion, the Court confirmed that ''[g]roundbreaking, innovative, or even brilliant discovery'' and ''extensive effort alone'' are insufficient to create patent-eligible subject matter.[31]

The Court also rejected Myriad's argument that cleaving chemical bonds creates a non-naturally occurring molecule. Myriad's position on the patent eligibility of ''isolated DNA'' was consistent with the long-standing practice of the Patent Office and the lower courts, which, for nearly 30 years, had maintained the validity of claims directed to isolated DNA.[32] The Court declined to defer to the Patent Office's past practice, noting that the United States argued that isolated DNA was not patent-eligible under Section 101.[33]

The Court concluded that ''Myriad's claims are simply not expressed in terms of chemical composition,'' but instead ''understandably focus on the genetic information'' encoded in the sequence.[34] As further support for its ''genetic not chemical'' reading of Myriad's claims, the Court observed that:

> a would-be infringer could arguably avoid at least Myriad's patent claims on entire genes . . . by isolating a DNA sequence that included both the BRCA1 or BRCA2 gene and one additional nucleotide pair.[35]

Although many might disagree with the Court's conclusion regarding infringement given the potential application of the doctrine of equivalents, its impact completely extinguishes the patent eligibility of isolated DNA as a unique chemical if that DNA molecule's sequence exists in nature.[36]

The Court concluded that cDNA sequences, on the other hand, are not naturally occurring. The Court rejected petitioners' argument that the actual sequences within the cDNA are a product of nature, and appeared satisfied that someone ''unquestionably creates something new when cDNA is made.''[37] On that basis, the Court held that ''cDNA is not a product of nature and is patent eligible under § 101,'' with the caveat that ''a short strand of cDNA may be indistinguishable from natural DNA,'' and not patent-eligible.[38]

The Court attempted to limit its opinion by reciting matters ''*not* implicated by this decision.''[39] The Court did not review any method claims, and noted:

> Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent.[40]

Although method claims were ''not at issue in this case,'' the Court characterized Myriad's processes as ''well understood by geneticists,'' implicitly casting doubt on any ''innovative method of manipulating genes'' Myriad could have invented and patented.[41] The Court pointed out that Myriad had other claims directed to ''applications'' of the BRCA gene sequences,[42] yet declined to comment on how those applications transformed sequences into patent-eligible subject matter.[43]

Finally, the Court expressed ''no opinion'' as to the patent eligibility of alterations to naturally occurring DNA sequences.[44] This last observation is interesting because, according to the Court's holding, naturally occurring DNA sequences are not patent-eligible and non-naturally occurring DNA sequences are patent-eligible. Under this rule, deliberately altered DNA sequences are patent-eligible under Section 101 if the alteration renders the sequence non-naturally occurring.

III. After *Myriad*—Where Does It End?

The *Myriad* opinion caps almost four years of litigation specifically designed to engage various communities and competing interests to debate whether human genetic information may be patented.[45] Although practitioners may disagree as to the immediate impact that the *Myriad* decision will have on affected areas of innovation, most would agree that we are left with fewer answers than questions.

The *Myriad* decision immediately ends the practice of treating DNA as ''a chemical compound, albeit a complex one'' when assessing patentability.[46] Before *Myriad*, a DNA molecule, like other chemicals, could be converted into a patentable composition of matter

[27] *Id.* (citation and internal quotation omitted).
[28] Slip Op. at 12 (citation omitted).
[29] Slip Op. at 12.
[30] Slip Op. at 13.
[31] Slip Op. at 12, 14.
[32] *See Myriad III*, 689 F.3d at 1333.
[33] Slip Op. at 16.
[34] Slip Op. at 14.
[35] Slip Op. at 15.
[36] Slip Op. at 1, 18 (holding that ''genes and the information they encode are not patent eligible under § 101 simply because they have been isolated from the surrounding genetic material'').
[37] Slip Op. at 17.
[38] *Id.*
[39] *Id.*
[40] *Id.*
[41] *Id.*
[42] *See Diamond v. Diehr*, 450 U.S. 175, 187 (1980).
[43] Slip Op. at 17-18.
[44] Slip Op. at 18.
[45] Press Release, ''ACLU, Gene Patents Stifle Patient Access to Medical Care and Critical Research'' (May 14, 2009) (available at http://www.aclu.org/free-speech-womens-rights/aclu-challenges-patents -breast-cancer-genes) (noting that ''the ACLU's lawsuit challenges the whole notion of gene patenting'').
[46] *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991); *see* Jon M. Harkness, *Dicta on Adrenalin(e): Myriad Problems with Learned Hand's Product-of-Nature*, 93 J. Pat. Trademark Office Society 363, 367 n.28 (2011) (citing law review articles discussing patentability of purified products of nature, including DNA).

