

THE SUPREME COURT’S *MYRIAD* EFFECTS ON SCIENTIFIC RESEARCH:
DEFINITIONAL FLUIDITY AND THE LEGAL CONSTRUCTION OF NATURE

Peter Lee
UC Davis School of Law

Contents

INTRODUCTION	1
PART I. THE IMPACT ON MYRIAD GENETICS AND BRCA RESEARCH	3
PART II. UPSTREAM-DOWNSTREAM DYNAMICS IN PATENT LAW	9
PART III. BROADER DOCTRINAL IMPLICATIONS	19
A. Elevating Patentable Subject Matter Doctrine to Police Patentability.....	19
B. Creating a Strong and Flexible Exception for Nature from Patent Eligibility	20
PART IV. ONGOING CHALLENGES AND LONG-TERM RAMIFICATIONS	28
CONCLUSION.....	31

INTRODUCTION

Although patent law rarely captures the popular imagination, such was not the case in the summer of 2013. That June, the Supreme Court issued its much-anticipated decision in *Association for Molecular Pathology v. Myriad Genetics*.¹ The decision culminated years of litigation over several patents held by Myriad Genetics, a Utah-based biotechnology company, covering two genes, BRCA 1 and BRCA 2. Mutations in these genes are correlated with a higher risk of developing breast and ovarian cancer. Based significantly on its patents, Myriad Genetics enjoyed exclusive rights on clinical genetic diagnostic tests related to these diseases. A consortium of plaintiffs, including medical research groups and women’s health advocates, challenged the validity of Myriad’s patents based concerns that patent exclusivity was increasing the cost of testing and decreasing valuable access to these genes. This Article explores one of the important implications of this decision, namely its impact on scientific research.

On its face, the case addressed the rather narrow technical issue of patentable subject matter, the threshold inquiry of what sort of *thing* is eligible for patenting.² Reversing decades of accepted legal practice, the Court held that isolated DNA, which is DNA that is separated from its genomic environment, is not patentable subject matter.³ However, the Court held that complementary DNA (“cDNA”), which is synthetically

¹ *Ass’n for Molecular Pathology v. Myriad Genetics Inc.*, 133 S.Ct. 2107 (2013)

² See 35 U.S.C. § 101 (stating that patentable subject matter encompasses “any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof”).

³ 133 S.Ct. at 2111.

created DNA that omits nucleotide sequences that do not code for proteins, is eligible for patenting.⁴ Beyond its rather technical holdings, however, the decision holds significant implications for public health, biotech commercialization, and research. Most policy, media, and popular attention has focused on the impact of “gene patents” on the availability of diagnostic tests for breast and ovarian cancer, a matter of high personal and political salience.⁵ Within this view, Myriad’s patents—including those covering isolated DNA corresponding to the BRCA 1 and BRCA 2 genes—gave the company exclusive rights to diagnostic tests for breast and ovarian cancer, which raised prices and decreased the availability of such tests. A significant background consideration throughout the litigation, however, focused on the impact of Myriad’s isolated DNA patents on biomedical research itself. Although less immediate than concerns over patient access to testing, the prospect of gene patents blocking research could have greater long-term ramifications. After all, inhibited research could retard the expansion of biological knowledge and the development of future diagnostics and therapeutics.

Indeed, the potential for isolated DNA patents to inhibit biomedical research was a significant issue in the *Myriad* litigation. Plaintiffs challenging Myriad’s patents argued that “[c]laims on isolated DNA impermissibly preempt scientific and medical work, far beyond what Myriad’s contributions can justify.”⁶ *Amici* challenging the patents, including the American Medical Association and the National Women’s Health Network, argued similarly.⁷ Concerns over the ability of patents to deter research also permeated lower court decisions in this case. At the trial court, the Southern District of New York noted the “deep disagreement” regarding the impact of Myriad’s patents on scientific progress.⁸ Such concerns also arose at the Federal Circuit. In a partial concurrence arguing that isolated DNA should not comprise patentable subject matter, Judge Bryson cited with approval Justice Breyer’s earlier statement in *Lab. Corp. of Am. Holdings v. Metabolite Labs Inc.* stating that sometimes “too much patent protection can impede rather than ‘promote the Progress of Science and Useful Arts.’”⁹

⁴ 133 S.Ct. at 2111.

⁵ E. Richard Gold & Julia Carbone, *Myriad Genetics: In the Eye of the Policy Storm*, 12 *Genetics in Med.* S39, S39 (“It is perhaps because of the high profile of breast cancer that this test, patented by Myriad, struck a chord among politicians and the public.”).

⁶ Brief for Petitioners, *Ass’n for Molecular Pathology v. Myriad Genetics Inc.*, Jan. 24, 2013, at 41 [hereinafter AMP Brief]; *id.* at 43 (“The effect of the patents has been to prevent and deter research.”).

