AMP v. Myriad Genetics: the end of the beginning

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July 2013—The most remarkable fact about the June 13 decision of the Supreme Court in *Association for Molecular Pathology v. Myriad Genetics*, ___ U.S. ___ (2013), is that both sides are proclaiming victory. The physicians and geneticists who challenged efforts to enforce patents on the BRCA1 and BRCA2 genes are elated that the Court has squarely held that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated." (Opinion, at 1). Conversely, Myriad Genetics and its allies in the biotech community see themselves as having prevailed because the Court ruled that synthetically created DNA—or complementary DNA (cDNA)—"is patent eligible because it is not naturally occurring." *Id.*

So which side is right? In my opinion, it is far too early to tell. A host of issues remain to be played out in a variety of forums—the United States Patent and Trademark Office (PTO), the courts, Congress, and the negotiating table. This article examines three of these issues:

- The practical effects of the holding that genes and the information they encode are not patentable;
- The possible aftermath of the ruling that cDNA is patent eligible; and
- The patentability of methods used in genetic testing and next-generation sequencing, and the patentability of DNA that has been radiotagged or otherwise altered for use as probes or primers.

At this point, however, one conclusion seems clear: Contrary to what might at first blush appear, the Supreme Court has not replicated the long-lost DNA of King Solomon and announced a splitting of the baby that will produce a definitive resolution of the matters at issue.

Naturally occurring DNA

Of the two definitive holdings of the Supreme Court, the first is that extracted, native DNA cannot be patented. It is that holding that forms the basis of the claim to victory by the Association for Molecular Pathology and its co-plaintiffs. That claim is certainly justified in two respects. The position of the plaintiffs that no one can own human genes has been vindicated. Moreover, researchers and clinicians are now free to use naturally occurring DNA without fear of a patent infringement lawsuit.
But at least three issues must be of concern to those who side with the plaintiffs.

The first is the possibility of legislative modification of the decision. The relevant holding of the Court is that, under the Patent Act as currently written, naturally occurring DNA is not eligible for patent protection. There is nothing, however, to prevent the biotech industry from asking Congress to try to amend the Patent Act so as to permit the patenting of such DNA.

Indeed, the Supreme Court explicitly foresaw this possibility. Specifically, in its brief to the Court, Myriad Genetics noted that, in 2001, the PTO had stated that human genes are patentable—and that, in reliance on that pronouncement, hundreds of millions of dollars had been invested in genetic research. Myriad argued that the courts should not upset the reliance of the biotech industry through a judicial interpretation of the Patent Act that overturned the PTO position. This argument proved persuasive to at least one of the three judges of the Court of Appeals. (See *Assn. for Molecular Pathology v. U.S. P.T.O.*, 689 F.3d 1303, 1343-47 [Fed. Cir. 2012] [Moore, J., concurring].)

By contrast, the Supreme Court brushed off the reliance argument in a footnote (Opinion, at 16, n. 7):

> "Myriad also argues that we should uphold its patent so as not to disturb the reliance interests of patent holders like itself. Concerns about reliance interests arising from PTO determinations, insofar as they are relevant are better directed to Congress." (citations omitted)

Particularly given the statement by the Court that concerns about the reliance interests of holders of genetic patents "are better directed to Congress," it is quite possible that the fight over the patentability of isolated, native DNA will move from the courts to the legislature. And, of course, no one can predict how the issue might play out in Congress.

Second, an issue now arises regarding the impact of the Supreme Court's decision on existing licenses to use naturally occurring DNA. As just noted, the PTO had, for more than a decade, issued thousands of patents on extracted human genes. Moreover, the Federal Circuit had upheld these patents. Id. Faced with these facts and with the uncertainties and high costs of patent infringement litigation, some institutions took licenses under which they obligated themselves to pay royalties for the right to use genetic material on which a patent had been issued.

