

Diagnostic Patents at the Supreme Court

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2013 ANNUAL HELEN WILSON NIES LECTURE

DIAGNOSTIC PATENTS AT THE SUPREME COURT

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INTRODUCTION

In June 2013, the United States Supreme Court handed down a highly anticipated decision on DNA patenting, *Association for Molecular Pathology v. Myriad Genetics, Inc.*¹ Overturning the determination reached by the U.S. Court of Appeals for the Federal Circuit, but in line with the position of the U.S. solicitor general, the Court distinguished between DNA that has merely been isolated (genomic DNA, or “gDNA”) and DNA that has non-protein-coding regions excised (complementary DNA, or “cDNA”).² The Court held that, while gDNA is a patent-ineligible “product of nature,” cDNA is patent-eligible.³ The upshot of the Court’s decision is that certain patents generally associated with diagnostic medicine (gDNA) are invalid, but patents typically associated with therapeutics (cDNA) are valid.

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.*⁴ In *Mayo*, the Court similarly overturned the Federal Circuit’s approach to deciding whether subject matter associated with diagnostic medical practice should be eligible for patenting.⁵ There the Court

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1. *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013).
2. *Id.* at 2119.
3. *Id.*
4. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012).
5. *Id.* at 1296, 1302.

struck down method claims on measuring a thiopurine drug metabolite to adjust doses of a thiopurine drug, stating that the claims in question merely added routine activity to the law of nature that individuals metabolize thiopurine drugs differently.⁶

The Court's recent interest in diagnostic patents comes after years of heated public controversy over whether such patents pose an impediment to patient access and control of medical decision making. This controversy encompasses, but is also broader than, the controversy over DNA patenting.

Some critics of the *Myriad* and *Mayo* decisions fear that the Court was improperly swayed by concerns over access and patient control. In this view, conventional among patent lawyers, validity doctrine exists to promote innovation—and only innovation. The *Myriad* case, involving patents on BRCA1 and BRCA2 genes associated with breast cancer,⁷ is particularly troubling, as the momentum behind the case was clearly driven in part by concerns unrelated to innovation.

At least some critics of the decisions might concede that patents were not essential for innovation in the specific factual scenarios raised by those cases. Even so, they would argue that the Court's decisions are likely to have unintended consequences in areas where patents are more necessary. These include not only therapeutics but also diagnostic research that is more complex, or less enmeshed in federal funding, than the research in *Myriad* and *Mayo*.

In line with the conventional frame, this essay agrees that interpretation of patentable subject matter and other validity doctrines should be guided by innovation goals. Although innovation and access cannot be entirely separated in the case of physician-researchers who also provide clinical care, the conceptual emphasis should be on innovation. Promoting access should rely not on validity doctrine but rather on the carefully calibrated tools of infringement exemptions that borrow from antitrust principles, from agency use of background government rights to persuade those who receive federal funding to engage in appropriate licensing practices, and from insurer bargaining over price.

Myriad and *Mayo* need not, however, be interpreted in a manner that is antithetical to innovation. This essay lays out a path forward from these cases that is compatible with innovation goals.

6. *Id.* at 1295.

7. *Myriad*, 133 S. Ct. at 2112.

I. INNOVATION, ACCESS, AND VALIDITY

As a historical matter, U.S. patent validity doctrine has focused on innovation. The Constitution's intellectual property provision, which discusses patents as promoting the "Progress of . . . useful Arts," puts the spotlight squarely on innovation.⁸ Moreover, although the Supreme Court has given Congress broad leeway to interpret this constitutional provision,⁹ U.S. patent legislation, unlike legislation in other jurisdictions (e.g., Europe),¹⁰ rarely imposes nonutilitarian limits on patent eligibility.

This historical focus is reinforced by functional considerations. As a functional matter, patent validity is a blunt and over-inclusive mechanism for policing concerns about access. In many cases where access concerns are raised, problems could be alleviated by the patent owner's being forced to adopt a different enforcement strategy. In the *Myriad* case, for example, one very significant complaint was Myriad's alleged use of its patent to deny women the option of a second opinion after having received Myriad's test.¹¹ In that situation, principles of patent exhaustion drawing upon antitrust law suggest that patients who have already given Myriad a monopoly profit by using its services should have the option of using another provider to get a second opinion. Conversely, providers who offer those second opinions shouldn't be liable for patent infringement. Efforts to create a safe harbor from infringement liability for second-opinion testing reflect these exhaustion principles.¹²

Additionally, in many diagnostic-testing cases, including *Myriad*, flows of public funding from the National Institutes of Health ("NIH") to universities were heavily involved in the research that led to patenting.¹³ In *Myriad* itself, the relevant university was the University of Utah.¹⁴ Unlike the University of Utah, most universities have endorsed, and tend to follow, norms for licensing

8. U.S. CONST. art. I, § 8, cl. 8.

9. See *Golan v. Holder*, 132 S. Ct. 873, 884, 887-889 (2012).

10. See generally Directive 98/44, of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions, 1998 O.J. (L 213) 13 (EC).