⁷ See, e.g., Brief of Amici Curiae American Medical Association et al. in Support of Petitioners, *Ass’n for Molecular Pathology v. Myriad Genetics Inc.*, Jan. 29, 2013, at 13 (arguing that patents on isolated DNA impede both research and diagnosis) [hereinafter AMA Brief]; Brief of Amici Curiae the National Women’s Health Network et al. in Support of Petitioners, *Ass’n for Molecular Pathology v. Myriad Genetics Inc.*, Jan. 30, 2013, at 27 (“Myriad’s patents on the embodied information of the BRCA 1/2 genes inhibit important scientific work in biomedical research and treatment for breast and ovarian cancer....”) [hereinafter National Women’s Health Network Brief].

⁸ *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 702 F.Supp.2d 181, 207-11 (S.D.N.Y. 2010).

⁹ *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 653 F.3d 1329, 1380 (Fed. Cir. 2011) (Bryson, J., concurring in part and dissenting in part); Dianne Nicol, *Implications of DNA Patenting: Reviewing the Evidence*, 21 *J. L. Info. Sci.* 7, 28 (2011).

The question of *Myriad*'s impact on scientific research is a complicated one, and this Article argues that it depends significantly on context. This Article will examine this question on three different levels.¹⁰ Part I considers the decision's impact on Myriad Genetics itself and its enforcement (or nonenforcement) of its patents. Among other observations, it notes that debates in this context are plagued with definitional difficulties. For instance, terms such as "research" versus "commercial" uses of isolated DNA patents are rife with ambiguity, and one use often informs the other. This Article argues that Court's decision removes some of the real and perceived threat of enforcement actions by Myriad, thus increasing freedom to operate for biomedical scientists. Part II expands the perspective, drawing on the Supreme Court's holding to revisit a longstanding debate regarding the potential for patents to stymie research activities. Although empirical studies reveal little chilling and anticommons effects generally from patents on research inputs, a significant exception applies to diagnostics. Thus, the Court's invalidation of isolated DNA patents will provide greater access to important genetic research inputs beyond BRCA. Part III expands the perspective further and considers *Myriad*'s long-term doctrinal implications. It argues that the opinion reflects both a strong prudential interest in exempting "nature" from patentable subject matter as well as a remarkable degree of flexibility in defining nature for this purpose. A strong and flexible zone of nonpatentability for nature, moreover, may have significant implications for scientific research.

PART I. THE IMPACT ON MYRIAD GENETICS AND BRCA RESEARCH

This Part examines the impact of *Myriad*'s holding that isolated DNA does not comprise patentable subject matter on Myriad's own efforts to control research. This is a complicated issue, partly due to Myriad's insistence that it has always permitted noncommercial research on BRCA genes to proceed without a license. This debate reveals the importance and ambiguity of definitions in determining whether patents impede research activities. After all, definitions of "research" and "commercial" uses of genes are rather subjective, and commercial uses of genes may yield important research insights. Additionally, perceptions of the law or of a patentee's proclivity to enforce its rights may be more important than actual reality in shaping (and chilling) behavior in the research community. Taken together, the Court's invalidation of Myriad's isolated DNA patents creates real and perceived freedom to operate, thus freeing up space for more BRCA research to proceed

At the outset, it is important to acknowledge that from several practical perspectives, the significance of Supreme Court's holding is quite modest. First, Myriad's

¹⁰ This Article focuses on the Supreme Court's holding that isolated DNA does not comprise patentable subject matter, and it also considers the Court's holding that cDNA remains eligible for patenting. It will not address the important lower court holdings regarding the patent eligibility of Myriad's patented *processes*. These patents, however, may be quite significant. Cf. Christopher M. Holman, The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation, 76 UMKC L. Rev. 295, 314 (2007) [hereinafter Holman, Impact] ("In many cases, the most dominating patent claims relating to human genetic sequences are process claims, particularly those that broadly claim methods of identifying mutations.").

patents in suit were set to expire in 2015.¹¹ Therefore, even if the Court upheld the validity of Myriad's isolated DNA claims, exclusivity would have only remained for two more years. Second, patentable subject matter was not the only doctrinal ground upon which Myriad's patents were open to attack. In particular, nonobviousness doctrine represented another promising avenue to challenge these patents.¹² Third, Myriad maintained other patents to assert exclusivity over clinical genetic diagnostic tests. Prior to the decision, Myriad even downplayed the importance of its isolated DNA patents and suggested that their potential invalidation would be rather insignificant.¹³ Indeed, about three-fourths of Myriad's BRCA-related patents are on cDNA, probes, and methods that were by undisturbed by the Supreme Court's ruling on isolated DNA.