The holding of the Supreme Court that naturally occurring DNA is not patentable does not automatically invalidate these licenses. Rather, the continuing vitality of each such license depends on the specific wording of the document. Does the license contain a provision calling for termination if genetic patents are generally invalidated—as they were in Myriad Genetics? Does the license provide for termination in the event of invalidation of the specific patent? (For now, only the patents on the BRCA1 and BRCA2 genes have been specifically struck down). Or does the license make no provision for early termination?

The termination provisions of each license will have to be individually examined. The correct interpretation may be murky, particularly if a specific license includes rights to cDNA, methods of genetic testing, or other items whose status under the Patent Act is less than clear. In any event, insofar as the obligation to pay royalties under existing contracts survives the decision in Myriad Genetics, the goal of reducing the costs of genetic testing will, at least to some degree, be thwarted.

Third, and relatedly, to what extent will the decision of the Supreme Court actually result in fulfillment of the plaintiffs' hopes for lower cost, more accessible genetic testing? Here, it should be recalled that patents are not the only intellectual property in Myriad Genetics' arsenal. Specifically, over the many years in which it enforced its patents, Myriad gained an enormous amount of information about various mutations in the BRCA1 and BRCA2 genes—information that might be critical in identifying less common mutations.

Myriad is likely to take the position that, because of the potential diagnostic value of its data bank regarding these genes, that bank is a protectable trade secret that it will not share with any other diagnostic laboratory. Certainly, nothing in the recent decision speaks to the trade secrets issue. Thus, insofar as decisions are made to send specimens to Myriad because of Myriad's unrivaled database, the objective of reducing the cost of genetic testing may not be realized to the degree hoped for by the plaintiffs in the case. More generally, if the holders of patents on other genes have developed databases with significant diagnostic value, the decision in *Myriad Genetics* might not have the hoped-for effect of significantly reducing the costs of genetic testing.

cDNA

Just as plaintiffs cheered the holding that naturally occurring DNA is not patentable, Myriad Genetics and its allies found cause to rejoice in the ruling that cDNA is not naturally occurring and is, therefore, patent eligible—or, more accurately, is patent eligible unless it is a "very short series of DNA … [with] no intervening introns to remove." (Op. at 17). The biotech industry may see synthetic DNA as the hook to recapture the huge investment that has been made in mapping various genes and in other forms of genetic research. Once again, however, that result is by no means a foregone conclusion.

Notably, the conclusion that cDNA is not a product of nature and is therefore eligible for patent protection does not necessarily mean that patents on cDNA will be granted or enforced. Rather, to be enforceable, a patent must be the invention or discovery of the patent holder, 35 U.S.C. § 101, and must, *inter alia*, be both novel (*id.* at § 102) and non-obvious (*id.* at § 103). The battle will now shift, therefore, from patent eligibility to whether those who assert a patent have met the other tests for patentability.

Here, another footnote in the Supreme Court's recent decision may have ominous portent for the biotech industry. Specifically, in footnote 9 (Op. at 17), the Court stated as follows:

> "We express no opinion whether cDNA satisfies the other statutory requirements of patentability." (citations omitted)

The Court may not have expressed an opinion on whether cDNA will satisfy the other statutory requirements of patentability, but those who oppose genetic patents certainly will: They will undoubtedly argue that no patent on synthetic DNA can meet the other relevant requirements.

With respect to the BRCA1 and BRCA2 genes, the opponents of patentability will point out that there is considerable doubt as to whether Myriad Genetics was the sole entity that isolated and mapped those genes. (See *Assn. for Molecular Pathology v. US PTO*, 702 F. Supp. 2d, 181, 200-203 [S.D.N.Y. 2010] [describing the development of the Myriad patents].) More generally, opponents of patents on cDNA will argue that, once the nucleotide sequence of a gene is known, there is nothing novel or non-obvious in synthesizing the gene. Rather, they can be expected to assert that the gene can be synthesized by any knowledgeable researcher using well-understood laboratory techniques. Thus, while acknowledging the tremendous work and creativity involved in isolating and mapping any gene in the first instance, they will deny that there is anything patentable about synthesizing a gene once its sequence is identified. This sort of argument will simply have to work its way through the courts.

