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U.S. Supreme Court Concludes That "Isolated" DNA Is Not Patent-Eligible But cDNA Is

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On June 13, 2013, the Supreme Court issued its decision in *Association for Molecular Pathology v. Myriad Genetics, Inc*., addressing the eligibility for patenting of certain kinds of DNA. The Court held that so-called "isolated" DNA is not eligible for patenting but that complementary DNA (cDNA) is.

A. Background

In most cells of the human body, there are 23 pairs of chromosomes, each comprising a DNA molecule containing sequences of millions of nucleotides. There are four kinds of nucleotides in DNA: adenine (A), thymine (T), cytosine (C), and guanine (G). A given sequence of these nucleotides in a chromosome constitutes a gene, and each gene controls a particular trait or function within the body. A human's 23 pairs of chromosomes contain approximately 22,000 genes. Changes in a sequence of nucleotides are called mutations. Some mutations are harmless; others can cause disease or increase the risk of disease.

About 20 years ago, scientists at Myriad Genetics, headquartered in Salt Lake City, discovered the location and sequence of the nucleotides for two genes, mutations of which can substantially increase the risks of breast and ovarian cancer. These genes are known as the "BRCA1" and "BRCA2" genes. They are located on chromosomes 17 and 13, and each is about 80,000 nucleotides long. This sequence of nucleotides can be severed from the chromosome to form a new molecule, referred to in this case as "isolated" DNA. The isolated DNA molecule formed in this fashion does have the same sequence of nucleotides as occurs naturally in the body, but it does not occur naturally in the body because—at the very least—the chemical structure at the ends of those nucleotides is different than in the body. Before Myriad's discovery, scientists knew that heredity played a role in establishing a risk for breast and ovarian cancer, but they did not know which genes were associated with those cancers. As a result, Myriad obtained patents covering an isolated DNA molecule with the BRCA1 or BRCA2 nucleotide sequences (or portions of those sequences), allowing Myriad to prevent others from "making" or "using" such isolated DNA molecules. *See* 35 U.S.C. §§ 154(a)(1), 271(a).

However, in order to determine whether someone has a harmful mutation in their BRCA1 or BRCA2 genes, it is necessary to determine the sequence of nucleotides in at least parts of those genes. And in order to determine that sequence, it is necessary—at least using current technology—to "isolate" the DNA corresponding to that sequence. The plaintiffs in this case wished to provide genetic testing without paying for Myriad's genetic test but viewed Myriad's patents as precluding this activity, and therefore sought to have those patents declared invalid.

B. Eligibility of Isolated DNA

Congress has declared 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 other conditions and requirements of the patent laws, such as novelty and non-obviousness. 35 U.S.C. § 101. There can be no question that isolated DNA is a "composition of

matter." However, the Supreme Court has created three exceptions, holding that "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." In 2001, the U.S. Patent and Trademark Office (USPTO) issued guidelines observing that isolated DNA was not naturally occurring and therefore concluding that it did not fall within the Supreme Court's exception prohibiting the patenting of "natural phenomena." Justice Thomas's opinion for the Court acknowledged that isolating a particular strand of DNA creates "a nonnaturally occurring molecule," but concluded that the isolated DNA still does violate the prohibition against patenting "natural phenomena." The Court observed that "[t]he location and order of the nucleotides existed in nature before Myriad found them" and concluded that merely "separating that gene from its surrounding genetic material" was insufficient. The Court found it significant that the claims in Myriad's patents are "not expressed in terms of chemical composition" but "focus on the genetic information encoded in the BRCA1 and BRCA2 genes," demonstrating that its claim "is concerned primarily with the information contained in the genetic sequence, not with the specific chemical composition of a particular molecule." In effect, the Court concluded that isolated DNA is different from naturally occurring DNA but not different enough to be eligible for patenting.