Notwithstanding these considerations, the Court's decision remains significant as immediately eliminating an important and highly visible mechanism of exclusivity. It also provides an opportunity to assess the degree to which Myriad's isolated DNA patents actually inhibited or threatened to inhibit biomedical research. Throughout the Myriad litigation, there was concern that exclusive rights would inhibit "basic" research. As a general matter, however, defining the contours such research is rather difficult. In the traditional view, "basic" research refers to foundational, upstream research that advances scientific knowledge while "applied" research applies scientific knowledge to solve practical problems.¹⁴ Contemporary science, however, blurs these definitional boundaries. These days, much biomedical research occurs in "Pasteur's Quadrant": it both strives for fundamental understanding and is intrinsically oriented toward practical application.¹⁵ For instance, discovery of the BRCA 1 and BRCA 2 genes advanced basic biological knowledge as well as led directly to diagnostic tests. Importantly, just as "basic" research can have clear practical applications, commercial uses of genes can yield

¹¹ Cf. Rose-Ellen Lessy, What's At Stake in the Supreme Court Decision in 'AMP v. Myriad Genetics,' *The Nation*, June 5, 2013, at <http://www.thenation.com/article/174681/whats-stake-supreme-court-decision-amp-v-myriad-genetics> (noting that Myriad's patents expire in 2015).

¹² See *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009) (invalidating claims covering an isolated DNA encoding a particular protein as obvious); *infra* notes – and accompanying text.

¹³ John Conley, Myriad, Finally; Supreme Court Surprises by not Surprising, *Genomics Law Report*, June 18, 2003, at <http://www.genomicslawreport.com/index.php/2013/06/18/myriad-finally-supreme-court-surprises-by-not-surprising/>.

¹⁴ See Fiona Murray & Scott Stern, Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-commons Hypothesis, 63 *J. Econ. Behav. & Org.* 648, 651 (2007). This distinction has a long provenance and relates to the massive increase in federal science funding following World War II. See Peter Lee Toward a Distributive Commons in Patent Law, 2009 *Wisc. L. Rev.* 917, 944-45 n.160. Vannevar Bush, chief scientific advisor to President Roosevelt and architect of postwar U.S. science policy, envisioned that federal funding of basic academic research would create a "reservoir of knowledge" that would facilitate downstream, applied research and innovation. Timothy L. Faley & Michael Sharer, Technology Transfer and Innovation: Reexamining and Broadening the Perspective of the Transfer of Discoveries Resulting from Government-Sponsored Research, 3 *Comp. Tech. Transfer & Soc'y* 109, 111 & fig.1 (2005); see generally Vannevar Bush, *Science: The Endless Frontier* (1945).

¹⁵ Francis Narin et al., The Increasing Linkage Between U.S. Technology and Public Science, 26 *Res. Pol'y* 317, 317 (1997); Richard R. Nelson, The Market Economy, and the Scientific Commons, 33 *Res. Pol'y* 455, 457 (2004) [hereinafter Nelson, *Scientific Commons*]; see Katherine J. Strandburg, User Innovator Community Norms, At the Boundary Between Academic and Industry Research, 77 *Fordham L. Rev.* 2237 (2009); Nicol, *supra* note , at 13; see generally Donald E Stokes, *Pasteur's Quadrant: Basic Science and Technological Innovation* (1996).

foundational scientific insights. As we will see, clinical (“commercial”) diagnostic testing can reveal previously unknown disease-causing mutations,¹⁶ thus enhancing basic knowledge as well as leading to more refined tests. Therefore, the impact of Myriad’s isolated DNA patents on research is a function of not only direct enforcement against researchers but against clinical testing in general.

The subjective nature of defining “research” uses of assets like isolated BRCA DNA complicates the debate over how much Myriad’s patents threatened research activities. To understand this debate, some background on Myriad’s services is helpful. Myriad developed several genetic diagnostic tests based on its discoveries, including the Comprehensive BRCAAnalysis, which comprises full sequence testing of BRCA 1 and BRCA 2¹⁷ as well as Single Site BRCAAnalysis tests, which only tests for a single mutation.¹⁸ Myriad performed the Comprehensive BRCAAnalysis at its own laboratory in Utah.¹⁹ However, it granted licenses to several laboratories around the nation to perform Single Site BRCAAnalysis.²⁰ These licenses included special provisions for research activities, as defined by Myriad, though these policies seemed to evolve over time. According to Myriad, licensees were allowed to perform genetic tests for research purposes as long they did not charge fees or share results with patients. If, however, the researcher shared results with patients, then “it crosses over the line,” and becomes commercial use, thus violating the license.²¹ Furthermore, although the licenses did not allow laboratories to perform comprehensive genetic testing for patients, Myriad made this service available at a discounted price for research purposes.²² Researchers at these institutions could submit test samples to Myriad to perform comprehensive analysis at its Utah laboratory; based on a negotiated agreement, Myriad would perform these tests for NIH-funded researchers for \$1,200 rather than the ordinary cost of \$2,680 for patients.²³

In a variety of ways, Myriad’s actual and threatened enforcements of its patents—including isolated DNA patents—helped chill research prior to the Supreme Court’s holding. To understand this dynamic, one must understand that there is no clear separation between “clinical” and “research” uses of the BRCA diagnostic test; one informs the other. In particular, widespread clinical genetic diagnostic testing plays an important role in illuminating new BRCA mutations that may have biological significance. Although Myriad maintained that it allowed wide, unlicensed use the BRCA genes for research purposes, it still asserted its exclusive rights in what it defined as commercial contexts. Such assertions threatened research as well. As Jon Merz testified

¹⁶ Rochelle Cooper Dreyfuss, Implications of the DNA Patenting Dispute: A US Response to Dianne Nicol, 22(1) J. of L. Info. & Sci. 1, 9 (2012).