Moreover, the courts may not be the only battleground. This article has already pointed out that the biotech industry might well take the patentability issue to Congress. Similarly, the research and medical communities can equally make their case in Congress. And once the Pandora's box of patent protection for genetic discoveries and implementation of those discoveries is opened in the legislature, there is simply no telling what is ultimately going to come out.

Method patents and genetic alterations

Thus far, this article has dealt with the likely sequelae of the two issues that were explicitly addressed by the Supreme Court in *Myriad Genetics*. However, a number of issues that the Court did not confront are also relevant.

The first of these relates to method patents that cover diagnostic testing using isolated or synthesized genetic material. As Justice Thomas observed (Op. at 17), "there are no method claims before this Court." However, the Federal Circuit had previously invalidated several Myriad patents on methods for analyzing and comparing DNA sequences. (See *Assn. for Molecular Pathology v. U.S. P.T.O*, supra, 689 F.3d at 1333.) On the other hand, that Court upheld a Myriad patent on a method for screening potential cancer therapeutics via changes in growth rates of transformed cells where that method involved growing host cells transformed with an altered BRCA1 gene in the presence or absence of a potential cancer therapeutic. Id. at 1335–1336.

On the patentability of diagnostic methods using products of the human genome, the decision of the Supreme Court a year earlier in *Mayo Collaborative Services v. Prometheus Laboratories*, 132 S. Ct. 1289 (2012), is relevant. There the Court announced that, to be patentable, a method based on a law of nature has to "provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself." Id. at 1297. I anticipate considerable litigation in which courts will be called upon to draw the line between: 1) a method that involves nothing of substance beyond instructions to use an isolated gene in a diagnostic procedure (not patentable) and 2) a method that qualifies as a patent-eligible process for using the gene for diagnostic purposes (patentable).

In this connection, a memo to the Patent Examining Corps from Andrew H. Hirshfeld, deputy commissioner for patent examination policy, provides insight into the thinking of the PTO. Written on June 13, 2013—the same day as the Court issued its decision in *Myriad Genetics*, the memo instructs patent examiners at the PTO to "reject product claims drawn solely to naturally occurring nucleic acids or fragments thereof, whether isolated or not." But, the memo goes on to state that "(o)ther claims, including method claims that involve naturally occurring nucleic acids may give rise to eligibility issues and should be examined under the existing guidance in MPEP 2016, *Patent Subject Matter Eligibility.*" In other words, method claims will have to be evaluated on a case-by-case basis. Until there have been judicial decisions on the patentability of methods using extracted or synthesized DNA, it is too early to know whose claims of victory will turn out to be correct.

Two related questions are whether isolated DNA that has been radiolabeled for use as primers or probes—or isolated DNA that has had its nucleotide sequences altered—will be held to be patentable. The June 13 memo to the Patent Examining Corps suggests that at least the PTO considers such DNA to be patent eligible:

> "Claims clearly limited to non-naturally-occurring nucleic acids, such as a cDNA or a nucleic acid in which the order of the naturally-occurring nucleotides has been altered (e.g. a man-made variant sequence), remain eligible."

However, as the decision in *Myriad Genetics* confirms, the PTO is hardly the last word on these issues. Moreover, even if coded DNA or altered DNA sequences are deemed to be the work of human beings and therefore patent eligible, patents on these items may, or may not, survive scrutiny under tests for novelty and non-obviousness. Finally, as noted earlier, Congress may well intervene and craft a legislative resolution of these perplexing issues.

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In the final analysis, the words of Winston Churchill on Nov. 9, 1942 at the conclusion of the Battle of Egypt are equally fitting to describe the decision in *Association for Molecular Pathology v. Myriad Genetics:* "This is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning." The decision of the Supreme Court on June 13, 2013 is neither the end, nor even the beginning of the end, of the controversy over the patentability of discoveries and methods relating to the human genome. However, it is the end of the beginning. On the question of who will emerge victorious in that ongoing controversy, "the jury" is, as lawyers like to say, "still out." And it will, I suspect, be a long time before the verdict is in.

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