through purification and isolation. The Patent Office's directives to patent examiners regarding patent eligibility have long confirmed this point—for example, in 2001:

> An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound.[47]

Isolation and purification as a key indicator of patent eligibility has a long history. In 1911, Judge Learned Hand held that an ''extracted product [of nature] without change'' ''was good ground for a patent'' because, after purification, ''it became for every practical purpose a new thing commercially and therapeutically.''[48] Later cases suggested that purified natural products could be patent-eligible if purification created a ''marked change in functionality.''[49]

But after *Myriad*, sequence alone establishes the patent eligibility of any given DNA sequence—only those sequences not existing in nature may be patented. This bright line makes DNA a very special chemical indeed. In fact, the Patent Office issued new rules for examination consistent with the *Myriad* decision later that day:

> As of today, naturally occurring nucleic acids are not patent eligible merely because they have been isolated. Examiners *should now reject product claims drawn solely to naturally occurring nucleic acids or fragments thereof, whether isolated or not,* as being ineligible subject matter under 35 U.S.C. § 101.[50]

Moreover, *Myriad* places no restriction on the genome in which a naturally occurring sequence may be found, meaning that any DNA sequence might be ineligible for patenting should it be found in any living organism.

Now that ''a naturally occurring DNA segment'' is excluded from patenting, the actual origin of a DNA segment—whether derived from a natural source or synthesized in the laboratory—is irrelevant to a patent eligibility analysis. The Court characterized cDNA as ''not naturally occurring,'' a conclusion that some may continue to dispute.[51] Nevertheless, the *Myriad* opinion is clear that cDNA is patent-eligible insofar as it is ''distinct'' and ''not a 'product of nature' ''; this distinctiveness is lost for those short strands of cDNA that are ''indistinguishable from natural DNA.''[52]

Myriad removes any significance to isolation, as a DNA sequence alone determines whether a particular DNA molecule is non-naturally occurring and eligible for patenting. This result is consistent with the Court's long-held view that labor alone is insufficient to create an article of manufacture that could be patent-eligible—''something more is necessary'':

> There must be a transformation; a new and different article must emerge having a distinctive name, character, or use.[53]

For this reason, simply adding ''borax to the rind of natural fruit'' was not a ''manufacture'' according to the patent laws, as there was ''no change in the name, appearance, or general character of the fruit.''[54] Later, in *Funk Bros. Co. v. Kalo Inoculant Co.*, the Court held that a simple mixture of different strains of bacteria retaining the natural properties of each strain was not patent eligible, because the bacterial species in the mixture merely ''serve the ends nature originally provided and act quite independently of any effort of the patentee.''[55]

A few years after *Funk Bros.*, in connection with the 1952 amendments to the Patent Act, Congress stated that a:

> person may have ''invented'' a machine or manufacture, which may include anything under the sun that is made by man, but it is not necessarily patentable under section 101 unless the conditions of the title are fulfilled.[56]

As discussed above, the Court confirmed Congress' intent in *Chakrabarty* when it held *bacteria* made at the hands of man to be markedly different and non-naturally occurring. As to the *sequences* present in the Chakrabarty bacterium, however, those originated from naturally occurring bacteria and were *not* markedly different. After *Myriad*, it is clear that those DNA sequences conferring bacteria with useful properties not occurring in nature could not themselves be patented, even though the actual manufactured bacteria might be patent-eligible like the strain created in *Chakrabarty*.