¹⁷ Gold & Carbone, *supra* note , at S42.

¹⁸ Gold & Carbone, *supra* note , at S42.

¹⁹ Gold & Carbone, *supra* note , at S42.

²⁰ Gold & Carbone, *supra* note , at S42.

²¹ See John P. Walsh et al., Effects of Research Tool Patents and Licensing on Biomedical Innovation, in *Patents in the Knowledge-Based Economy* 285, 318 (Wesley M. Cohen & Stephen A. Merrill eds., 2003) (quoting Gregory Critchfield, Myriad Genetics) [hereinafter Walsh et al., Effects]; see Aaron S. Kesselheim & Michelle M. Mello, Gene Patenting—Is the Pendulum Swinging Back?, 362 N. Eng. J. Med. 1855, 1857 (2010).

²² Kimberly Stanton, Corporate Takeover, Boston Globe, Feb. 24, 2002, at .

²³ Stanton, *supra* note , at .

to Congress, “There is no clear line to be drawn between clinical testing and research testing, because the state of the art of genetic tests is such that much more clinical study is necessary to validate and extend the early discovery of a disease gene. Thus, the restriction of physicians from performing clinical testing will directly reduce the knowledge about these genes.”²⁴ For academic medical centers, the inability to share diagnostic results with test subjects made it more difficult to enlist patients in research studies.²⁵ This restriction particularly discouraged the most important potential research subjects—those with a family history of breast cancer—from participating in studies.²⁶ Although Myriad offered to perform full-gene “research” sequencing at its own laboratory for a discount, the fee was still substantial. Furthermore, the requirement of submitting samples to Myriad would have foreclosed researchers from utilizing their own, preferred sequencing techniques.²⁷ Commentators suggest that chilled research on the BRCA 1 and BRCA 2 genes may have delayed important discoveries, such as the role of “big mutations” in developing breast cancer.²⁸

The definitional difficulties of distinguishing “research” and “commercial” use are evident in a specific instance where Myriad’s patents threatened an academic laboratory. In 1998, Myriad sent a letter to the University of Pennsylvania’s Genetics Diagnostic Laboratory (GDL) in response to the lab’s performance of BRCA 1 testing for other institutions.²⁹ The letter described Myriad’s ownership of relevant patents and informed GDL that Myriad would allow the lab to continue diagnostic tests only if it agreed to certain restrictions and paid a license fee.³⁰ Interestingly, GDL initially refused to accede to Myriad’s request, claiming a “research exemption” from Myriad’s patent because it was working under protocols from the National Cancer Institute’s Cancer Genetics Network.³¹

In response, Myriad somewhat modified its research policy, but still asserted its rights against GDL. In so doing, the dispute with GDL depended centrally on “a question of how one defines research in deciding whether to enforce a patent.”³² Myriad entered into an agreement with NCI that articulated a rather complicated definition of “research use” that was permitted under Myriad’s license. Additionally, Myriad entered into an MOU with NCI to allow for discounted testing for any researcher working under an NCI-funded project, as noted above.³³ The MOU defined research testing services as “part of the grant supported research of an investigator, and *not in performance of a technical*

²⁴ Walsh et al., Effects, supra note , at 318-19 (citing testimony of Jon F. Merz before House Judiciary committee, July 13, 2000)

²⁵ Stanton, supra note , at .

²⁶ Stanton, supra note , at .

²⁷ Stanton, supra note , at .

²⁸ Stanton, supra note , at . Myriad’s diagnostic tests screen for relatively small point mutations rather than big deletions where long stretches of sequences are missing. Stanton, supra note , at .

²⁹ Steve Bunk, Researchers Feel Threatened by Disease Gene Patents, The Scientist, Oct. 11, 1999, at 7.

³⁰ Bunk, supra note , at 7. In 1998, Myriad actually filed a lawsuit against the University of Pennsylvania, but the district court dismissed it because Myriad failed to serve process on the defendant. Holman, Impact, supra note , at 347-48.

³¹ Gold & Carbone, supra note , at S42.

³² Gold & Carbone, supra note , at S64.

³³ Gold & Carbone, supra note , at S42.

service for the grant supported research of another (as a core facility, for example).”³⁴ Research testing services were further defined as paid for by grant funds and not by the patient or insurance. Notably, if these conditions were satisfied, patients participating in research could obtain their test results. However, because GDL performed tests for other NCI-funded researchers, it did not itself qualify for “research testing” under the MOU.³⁵ According to GDL, the prospect of paying royalties to Myriad for tests conducted on behalf of other institutions made this activity financially untenable,³⁶ and it stopped testing.