11. See *Myriad*, 133 S. Ct. at 2114.

12. See Dan Vorhaus, *House Introduces Patent Reform Proposal to Permit Second Opinions in Genetic Diagnostic Testing*, GENOMICS LAW REPORT (June 15, 2011), <http://www.genomicslawreport.com/index.php/2011/06/15/house-introduces-patent-reform-proposal-to-permit-second-opinions-in-genetic-diagnostic-testing>.

13. See SECRETARY'S ADVISORY COMM. ON GENETICS, HEALTH, AND SOCIETY, U.S. DEP'T OF HEALTH & HUM. SERVS., GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 28 (2010) [hereinafter SACGHS Report], available at http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_patents_report_2010.pdf.

14. SACGHS Report, *supra* note 13, at A-11.

diagnostic patents similar to those suggested by NIH.¹⁵ These norms include a recognition that exclusive licensing of diagnostic patents should be used primarily in those cases where substantial additional development associated with regulatory approval by the Food and Drug Administration (“FDA”) is needed and exclusivity will provide the economic motivation for such development.¹⁶

In cases like *Myriad*, where FDA regulatory approval did not need to be pursued (and was not pursued), the rationale for exclusive licensing is less clear. Moreover, even in cases of exclusive licensing, university norms endorse preserving the option of second-opinion testing and shielding physician-researchers from the threat of infringement liability. In this regard, the University of Utah and its exclusive licensee Myriad have been outliers. Outlier cases are not a reason to revise validity doctrine.

In addition, insurance carriers, private and public, can and should bargain with patent owners over conditions of access. The current reimbursement regime for diagnostics, in which insurers require proof of clinical efficacy before they provide coverage, may have limitations,¹⁷ but it gives insurers bargaining leverage. Notably, in other countries, purchasers have exercised bargaining power to promote access to diagnostic testing.¹⁸

After the Supreme Court’s decision, Myriad pledged formally for the first time that it would not assert its patents against noncommercial academic research.¹⁹ It also pledged that it would not interfere with the ability of patients to secure a second opinion.²⁰ Had institutions such as NIH, other universities, and insurers applied pressure earlier, Myriad might have been forced to make this pledge earlier.

II. INNOVATION AND THE COURT’S RECENT SUBJECT MATTER DECISIONS

Let us consider next the issue of innovation. Although critics are right to argue that the Court’s decisions on patentable subject matter should focus on innovation, they mistakenly suggest that the recent decisions must be read in a manner that hampers innovation substantially. The following discussion of

15. See *Nine Points to Consider in Licensing University Technology*, ASS’N OF UNIV. TECH. MANAGERS (March 6, 2007), http://www.autm.net/Nine_Points_to_consider.htm.

16. See *id.*

17. See Kevin A. Schulman & Sean R. Tunis, *A Policy Approach to the Development of Diagnostic Tests*, 28 NATURE BIOTECHNOLOGY 1157, 1158 (2010).

18. See generally E. Richard Gold & Julia Carbone, *Myriad Genetics: In the Eye of the Policy Storm*, 12(4) GENETICS IN MED. S39–S70 (April 2010).

19. *Myriad’s Pledge to Our Patients and the Research Community*, MYRIAD GENETICS, INC., <http://www.myriad.com/responsibility/myriads-pledge> (last visited Oct. 31, 2013).

20. *Id.*

Mayo and *Myriad* suggests how the decisions can be interpreted through an innovation-focused lens.

For many decades, the Court has repeatedly stated that “abstract ideas,” “laws of nature,” and “products of nature” categorically fall outside the realm of patentability. However, since many inventions could be seen as obvious applications of laws or products of nature,²¹ the Court has the responsibility to articulate what the categories mean and why they are off limits. Unfortunately, the Court’s decisions have often been quite unhelpful in this regard. Indeed, decisions such as *Funk Brothers Seed Co. v. Kalo Inoculant Co.* (1948)²² fail to clarify whether the Court is actually addressing eligible subject matter or is instead referring to some other validity requirement. The problem of precisely parsing the Court’s discussions is particularly acute for cases decided before the 1952 Patent Act,²³ which first codified the obviousness requirement. Unfortunately for the current Court, it must contend with this old precedent as it goes forward.

One obvious option would be to overrule or narrowly limit past precedent. Instead, in keeping with the Court’s general reluctance to declare prior decisions wrong, the Court’s recent decisions have, at least to some extent, tried to shape this past precedent into an economic, innovation-oriented framework.

