

BIOMEDICAL PATENTS AT THE SUPREME COURT: A PATH FORWARD

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While software patents and patent trolls dominate most patent discussions, the Supreme Court has focused on patents in the biotechnology and pharmaceutical space. In addition to deciding a number of antitrust cases involving such patents,¹ the Court has in the last two Terms decided two cases involving the subject matter eligibility of biopharmaceutical patent claims. In June 2013, the Court handed down a unanimous decision on DNA patenting, *Association for Molecular Pathology v. Myriad Genetics, Inc.*² The Court's decision in *Myriad* came on the heels of its unanimous decision a year earlier in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*³

In both *Mayo* and *Myriad*, the Court struck down patent claims associated with diagnostic medical practice. *Mayo* rejected method claims on measuring a thiopurine drug metabolite to adjust doses of a thiopurine drug. *Myriad* rejected claims to DNA that has merely been isolated (genomic DNA or gDNA)—such claims are typically associated with diagnostic medicine.

The Court's recent interest in diagnostic medicine patents comes after many years of heated public controversy over whether such patents pose an undue impediment to patient access as well as patient and physician autonomy. Notably, however, the policy analysis in *Mayo* and *Myriad* focuses on innovation. That focus is appropriate. Although access and autonomy are important

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1. Fed. Trade Comm'n v. Actavis, 133 S. Ct. 2223 (2013); Bowman v. Monsanto Co., 133 S. Ct. 1761 (2013).

2. 133 S. Ct. 2107 (2013). Although the result in *Myriad* was unanimous, the case resulted in two opinions: an opinion by Justice Thomas for the Court and an opinion by Justice Scalia concurring in part and concurring in the judgment. *Id.* at 2110.

3. 132 S. Ct. 1289 (2012).

goals, patent validity doctrines are a very blunt mechanism for promoting them. Antitrust law aggressive insurer bargaining over price and other conditions of access, and proposals for various infringement exemptions offer more tailored solutions.

While the Supreme Court's opinions rightly focus on innovation, they fall short in their efforts to prescribe *how* patent eligibility can be used to promote innovation goals. Critics have bemoaned the uncertainty created by the Court's decisions.⁴ The *Mayo* case in particular has prompted justifiable concern that its resuscitation of old, and long-criticized, approaches to subject matter eligibility will undermine the promise of personalized medicine.⁵ Against this background of negative reaction, I sketch a path forward for how *Mayo* and *Myriad* could be read through an innovation-focused lens.

INNOVATION AND THE COURT'S DECISIONS

Although the patent statute does not speak to the question, the Court has long held as a matter of common law that "abstract ideas," "laws of nature," and "products of nature" fall outside the realm of patent eligibility. On the other hand, the Court has also repeatedly warned (including in the *Mayo* case) that these categorical exemptions must be carefully deployed, since all inventions can be reduced to principles of nature.⁶ The Court therefore has the responsibility to articulate clearly how far its excluded categories extend, and equally important, *why* the categories are off limits.

In this regard, portions of the *Mayo* decision are quite problematic. The *Mayo* Court held that the claims at issue were invalid because they added only conventional activity to the natural law that individuals metabolize thiopurine drugs differently. In reaching this conclusion, the *Mayo* Court resuscitated a much-criticized 1978 case, *Parker v. Flook*,⁷ in which the Court had, for purposes of determining patent eligibility, dissected out the patent-ineligible "abstract idea" and then determined whether what remained was novel. The *Mayo* Court suggested the continuing viability of this "point of novelty" approach even though a 1981 case, *Diamond v. Diehr*,⁸ had disparaged the approach.

Fortunately, the result in *Myriad* could be seen as walking back this part of the *Mayo* case. Although the *Myriad* Court rejected gDNA claims, it affirmed claims to DNA with regions that don't code for a protein excised. Notably, this complementary or cDNA represents nothing more than the conventional appli-

4. See, e.g., Christopher M. Holman, *In Myriad the Supreme Court Has, Once Again, Increased the Uncertainty of U.S. Patent Law*, 32 BIOTECH. L. REP. 1, 1 (2013).