Complicating matters further was Myriad’s public articulations of its patent policy as well as the issue of whether Myriad stood to gain from open use of BRCA diagnostic tests for research purposes. The company maintains that its position “is to not require a research license for anybody” and that it is only concerned with commercial infringement.³⁷ It states that it defines “noncommercial research” broadly,³⁸ but that is a debatable proposition. Furthermore, there appears to be some evolution or inconsistency in Myriad’s conception of noncommercial research; in some contexts, such activity was incompatible with sharing results with patients while in other context it was.³⁹ In a broader sense, Myriad has tried to corroborate its image as a “proresearch” company by reasoning that “[s]ince research performed on BRCA 1 and BRCA 2 could only confirm and expand the clinical utility of testing, it would have been counter productive to science or to Myriad’s commercial development to require researchers to obtain a license.”⁴⁰ The notion that research uses of the BRCA 1 and 2 tests would benefit Myriad shores up its claim that it never intended to chill such activities. However, constraining research may have actually commercially benefitted Myriad. Notably, a dearth of independent research on the BRCA 1 and 2 genes would shore up the value of Myriad’s own (proprietary) database of mutations.⁴¹

As in many areas of law, in the case of gene patents and the research community, perception is sometimes more important than reality.⁴² Although Myriad’s official position on unlicensed research uses of BRCA diagnostic tests was, at times, quite permissive, the company failed to articulate this message coherently and widely.⁴³ GDL helped fan the flames of controversy by widely publicizing Myriad’s cease-and-desist letter “with the accompanying message that Myriad was attempting to impede basic

³⁴ Gold & Carbone, *supra* note , at S42 (emphasis added).

³⁵ Gold & Carbone, *supra* note , at S42.

³⁶ Bunk, *supra* note , at 7.

³⁷ Bunk, *supra* note , at 7 (quoting Gregory C. Critchfield, president, Myriad Genetics).

³⁸ Gold & Carbone, *supra* note , at S58.

³⁹ See *supra* notes – and accompanying text.

⁴⁰ Gold & Carbone, *supra* note , at S44.

⁴¹ See Bunk, *supra* note , at 7.

⁴² Holman, *Impact*, *supra* note , at 359 (“[I]f academic researchers face little or no real threat of a lawsuit based on patent infringement but nevertheless avoid the use of certain patented genes and other technologies in their research, it is this misperception rather than patents per se that is having the impact.”).

⁴³ Gold & Carbone, *supra* note , at S44. See *id.* at S58 (“Much of the policy story surrounding Myriad and its genetic test stemmed from Myriad’s failure to communicate its position clearly, if indeed its position was clear and stable to itself.”).

scientific research.”⁴⁴ Due in part to these media accounts, some scientists were wary about identifying new BRCA mutations and depositing them in public databases, as they were concerned that such actions would constitute evidence of patent infringement.⁴⁵ Some investigators stopped research on BRCA 1 and 2 or at least stopped publicly disseminating their results.⁴⁶ Notably, Myriad has only recently formalized and publicized its policy of “not imped[ing] non-commercial, academic research that uses patented technology licensed or owned by us.”⁴⁷ Although Myriad claims that it has always permitted noncommercial use of the BRCA 1 and 2 genes, it is far from clear what this means, and some scientists understandably felt that BRCA research might expose them to patent infringement liability.

Given this state of affairs, it appears that the Supreme Court’s invalidation of Myriad’s isolated DNA patents may create greater freedom to operate for research scientists. The substantive impact of the decision operates on two levels. In terms of “pure” research, scientists may now study isolated BRCA 1 and BRCA 2 DNA without fear of infringement liability (assuming, of course, that they do not infringe any other patents). In terms of indirect gains, greater commercial diagnostic testing of BRCA 1 and 2 will ultimately enhance knowledge of these important genes. Of course, a complicating factor here is Myriad’s remaining intellectual property. In the wake of the Court’s ruling, several companies began offering clinical genetic diagnostic testing for mutations on BRCA 1 and 2. However, Myriad quickly filed patent infringement suits against several companies, including Ambry Genetics and Gene By Gene.⁴⁸ It has argued that notwithstanding its invalidated patents, it still holds significant intellectual property rights in BRCA testing via its other product and process patents.⁴⁹ Although litigation with Gene By Gene settled largely in Myriad’s favor,⁵⁰ a court has rejected Myriad’s motion

⁴⁴ Gold & Carbone, *supra* note , at S44.

⁴⁵ Gold & Carbone, *supra* note , at S44.

⁴⁶ Gold & Carbone, *supra* note , at S61.

⁴⁷ Myriad Genetics, Myriad’s Pledge to Our Patients and the Research Community, at <https://www.myriad.com/responsibility/myriads-pledge/>.

