

VIEWPOINT

The Future of Gene Patents and the Implications for Medicine

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On June 13, 2013, in *Association for Molecular Pathology v Myriad Genetics Inc*, the US Supreme Court unanimously ruled that naturally occurring genes cannot be patented. Synthetic transcripts of genes, however, can be patented.¹ The case involved patent claims covering *BRCA1* and *BRCA2*; mutations in these genes are linked to an increased risk for breast and ovarian cancer. Both sides quickly claimed victory. Harry Osterer, MD, a clinician and one of the plaintiffs, declared that the Court's decision would help society "feel more of the impact of the genomics revolution."² The Biotechnology Industry Organization claimed that the decision left intact patents on the synthetic transcripts, "the commercially most important form of DNA used in biotechnology."³ On the day the decision was announced, Myriad Genetics stock initially jumped 12% but finished down 6%. So what does this decision really mean, for both patent law and medicine?

The *Myriad* decision concerned one particular legal doctrine in patent law, termed "patentable subject matter" or "patent eligibility." Simply put, a patent can be granted only to someone who "invents or discovers" a "new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."⁴ Historically, courts and the US Patent and Trademark Office have interpreted these terms broadly to encompass "anything under the sun made by man." This has not included "laws of nature," "natural phenomena," "abstract ideas," or "products of nature."⁵ Yet, a famous 1911 lower court decision concluded that "products of nature" may constitute patentable subject matter if they were "isolated and purified" from their surroundings.⁶ Precisely what constitutes a "product of nature," or the propriety of this "isolated and purified" exception, has long been a puzzle. Nonetheless, human genes have been eligible for patent protection since at least 1982 under the theory that they were "isolated and purified" from their surrounding chromosomes. The *Myriad* case is the first time the Supreme Court addressed this practice.

In *Myriad*, the Court considered 2 types of patent claims for human genes. The first type covered "isolated genomic DNA," that is, DNA fragments of various sizes that have simply been removed from the surrounding genome. The second type were claims directed to "complementary DNA" (cDNA), specifically, reverse transcripts of messenger RNAs (mRNAs). The Court ruled that claims on isolated genomic DNA were not patent eligible—even if the genomic DNA were "isolated and purified" from the surrounding chromosome. Claims for cDNA, however, were patent eligible.

The Court's decision primarily focused on whether either type of DNA existed as such in nature. Because the Court viewed isolated genomic DNA as a stretch of DNA

simply excised from a larger chromosomal region, it concluded this was more like a "product of nature" than "a product of human ingenuity."¹ These DNAs did not have "a distinctive name, character [and] use," nor did they possess "markedly different characteristics from any found in nature."¹ Although the Court was careful not to negate Myriad's work in sequencing the *BRCA* genes, it declared that "separating [a] gene from its surrounding genetic material is not an act of invention" and that "[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy" patent eligibility. Under these circumstances, the Court was reluctant to extend the "isolated and purified" doctrine, despite its historical pedigree. Therefore, claims on isolated genomic DNA are now patent ineligible because they are "products of nature."¹

But cDNA does not exist, as such, in nature. Even though the "nucleotide sequence of cDNA is dictated by nature," in mRNA transcripts, "the lab technician unquestionably creates something new when cDNA is made," according to the Court.¹ Thus, claims on cDNA are potentially patentable, although, as the Court noted, other legal doctrines might still bar patenting of cDNA sequences in some cases. For example, patents covering cDNA sequences, although eligible for patent protection, might still not be patentable, if obvious or if previously disclosed elsewhere.

One result of *Myriad* is fairly clear: testing for *BRCA* genes should be cheaper. Within hours after the decision, several companies announced that they would offer *BRCA1* and *BRCA2* testing for much less than Myriad's then-current prices. Myriad has charged as much as \$4100 for full-sequence testing; some competitors have announced prices in the range of \$1000 to \$2200 for the same level of testing. These price declines will probably stick. Because Myriad's cDNA claims cover only testing methods that require the creation of cDNA, other companies will be able to compete with Myriad using newer sequencing technology that does not involve cDNA. (Myriad's claims for the method of assessing breast cancer risk based on *BRCA1* and *BRCA2* sequences were struck down at an earlier stage of the case.) Myriad will likely lower its prices for *BRCA* testing as it responds to the competition, although not without a fight; on July 10, 2013, Myriad sued one of its new *BRCA* testing competitors for patent infringement.

Yet, it remains to be seen just how much more widely available *BRCA* testing will be. Although Myriad no longer has a monopoly on sequencing the genes, it does have an extensive—and exclusive—database of its past customers' mutations. That database may help Myriad determine whether a patient with an unusual genetic variation has a higher risk of cancer or not, although patients with either wild-type *BRCA* sequences

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or well-known mutations will likely not need the added precision that the database can provide. In addition, others are actively trying to replicate Myriad's database of mutations.

What the *BRCA* testing landscape would have looked like if the Court had upheld all of Myriad's patent claims is unclear. The now-invalid claims for the most basic of Myriad's patents would have expired in February 2016, and new testing technologies might have produced *BRCA* tests that would not have infringed on those patents anyway.

What about the world beyond *BRCA*? Thousands of genes have been patented, and thousands of genetic tests are available, but almost no genetic tests have caused patent controversies. For example, the gene involved in Huntington disease, *HTT*, has long been patented, but there have been few complaints about Huntington's testing because the patents were either not asserted or licensed non-exclusively and on easy terms.⁷ The "gene patent problem" has been almost entirely a Myriad Genetics problem. Other firms that might have been tempted to enforce their gene patents aggressively would have confronted the same impending patent expirations and noninfringing technological advances that Myriad faces now. Thus, although the Court's decision brings some reassurance to those worried that hundreds of patents might be asserted against broad gene-sequencing technologies, that risk never seemed great. The end of Myriad's monopoly on *BRCA* testing is to be applauded, but the Court's decision is likely to have only have limited effects on genetic testing.

Will the *Myriad* decision chill investment in genetic research? Probably not. Fewer and fewer researchers have been receiving pat-

ents for isolated genomic DNA sequences. Many gene researchers are publicly funded, and many researchers are not substantially motivated by the potential for profits. Synthetically created, novel, nonobvious DNA sequences—important for purposes other than diagnostic testing, such as for creating recombinant biological products—are still eligible for patents, although it is not clear how important those patents might be. Nonetheless, some interpretations of the Court's decision might chill pharmaceutical research. If, for example, a drug company discovers a medically important molecule naturally produced by a fungus, the decision might prohibit the firm from patenting the molecule itself. But the company still should be able to patent medicinal uses of that molecule, as well as useful variations made in a laboratory. And, if the company shepherds that new chemical entity through FDA approval, the approval will include the exclusive right to sell the drug for 5 years.

In fact, on July 2, 2013, public interest organizations filed their brief in the appeal of their suit, *Consumer Watchdog v WARF*, to invalidate claims to human embryonic stem cells in patents of the Wisconsin Alumni Research Foundation. The appellate brief argues, among many other things, that the cells are "products of nature" and thus not patent eligible under the Myriad decision. It is not at all clear that those arguments will prevail, but it is more evidence that the decision will be good for the patent litigation business.

So what does the *Myriad* decision ultimately mean? In the short term, it means more competitive markets for diagnostic genetic testing, at least for testing for *BRCA1* and 2. But in the long term, probably not very much.

ARTICLE INFORMATION

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