The 2012 *Mayo* case shows both the promise and limitations of the Court’s efforts. In the opinion, the Court repeatedly focused on pragmatic consequences, most notably the possibility that claims on laws of nature—even claims that satisfied all requirements of patentability *other* than subject matter—could “preempt” future research.²⁴ It also recognized arguments made by the patentee and by various academics²⁵ that a pragmatic approach should distinguish broad laws of nature 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.²⁶

Unfortunately, the Court did not follow through on the promise of its

21. See Rebecca Eisenberg, *Wisdom of the Ages or Dead-Hand Control? Patentable Subject Matter for Diagnostic Methods After In re Bilski*, 3 CASE W. RES. J.L. TECH. & INTERNET 1, 46 (2012).

22. See *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948).

23. Patent Act of 1952, Pub. L. No. 82-593, 66 Stat. 792 (codified as amended in scattered sections of 35 U.S.C.).

24. *Mayo*, 132 S. Ct. at 1291-1292.

25. See Mark Lemley et al., *Life after Bilski*, 63 STAN. L. REV. 1315, 1334 (2011).

26. *Mayo*, 132 S. Ct. at 1302.

reasoning. Instead, it insisted that it needed to enunciate a “bright-line prohibition” striking down all patents covering laws of nature, no matter how narrow.²⁷ Although the Court invoked institutional-competence considerations, specifically the inability of the judiciary to distinguish between broad and narrow laws of nature,²⁸ it was likely mindful of the reality that prior case law had failed to draw such policy-laden distinctions.

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. In those cases, patents may be necessary to induce development of relevant evidence.²⁹ 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.³⁰ As the Court noted,³¹ the patent in question itself recognized that studies had already indicated that measurement of thiopurine metabolite level was important for predictions of efficacy. The patentee had simply quantified the precise correlation 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 test in *Mayo*. In other words, not all diagnostic associations are alike, and perhaps the reasoning in *Mayo* can be restricted to the simple category.

The Court’s reasoning and ultimate result in *Myriad* in 2013 can also be

27. *Id.* at 1303.

28. *Id.*

29. See Michael Hopkins & Stuart Hogarth, *Biomarker Patents for Diagnostics: Problem or Solution*, 30(6) NATURE BIOTECHNOLOGY 498, 499 (June 2012).

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

31. *Id.* at 1292 (citing U. S. Patent No. 6,355,623, col. 8, ll. 37–40, 2 App. 10. (“Previous studies suggested that measurement of 6-MP metabolite levels can be used to predict clinical efficacy and tolerance to azathioprine or 6-MP”) (citing Cuffari, Théorêt, Latour, & Seidman, 6-Mercaptopurine Metabolism in Crohn’s Disease: Correlation with Efficacy and Toxicity, 39 Gut 401 (1996)).

interpreted as tracking relevant economic considerations. Yet, as with *Mayo*, one's reading of the case has to be oriented in that direction.

In *Myriad*, the Court began by observing that under the “well-established” balance that patent law tries to strike between creating incentives for innovation and blocking future innovation, gDNA claims covering broad categories of information, rather than “the specific chemical composition of a particular molecule,” are suspect.³² Informational content is, however, only one factor in the calculus. Although the Court indicated that cDNA claims also cover information, it ultimately held that the removal of noncoding DNA makes cDNA molecules patent-eligible.³³

The Court's analysis 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 is significant and renders the opinion less useful as a stand-alone document. Nonetheless, lower courts could certainly read the Court's distinction through the economic lens invoked by the two amicus briefs that called the distinction to the Court's attention—those of the solicitor general and of the prominent geneticist Eric Lander.³⁴ 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.³⁵

With gDNA patents now out of the picture, concerns that the platform technology of whole genome sequencing could be impeded by such patents are now gone. Some have argued that these patents would not have posed a major obstacle.³⁶ But dissipating the shadow of infringement liability to the greatest extent possible was important for officials at 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 position, which allowed claims on “isolated” DNA molecules.

As it happens, NIH has a long history of helping to shape validity

32. *Myriad*, 133 S. Ct. at 2116, 2118-2119.

33. *Id.* at 2119-2120.

34. Brief for the U.S. as Amicus Curiae in Support of Neither Party, Ass'n for Molecular Pathology v. Myriad Genetics, 569 U.S. __ (2013) (No. 12-398), available at <http://www.justice.gov/osg/briefs/2012/3mer/1ami/2012-0398.mer.ami.pdf>; Brief for Amicus Curiae Eric S. Lander in Support of Neither Party, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. __ (2013) (No. 12-398), available at http://www.americanbar.org/content/dam/aba/publications/supreme_court_preview/briefs-v2/12-398_neither_amcu_lander.authcheckdam.pdf.