⁴⁸ 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); Brent Kendall, Myriad Genetics Presses Ahead After High Court Ruling on Patents, *Wall St. J.*, July 12, 2013, at . Myriad claims that even after the Court’s decision, it maintains 515 of 520 patent claims on the test. Brian Resnick, Why is Myriad Genetics Still Filing Patent Suits for Breast-Cancer Tests?, *National Journal*, Aug. 8, 2013, at <http://www.nationaljournal.com/healthcare/why-is-myriad-genetics-still-filing-patent-suits-for-breast-cancer-tests-20130808>. Ambry Genetics and Gene By Gene countersued, alleging antitrust violations on the part of Myriad. Gene By Gene Joins Ambry in Countersuit against Myriad Alleging Antitrust Violations, *GenomeWeb*, Aug. 15, 2013, at

⁴⁹ Myriad claims that even after the Court’s decision, it maintains 515 of 520 patent claims on the test. Brian Resnick, Why is Myriad Genetics Still Filing Patent Suits for Breast-Cancer Tests?, *Nat. J.*, Aug. 8, 2013, at <http://www.nationaljournal.com/healthcare/why-is-myriad-genetics-still-filing-patent-suits-for-breast-cancer-tests-20130808>.

⁵⁰ See Lora Hines, Local Company Settles Gene-Testing Patent Case, *Houston Chron.*, March 15, 2014, at . Under the settlement, Gene-By-Gene agreed to stop selling and marketing gene-based diagnostics in North America. However, it can still offer whole genome and exome products and services, plus custom products that test variants of BRCA genes. *Id.*

for a preliminary injunction against Ambry.⁵¹ For the time being, such testing—and its research benefits—are available on a wider basis.

Perhaps even more important, from the perspective of perception, the Court's ruling may also have significant implications for research involving BRCA genes. Myriad has long maintained that it would not enforce its rights against noncommercial research uses of its test. However, its policy was rather convoluted, and it didn't articulate it very clearly. Some researchers were likely chilled based on the (mis)perception that purely noncommercial studies involving BRCA may expose them to infringement liability. Notwithstanding Myriad's more recent and more explicit policy articulations, the Supreme Court's ruling may send a powerful message to the scientific community that research on isolated DNA corresponding to BRCA genes can proceed without any threat of patent enforcement.

PART II. UPSTREAM-DOWNSTREAM DYNAMICS IN PATENT LAW

Moving beyond the immediate impact on Myriad Genetics, the *Myriad* litigation provides an opportunity to revisit a longstanding debate regarding the impact of “upstream” patents, including patents on isolated DNA, on scientific research. Although theoretical concerns abound that DNA patents may impede scientific inquiry, most empirical research reveals little to no inhibitory effect. An important exception, however, pertains to diagnostics, a realm in which patentees (like Myriad Genetics itself) have asserted exclusive rights. Given the link between diagnostics and scientific knowledge, the Supreme Court's ruling may have more significance than anticipated in accelerating scientific research.

There are several mechanisms by which patents on the inputs to scientific research,⁵² such as genes, could stymie scientific inquiry.⁵³ After all, scientific progress is cumulative, building on previous discoveries.⁵⁴ First, a patent on an indispensable resource for which there are no substitutes may impede biomedical research.⁵⁵ For instance, the Wisconsin Alumni Research Foundation's patents on extracted and purified

⁵¹ Andrew Pollack, *Patentholder on Breast Cancer Tests Denied Injunction in Lawsuit*, March 10, 2014, N.Y. Times, at .

⁵² Such inputs are commonly referred to as “research tools.” See Peter Lee, *Inverting the Logic of Scientific Discovery: Applying Common Law Patentable Subject Matter Doctrine to Constrain Patents on Biotechnology Research Tools*, 19 Harv. J.L. & Tech. 79, 80 (2005) [hereinafter Lee, *Inverting the Logic*].

⁵³ See Rebecca S. Eisenberg, *A Technology Policy Perspective on the NIH Gene Patenting Controversy*, 55 Univ. Pitts. L.R. 633, 647 (1994) [hereinafter Eisenberg, *Technology Policy*].

⁵⁴ See Walsh et al., *Effects*, supra note , at 289-90.

⁵⁵ See Peter Lee, *Contracting to Preserve Open Science: Consideration-Based Regulation in Patent Law*, 58 Emory L.J. 889, 903 (2009) [hereinafter Lee, *Open Science*]; see generally, Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 Colum. L. Rev. 839 (1990); Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. Econ. Persp. 29 (1991). In gauging the potential for an upstream patent to inhibit research, “it is obviously of interest how essential or ‘foundational’ a research tool is for subsequent innovation, both in the sense of whether the tool is key to subsequent research and in the sense of the breadth of innovation that might depend on its use.” Walsh et al., *Effects*, supra note , at 332.

human embryonic stem cells have attracted such concern, as there is no scientifically adequate substitute for this kind of biological entity.⁵⁶ On a related note, Myriad's original isolated DNA patents elicited these types of fears, as there are no substitutes for these resources, either. Second, a proliferation of upstream exclusive rights can impede downstream productive activity, a concern articulated in Michael Heller and Rebecca Eisenberg's influential theory of the anticommons.⁵⁷ Although Heller and Eisenberg originally emphasized the potential for upstream patents to inhibit downstream *commercial* development,⁵⁸ the anticommons theory can also explain how upstream patents could inhibit basic research.⁵⁹ This concern also pertains to BRCA research given that by 2005, the BRCA 1 gene was subject to "14 different patents owned by 12 different entities."⁶⁰ Third, analytically distinct from the anticommons theory is the phenomenon of patent thickets, in which multiple overlapping patents cover a single technology.⁶¹ This is most relevant when a single integrated product, such as a semiconductor, reads on multiple patents. In theory, a patent thicket could inhibit lines of research that infringe multiple sets of exclusive rights.