Perhaps then it was never proper to consider that ''anything'' under the sun that is made by man may be patented under Section 101. Rather, only those naturally occurring things actually transformed by man into another markedly different thing are products that are ''made.'' In *Mayo*, the Court established the scope of an inventive transformation for processes: claimed subject matter must ''add *enough*'' to naturally occurring correlations to ''qualify as patent-eligible processes that ap-

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[47] Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

[48] *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (C.C.S.D.N.Y. 1911) (citations omitted); *see also* Utility Examination Guidelines, 66 Fed. Reg. at 1093; *Myriad I*, 702 F. Supp. 2d at 224 (noting that Myriad's arguments relied heavily on Judge Hand's statement in *Parke-Davis*).

[49] *Myriad III*, 689 F.3d at 1354 (Bryson, J., dissenting) (citing several purification cases as employing an analysis consistent with *Chakrabarty*'s requirement for ''markedly different characteristics'').

[50] Memorandum from Andrew H. Hirschfeld, Deputy Commissioner for Patent Examination Policy, to Patent Examination Corps (June 13, 2013) (available at http://www.uspto.gov/patents/law/exam/myriad_20130613.pdf) (underlining in original).

[51] Slip Op. at 16 & n.8; *see also* Pet. Br. at 49-52.

[52] Slip Op. at 17; *see also* Brief for Amicus Curiae Eric S. Lander in Support of Neither Party at 4-5, *Ass'n for Molecular Pathology v. Myriad Genetics Inc.* (No. 12-398) (filed Jan. 31, 2013) (distinguishing ''non-natural DNA molecules'' from ''naturally occurring genomic DNA'').

[53] *American Fruit Growers Inc. v. Brogdex Co.*, 283 U.S. 1, 12-13 (1931) (internal quotation marks omitted).

[54] *Id.* at 11-12 (discussing a ''manufacture'' in the context of the tariff laws in *Hartranft v. Wiegmann*, 121 U.S. 609, 613, 615 (1887)).

[55] 333 U.S. 127, 131 (1948).

[56] H.R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952).

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ply natural laws.''[57] After *Myriad*, the same requirement for transformation now governs patent eligibility of naturally occurring DNA sequences. It stands to reason that the same transformation requirement exists for any naturally occurring product, perhaps establishing a bright-line rule precluding patent eligibility for any product of nature. It remains to be seen whether courts will reach this conclusion, but this argument has already been put before the Federal Circuit in the context of patents covering in vitro cultures of human embryonic stem cells.[58]

It is likely that the *Myriad* decision will impact the validity of patent claims beyond the relatively narrow question of patent-eligible subject matter under Section 101. Because the identity, functionality, and utility of a DNA molecule largely depend on its specific sequence, *Myriad* creates an argument that any application of a naturally occurring DNA sequence may be obvious, especially those processes ''well understood by geneticists at the time'' of the invention.[59] *Myriad*'s identification—in dicta—of an ''innovative method of manipulating genes'' as a potential point of patent eligibility raises the unsettling notion that patenting a new and useful invention based on a naturally occurring DNA sequence requires *additional* activity that is itself new in the art.[60]

IV. Conclusion

In *Myriad*, the Supreme Court at first blush delivered the straightforward, bright-line rule that the public demanded—naturally occurring DNA, like human genes, cannot be patented. The Court's rule does allow invention for synthetic DNA having a sequence that does not occur in nature. Additional interpretation from the lower courts will be needed to fully understand the contours of this seemingly simple recipe for patent eligibility of DNA.

In the meantime, claims directed to purified, separated, or isolated substances are vulnerable if those substances are essentially the same as found in nature. The Court's reasoning in *Myriad* strongly suggests that ''products of nature'' are not patent-eligible subject matter under Section 101 like other fundamental principles—''laws of nature, natural phenomena, or abstract ideas.''[61] It will be interesting to see how *Myriad* is applied in future analyses of patentable inventions.

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[57] *Mayo Collaborative Svcs. v. Prometheus Labs. Inc.*, 132 S.Ct. 1289, 1297 (2012) (emphasis in original).

[58] Opening Brief of Appellant at 13-15, *Consumer Watchdog v. Wisconsin Alumni Research Foundation*, No. 2013-1377 (Fed. Cir. July 2, 2013), ECF No. 12.

[59] Slip Op. at 17.

[60] *See* Slip Op. at 17.

[61] *Chakrabarty*, 447 U.S. at 313.