5. See, e.g., Rebecca S. Eisenberg, *Prometheus Rebound: Diagnostics, Nature, and Mathematical Algorithms*, 122 YALE L.J. ONLINE 341, 341 (2013), <http://yalelawjournal.org/2013/04/01/eisenberg.html>.

6. *Mayo*, 133 S. Ct. at 1304.

7. 437 U.S. 584 (1978).

8. 450 U.S. 175 (1981).

cation of routine laboratory techniques to a product of nature—chromosomal DNA.

Additionally, other portions of the *Mayo* opinion are more promising. Throughout the opinion, the Court did allude to policy considerations, most notably the possibility that claims on laws of nature, even claims that satisfied all requirements of patentability *other* than subject matter, could unduly “preempt” future research. In this context, it recognized arguments made by the patentee and by various academics⁹ regarding the importance of distinguishing broad laws that interfere with large areas of future innovation from narrower laws. After recognizing these arguments, the Court further acknowledged that the law of nature it was addressing—that individuals metabolize thiopurine-containing drugs differently—was in fact quite narrow. Unfortunately, the Court did not follow through on the promise of its reasoning. Instead, the Court insisted that it needed to enunciate a “bright-line prohibition” striking down all patents covering laws of nature, no matter how narrow.¹⁰

The patents affected by *Mayo* could include many that relate to the burgeoning field of personalized medicine. Personalized medicine revolves around “natural” associations between biomarkers such as DNA variations and patient prognosis or drug response. Like the association at issue in *Mayo*, personalized medicine associations typically cover narrow laws of nature. Unlike the association in *Mayo*, however, some of these associations may be quite difficult to find and validate clinically.¹¹ Although the Food and Drug Administration does not currently require such clinical validation in all cases, insurers are, quite justifiably, increasingly requiring validation.¹² Patents may be necessary to induce development of relevant evidence. On its face, then, *Mayo*’s reasoning is in tension with an economically oriented approach.

From the standpoint of those who care about innovation policy, all is not lost, however. In the context of conceding that the law of nature in question was narrow, the *Mayo* Court did emphasize the relatively trivial contribution made by the patentee. According to the Court, studies had already indicated that measurement of thiopurine metabolite level was important for predictions of efficacy.¹³ The patentee had simply quantified the precise correlation

9. See *Mayo*, 132 S. Ct. at 1301-02 (citing Mark A. Lemley et al., *Life After Bilski*, 63 STAN. L. REV. 1315 (2011)); see also Rochelle C. Dreyfuss & James P. Evans, *From Bilski Back to Benson: Preemption, Inventing Around, and the Case of Genetic Diagnostics*, 63 STAN. L. REV. 1349, 1371 (2011) (discussing problems raised by claims covering broad prospects that are difficult to invent around); cf. Kevin Emerson Collins, *Prometheus Laboratories, Mental Steps, and Printed Matter*, 50 HOUS. L. REV. 391, 429 (2012) (discussing use of patent eligibility as a filter against claims covering human cognition); Katherine J. Strandburg, *Much Ado About Preemption*, 50 HOUS. L. REV. 563, 585 (2012) (arguing that the Court’s cases have recognized *per se* exclusions that don’t involve broad claims).

10. *Mayo*, 132 S. Ct. at 1303.

11. See, e.g., Michael M. Hopkins & Stuart Hogarth, *Biomarker Patents for Diagnostics: Problem or Solution?*, 30 NATURE BIOTECH. 498, 499 (2012).

12. Kevin A. Schulman & Sean R. Tunis, *A Policy Approach to the Development of Diagnostic Tests*, 28 NATURE BIOTECH. 1157 (2010).