An important background consideration that exacerbates the chilling potential of patents is that the United States lacks a robust research exception to infringement.⁶² Since at least the nineteenth century, U.S. patent doctrine has recognized an exception for infringement for purely noncommercial, "philosophical" uses of a patented invention.⁶³ At least one twentieth century case suggested that the exception may extend to a university's unlicensed use of a patented invention for academic purposes.⁶⁴ However, in

⁵⁶ See Lee, *Inverting the Logic*, supra note , at 91-92; Christopher D. Hazuka, *Supporting the Work of Lesser Geniuses: An Argument for Removing Obstructions to Human Embryonic Stem Cell Research*, 57 U. Miami L. Rev. 157, 198 (2002).

⁵⁷ Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 698-99 (1998); see also Lee, *Open Science*, supra note 21, at 892; Lee, *Inverting the Logic*, supra note , at 83-86; Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 L. & Contemp. Probs. 289, 295 (Winter/Spring 2003).

⁵⁸ Heller & Eisenberg, supra note , at 699 ("Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.").

⁵⁹ Indeed, the potential for aggressive patenting strategies to inhibit biomedical research informed the findings of an NIH working group on research tools, which was chaired by Professor Eisenberg. See Report of the National Institutes of Health (NIH) Working Group on Research Tools, June 4, 1998, available at <http://biotech.law.lsu.edu/research/fed/NIH/researchtools/Report98.htm>; Rebecca S. Eisenberg, *Bargaining Over the Transfer of Proprietary Research Tools: Is this Marketing Failing or Emerging?*, in *Expanding the Boundaries of Intellectual Property* 223, 248 (Rochelle Cooper Dreyfuss et al. eds., 2004) (describing the findings of the working group).

⁶⁰ Louis M. Solomon & Gregory J. Sieczkiewicz, 4 *Gender Med.* 187, 189 (2007).

⁶¹ See Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting*, in *1 Innovation Policy and the Economy* 119 (Adam B. Jaffe et al. eds., 2001); Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 Va. L. Rev. 1575, 1627 (2003); Peter Lee, *Patents and the University*, 63 Duke L.J. 1, 26 (2013) [hereinafter Lee, *Patents and the University*].

⁶² See Lee, *Inverting the Logic*, supra note , at 86-87; Timothy Caulfield et al., *Patenting Human Genetic Material: Refocusing the Debate*, 1 *Nature Reviews Genetics* 227, 229 (2000) ("[T]here is no general statutory exemption for experimental use in the United States.") [hereinafter Caulfield et al., *Patenting Human Genetic Material*].

⁶³ See *Whittemore v. Cutter*, 29 F. Cas. 1120 (C.C.D. Mass. 1813) (No. 17,600).

⁶⁴ See *Ruth v. Stears-Roger Manufacturing*, 13 F. Supp. 697 (D. Colo. 1935).

2002, in a case called *Madey v. Duke University*,⁶⁵ the Federal Circuit construed the common law experimental use exception very narrowly.⁶⁶ Notwithstanding earlier perceptions, as a doctrinal matter, the common law experimental use exception does not apply to the vast majority of university-based research. The absence of this “safe harbor” heightens the possibility that patents on inputs to scientific inquiry—including isolated DNA—may impede research.

Concern over the potential for “upstream” patents to inhibit research has been particularly acute in biomedicine.⁶⁷ Indeed, Heller and Eisenberg’s paragon example of the anticommons involved multiple patents on gene fragments that would be costly to aggregate.⁶⁸ This concern has been so serious that it has informed agency policy and action, most notably in the Human Genome Project (HGP). Organizers of the project “emphasized that, in order to reap the maximum benefit from the HGP, human DNA sequence should be freely available in the public domain.”⁶⁹ This sentiment was echoed in the so-called Bermuda Principles from 1996, in which an international consortium of genomic scientists unanimously agreed that “all human genomic DNA sequence information, generated by centers funded for large-scale human sequencing, should be freely available and in the public domain in order to encourage research and development and to maximize benefit to society.”⁷⁰ Rapid disclosure was intended to serve several purposes, including preempting patents on DNA sequences.⁷¹

Although provocative, the threat of upstream patents chilling downstream research has been subject to significant empirical challenge. Influential studies by John Walsh and his colleagues have cast doubt on the presence of an anticommons phenomenon in basic biomedical research.⁷² One study found that only 1% of a random sample of academic scientists reported a project delay of more than one month due to

⁶⁵ 307 F.3d 1351 (Fed. Cir. 2002).

⁶⁶ See Lee, Patents and the University, *supra* note , at 57.

⁶⁷ See, e.g., John J. Doll, The Patenting of DNA, 280 Science 689, 689 (1998); Jon F. Merz & Mildred K. Cho, What Are Gene Patents and Why Are People Worried about Them?, 9 Community Genetics 203, 207 (2005).