C. Eligibility of Complementary DNA (cDNA)

The Court's opinion also addressed the eligibility of complementary DNA (cDNA). A few additional facts are required to understand the structure of cDNA. When the body uses its natural DNA, the DNA helix unwinds into two separate strands, and the body uses one of the DNA strands to create a complementary "pre-RNA" strand. The pre-RNA strand is considered "complementary" because it is like an inverted "mirror image" of the DNA. In each location that the DNA has a cytosine (C) nucleotide, the pre-RNA will have a guanine (G) nucleotide instead, and everywhere the DNA has a guanine (G) nucleotide, the pre-RNA will have a cytosine (C) nucleotide. Similarly, everywhere the DNA strand has an adenine (A) nucleotide, the pre-RNA will instead have a uracil (U) nucleotide, and everywhere the DNA has a thymine (T) nucleotide, the pre-RNA will have an adenine (A) nucleotide. After creating this pre-RNA molecule, the body then removes certain sequences of nucleotides from it and splices together the remaining nucleotides. The nucleotide sequences that are removed are called "introns," and the nucleotides sequences that remain are called "exons." The exons-only strand is called "messenger RNA" (mRNA). The body then uses the mRNA as a blueprint for producing proteins. Complementary DNA (cDNA) is created in the laboratory as a strand that is "complementary" to the mRNA. In other words, in each location that the mRNA has a cytosine (C) nucleotide, the cDNA will have a guanine (G) nucleotide instead, and everywhere the mRNA has a guanine (G) nucleotide, the cDNA will have a cytosine (C) nucleotide. Similarly, everywhere the mRNA strand has an adenine (A) nucleotide, the cDNA will instead have a thymine (T) nucleotide, and everywhere the mRNA has a uracil (U) nucleotide, the cDNA will have an adenine (A) nucleotide. Thus, the sequence of nucleotides in the cDNA are identical to the sequence of nucleotides in the natural DNA except that the cDNA does not have the nucleotides referred to as "introns." The introns can make up a significant percentage of a gene. Although the BRCA1 gene is about 80,000 nucleotides long, all but about 5,500 of those nucleotides are "introns." Likewise, the BRCA2 gene is about 80,000 nucleotides long, but all but about 10,200 of those nucleotides are "introns." In addition to its isolated DNA patents, Myriad obtained patents covering DNA molecules with the exon-only nucleotide sequences of the BRCA1 or BRCA2 genes (or portions of those sequences), *i.e.*, cDNA molecules for the BRCA1 or BRCA2 genes.

The Supreme Court held that Myriad's cDNA claims are patent-eligible. The plaintiffs argued that these claims should not be eligible because although the nucleotide sequence of cDNA is different from that of natural DNA, "[t]he nucleotide sequence of cDNA is *dictated by* nature, not by the lab technician." In other words, it is the body that determines what the exons are, and the only difference between natural

DNA and cDNA is the omission of the exons. The Court concluded that this fact was not sufficient to disqualify cDNA as a "natural phenomenon," explaining only that "the lab technician unquestionably creates something new when cDNA is made." This explanation leaves much to be desired because as the Court had previously recognized, the lab technician also creates something "nonnaturally occurring" (or "new") when isolated DNA is made, yet in that context the Court concluded that this fact was insufficient to confer eligibility. Perhaps the Court's reference to "something new" in this context is a reference to a *new sequence of nucleotides*. The Court suggests that this may be the case because its holding for cDNA is immediately followed by an exception when "very short series of DNA may have no intervening introns to remove when creating cDNA," in which situation "a short strand of cDNA maybe indistinguishable from natural DNA." Conspicuously absent from the Court's discussion of cDNA was any reference to its 2012 decision in *Mayo v. Prometheus*. Many expected the Court to conclude that *Mayo* required a finding of ineligibility because the process used to get from natural DNA to cDNA would have been well-known and conventional.

D. Conclusion

It remains to be seen what ramifications this decision will have going forward. As Myriad argued in its brief in opposition to the petition for certiorari, "the relevance of patenting isolated human DNA is ever diminishing in light of the publication of the entire human genome in 2001 . . . , thus presenting arguable bars to patentability under other provisions of the Patent Act (such as obviousness under § 103) for any claims to isolated human DNA molecules sought after that date." But it is possible that the Supreme Court's decision in this case could have consequences for the eligibility of purified and/or concentrated versions of naturally-occurring compounds. Significantly, the Court made a point of explaining that it was not addressing any method claims or any of Myriad's other claims directed to applications of its knowledge about the BRCA1 and BRCA2 genes. The Court also clarified that it was expressing no opinion on whether Myriad's cDNA claims would satisfy the other requirements for patentability such as novelty and nonobviousness.

The full text of Justice Thomas's opinion for the Court can be found at:

http://www.supremecourt.gov/opinions/12pdf/12-398_1b7d.pdf