13. *Mayo*, 132 S. Ct. at 1295.

between metabolite levels and effectiveness. In contrast, certain advances in personalized medicine—for example, the development of tests that analyze the expression of multiple genes in a tumor sample as a guide to prognosis and future treatment—could be distinguished as much more complex than the simple laboratory test in *Mayo*. In other words, all diagnostic associations are not alike, and perhaps the reasoning in *Mayo* can be restricted to the simple category.

As with *Mayo*, portions of the *Myriad* decision are quite promising. In that case, which involved claims to two genes, BRCA1 and BRCA2, determined to be associated with breast cancer, the Court made the acute observation that Myriad's claims were deliberately drawn to be very difficult to invent around. Myriad claimed not “the specific chemical composition of a particular molecule” but, instead, the information “encoded in the BRCA1 and BRCA2 genes.”¹⁴

To be sure, the Court did uphold Myriad's cDNA claims, even though it viewed those as drawn to information as well. Moreover, the Court failed to enunciate *why* claims to information in the form of cDNA are less problematic than claims to information in the form of gDNA. This failure renders the opinion's own language much less useful to lower courts struggling to distinguish between different types of claims to information. Claims to information arise not only in the context of DNA and bioinformatics, but also in all contexts where data processing plays a major role. The Court could therefore have provided a blueprint not simply for the biopharmaceutical industry, but also to the many industries dependent on software. *Myriad* therefore represents a missed opportunity.

Nonetheless, lower courts could certainly read the Court's distinction between cDNA and gDNA through the economic lens invoked by the two amicus briefs that called the distinction to the attention of the Court—that of the Solicitor General and of the prominent geneticist Eric Lander.¹⁵ Both of these briefs emphasized that while gDNA claims could interfere with a broad range of downstream uses, cDNA claims had narrower application specific to therapeutic development and could be worked around for other purposes. Although patent lawyers typically view breadth as an issue to be addressed by sections of the patent statute other than section 101, in certain cases (including the case of some of the gDNA claims at issue in the *Myriad* case), these sections may not do the job as efficiently as section 101.

With gDNA patents now out of the picture, concerns that the platform technology of whole genome sequencing could be impeded by such patents are gone. Although some had argued that these patents would not have posed a ma-

14. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2118 (2013).

15. *See* Brief for Amicus Curiae Eric S. Lander in Support of Neither Party, *Myriad*, 133 S. Ct. 2107 (No. 12-398), 2013 WL 432959; Brief for the United States as Amicus Curiae in Support of Neither Party, *Myriad*, 133 S. Ct. 2107 (2013) (No. 12-398), 2013 WL 390999.

major obstacle,¹⁶ dissipating the shadow of infringement liability to the greatest extent possible was important for officials at the National Institutes of Health (NIH) and the U.S. Office of Science and Technology Policy. They successfully convinced the Solicitor General to reject the U.S. Patent and Trademark Office's long-held, but only lightly theorized, position of allowing claims on all "isolated" DNA molecules.

As it happens, NIH has a long history of helping to shape validity requirements in the context of DNA patents.¹⁷ NIH played that role again in the *Myriad* case. As with many areas of law, patent law in the area of DNA has been an example of "shared regulatory space."¹⁸

The day the opinion was announced, a number of firms stated that they would begin commercial testing for BRCA1 and BRCA2 mutations. Relying primarily on patents with method claims that have not thus far been challenged,¹⁹ Myriad has now sued two firms, Ambry Genetics and Gene-by-Gene.²⁰ The question of whether these method claims survive *Mayo* is an interesting one. Under the approach advanced here, these method claims should fail on patent eligibility grounds if they inevitably block broad areas of future research. For example, to the extent that Myriad's interpretation of its remaining claims would cover all whole exome sequencing (whole exome sequencing is similar to whole genome sequencing except that introns are not sequenced), such an interpretation should call into question patent eligibility under section 101.