35. See Brief for the United States as Amicus Curiae in Support of Neither Party, *supra* note 31, at 9-11; Brief for Amicus Curiae Eric S. Lander in Support of Neither Party, *supra* note 31, at 27.

36. See Christopher Holman, *Debunking the Myth that Whole-Genome Sequencing Infringes Thousands of Gene Patents*, 30(3) NATURE BIOTECHNOLOGY 240 (March 2012).

requirements in the context of DNA patents.³⁷ Befitting its role as a research funder, its concerns have been innovation, not access. NIH played that role again in the *Myriad* case.

To be sure, the Court's decision may also weaken the diagnostic service monopoly model of firms such as Myriad, at least to the degree that this model relies on patents. The day the opinion was announced, Ambry Genetics, GeneDx, DNA Traits, Quest Diagnostics, and Pathway Genomics, as well as a number of academic institutions, stated that they would begin testing for BRCA1 and BRCA2 mutations.³⁸ That said, the opinion leaves Myriad room to sue on a variety of claims, particularly method claims, not at issue in the Supreme Court case. And Myriad has in fact sued several firms, including Ambry Genetics and Gene by Gene.³⁹

NIH, which appears to have funded research that led to at least some of the patents in the suits against Ambry and Gene by Gene, would be well-advised to track these lawsuits closely. Under the Bayh-Dole Act of 1980, agencies can force additional licensing of federally funded patents where such "action is necessary to alleviate health or safety needs which are not reasonably satisfied" by the federal grantee or its licensee.⁴⁰ In its briefing seeking a preliminary injunction, Myriad is making the perhaps counterintuitive argument that such relief would *promote* public health by prohibiting patients from using diagnostic laboratories that do not have its track record in interpreting mutations.⁴¹ If a court were to agree with these arguments (and of course agree with Myriad's argument that its claims are likely to be valid, also a contested proposition), NIH should consider counterarguments that the Myriad track record is not as unequivocally superior as the firm claims. If these arguments appear meritorious, NIH might evaluate whether licensing to other firms would promote Bayh-Dole's objectives with respect to health and safety. Even though NIH appears to have background rights in only some of the patents that are being asserted, even an incomplete stake might provide some leverage.

37. Arti K. Rai, *Patent Validity Across the Executive Branch: Ex Ante Foundations for Policy Development*, 61 DUKE L.J. 1237, 1241 (2012).

38. Arti K. Rai & Robert Cook-Deegan, *Moving Beyond "Isolated" Gene Patents*, 341 SCIENCE 137, 138 (12 July 2013).

39. See Univ. of Utah Research Found. v. Ambry Genetics Corp., No. 2:13-cv-00640-RJS (C.D. Utah July 9, 2013); Univ. of Utah Research Found. v. Gene by Gene, No. 2:13-cv-00643 (C.D. Utah July 10, 2013).

40. 35 U.S.C. § 203(a)(2).

41. See Plaintiff's Motion for Preliminary Injunctive Relief and Memorandum in Support at 40, Univ. of Utah Research Found. v. Ambry Genetics Corp., No. 2:13-cv-00640-RJS (C.D. Utah July 9, 2013).

III. 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. The amicus briefs filed by the solicitor general and Eric Lander called specifically for upholding cDNA claims typically associated with therapeutics.⁴²

Therapeutic products that could be affected include proteins and antibodies. Although many protein and antibody patents now claim molecules that are clearly synthetic, certain claims could be seen as encompassing naturally occurring molecules. Even in these cases, however, the claims would not necessarily be invalid. Presumably the antibodies and proteins would, in the words of the *Myriad* Court, be claimed as something closer to “specific chemical compositions” than to information.⁴³ 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,⁴⁴ courts could focus on the fact that these patents typically claim “specific chemical compositions.”

CONCLUSION

Without a doubt, the Court’s recent spate of activity in the area of diagnostic patenting has caused considerable anxiety for those concerned about innovation. To some extent, the anxiety is justified. But lower courts could choose to read the Court’s opinions in a manner that is friendly to innovation. This essay has attempted to provide a path forward for lower courts.

42. Brief for the United States as Amicus Curiae in Support of Neither Party, *supra* note 31, at 26; Brief for Amicus Curiae Eric S. Lander in Support of Neither Party, *supra* note 31, at 27.

43. *Myriad*, 133 S. Ct. at 2118.

44. Many such molecules are listed in an amicus brief filed by the Biotechnology Industry Organization. Brief for Amicus Curiae the Biotechnology Industry Organization in Support of Respondents at 20–21, *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. __ (2013) (No. 12-398), available at http://www.americanbar.org/content/dam/aba/publications/supreme_court_preview/briefs-v2/12-398_resp_amcu_bio.authcheckdam.pdf.