Although Myriad has sued several firms, it has also formally announced for the first time that it will not sue noncommercial academic researchers.²¹ NIH, which funded a substantial portion of the research that led to Myriad's patents, could play a role in ensuring that promise is kept. NIH is a co-owner of certain patents that Myriad is currently asserting,²² and it may have funded research underlying some of the other patents. Both the terms of NIH co-ownership and the Bayh-Dole Act of 1980, under which government agencies have background rights in patents emerging from research they fund,²³ give NIH some

16. See Christopher M. Holman, *Debunking the Myth That Whole-Genome Sequencing Infringes Thousands of Gene Patents*, 30 NATURE BIOTECH. 240, 240 (2012).

17. See Arti K. Rai, *Patent Validity Across the Executive Branch: Ex Ante Foundations for Policy Development*, 61 DUKE L.J. 1237, 1249 (2012).

18. Cf. Jody Freeman & Jim Rossi, *Agency Coordination in Shared Regulatory Space*, 125 HARV. L. REV. 1131 (2012).

19. Myriad also relies on one claim (claim 6 of U.S. Patent No. 5,747,282 (filed June 7, 1995)) that was at issue in the Supreme Court case. However, this claim covers short DNA fragments that don't have introns excised and appears invalid under the reasoning of the Court's decision.

20. Andrew Pollack, *2 Competitors Sued by Genetics Company for Patent Infringement*, N.Y. TIMES, July 10, 2013, http://www.nytimes.com/2013/07/11/business/2-competitors-sued-by-genetics-company-for-patent-infringement.html?_r=0.

21. See *Myriad's Pledge to Our Patients and the Research Community*, MYRIAD, <http://www.myriad.com/responsibility/myriads-pledge> (last visited Oct. 10, 2013).

22. NIH is a co-owner of U.S. Patent No. 5,747,282 (filed June 7, 1995) and U.S. Patent No. 5,753,441 (Jan. 5, 1996).

23. 35 U.S.C. § 202 (2011).

leverage. Because U.S. patent law unfortunately lacks the type of formal research-use exemption that exists in many other countries, NIH's role in promoting innovation should not end with the Supreme Court decision.

BEYOND DIAGNOSTICS

For many in the biopharmaceutical industry, the concern raised by *Myriad* is not invalidation of gDNA patents, but instead unintended consequences for patents associated with therapeutic molecules. All therapeutic molecules require approval by the FDA, and most analysts agree that patents provide important incentives for expending the resources necessary to secure such approval.²⁴ The amicus briefs filed by the Solicitor General and Eric Lander specifically called for upholding cDNA claims typically associated with therapeutics.

Therapeutic products that could be affected include proteins and antibodies. Although many protein and antibody patents now claim molecules to which the "chemical changes" favored by the *Myriad* Court have been made, certain claims could be seen as encompassing naturally occurring molecules. Even in these cases, however, the claims wouldn't necessarily be invalid. Even when chemical changes are not claimed, the antibodies and proteins are nonetheless probably claimed as something closer to "specific chemical compositions" than to information. Lower courts could focus on this aspect of the *Myriad* opinion in upholding such claims. Similarly, in addressing patents covering small molecule chemicals with important therapeutic uses that have been isolated from nature,²⁵ courts could focus on the fact that these patents narrowly claim "specific chemical compositions."

CONCLUSION

Without a doubt, the Court's recent spate of activity in the area of patent eligibility and diagnostic patenting has caused considerable anxiety for those concerned about innovation. Ideally, the question of subject matter eligibility would have been addressed more fully decades earlier. At least on the reading advanced here, however, the Court's opinions may not pose the barrier to innovation that some fear.

24. That said, most protein and antibody therapeutics now enjoy a twelve-year period of regulatory protection from generic competition by virtue of the Biologics Price Competition and Innovation Act (incorporated as Title VII of the Patient Protection and Affordable Care Act). This regulatory exclusivity may provide an incentive at least as important as patent protection.

25. Many such molecules are listed in an amicus brief filed by the Biotechnology Industry Organization. Brief for Amicus Curiae the Biotechnology Indus. Org. in Support of Respondents at 26-28, *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013) (No. 12-398), 2013 WL 1209142.