⁶⁸ Heller & Eisenberg, *supra* note , at 698.

⁶⁹ National Human Genome Research Institute, Policy on Availability of Genomic DNA Sequence Funded by NHGRI, July 1, 1999, at <http://www.genome.gov/pfv.cfm?pageID=10001802>.

⁷⁰ Summary of Principles Agreed Upon at the First International Strategy Meeting on Human Genome Sequencing (Bermuda, 25-28 February 1996) as reported by Hugo, at http://web.ornl.gov/sci/techresources/Human_Genome/research/bermuda.shtml#1; see Jorge L. Contreras, Bermuda’s Legacy: Policy, Patents and the Design of the Genome Commons, 12 Minn. J.L. Sci. & Tech. 1 (2011).

⁷¹ This effort was consistent with NIH’s evolving policy of not pursuing patents on cDNAs of unknown function. See Eisenberg, Technology Policy, *supra* note , at 633-34.

⁷² John P. Walsh et al., Patents, Material Transfers and Access to Research Inputs in Biomedical Research, FINAL REPORT TO THE NATIONAL ACADEMY OF SCIENCES’ COMMITTEE [ON] INTELLECTUAL PROPERTY RIGHTS IN GENOMIC AND PROTEIN-RELATED INVENTIONS, PATENTS, MATERIAL TRANSFER AND ACCESS TO RESEARCH INPUTS IN BIOMEDICAL RESEARCH (2005), available at <http://www2.druid.dk/conferences/viewpaper.php?id=776&cf=8> (finding minimal blocking effects from patents) [hereinafter Walsh et al., Patents, Material Transfers and Access]; Walsh et al., Effects, *supra* note 289, 331.

patents on research inputs.⁷³ Another found “only limited support for the idea that negotiations over rights stymie precommercial research conducted in universities.”⁷⁴ A survey of the American Association for the Advancement of Science found “very little evidence of an ‘anticommons problem’” in the United States and Japan.⁷⁵ Although the bulk of empirical analysis finds little or no evidence of an anticommons phenomenon in biomedical research, it has garnered some support. For example, Fiona Murray and Scott Stern have found “robust evidence for a quantitatively modest but statistically significant anti-commons effect.”⁷⁶ For example, citations to scientific articles decline after a patent is granted on the research described in the article.⁷⁷ The bulk of empirical studies, however, suggest a very modest general chilling effect for patents in biomedical research.

Several factors explain why patents may not inhibit research as much as anticipated. First, a de facto experimental use exception exists whereby patentees often refrain from suing basic researchers—especially university scientists—for patent infringement.⁷⁸ The lack of satisfactory remedies, the fear of undermining potential licensing relationships, and the specter of harmful public relations all dissuade patentees from suing universities.⁷⁹ Indeed, some patentees may welcome unlicensed use of their technologies by academics because those patentees are well positioned to exploit any new discoveries related to their invention.⁸⁰ A similar principle informed Myriad’s rather permissive approach to research use of BRCA 1 and 2 patents.⁸¹ Similarly, Ariad Pharmaceuticals, which holds a patent on the NF-kB molecular pathway, actively encouraged noncommercial use of its patent without a license.⁸² Short of simply tolerating infringement, patentees also routinely charge lower licensing fees to academic versus for-profit uses of their patents.⁸³ As mentioned earlier, Myriad offered a significant discount on whole-gene testing for academics conducting NIH-funded breast cancer research.⁸⁴

⁷³ Walsh et al., Patents, Material Transfers, and Access, *supra* note , at 2.

⁷⁴ Walsh et al., Effects, *supra* note , at 317.

⁷⁵ Am. Ass’n for the Advancement of Sci., International Intellectual Property Experiences: A Report of Four Countries 12 (2007).

⁷⁶ Murray & Stern, *supra* note .

⁷⁷ Murray & Stern, *supra* note ; see also Kenneth G. Huang & Fiona Murray, Does Patent Strategy Shape the Long-Run Supply of Public Knowledge? Evidence from Human Genetics, 52 Acad. Mgmt. J. 1193 (2009).

⁷⁸ Rai & Eisenberg, *supra* note 21, at 296 (characterizing the informal norm against suing nonprofit researchers as a form of price discrimination).

⁷⁹ Walsh et al., Effects, *supra* note , at 325.

⁸⁰ Walsh et al., Effects, *supra* note , at 326; *see* Dreyfuss, *supra* note , at 8 (“Until there are ways to translate the advances in the sciences of biotechnology into products, patent holders may be very happy to let researchers infringe, in the hope that the infringers will find therapies (or methods for developing them).”).

⁸¹ Gold & Carbone, *supra* note , at S64.

⁸² Walsh et al., Patents, Material Transfers, and Access, *supra* note , at 30.

⁸³ Walsh et al., Effects, *supra* note , at 302.

⁸⁴ Walsh et al., Effects, *supra* note , at 302.

Second, in addition to patentees frequently not enforcing their patents, university scientists routinely ignore patents when conducting their research.⁸⁵ The norm of ignoring patents thus represents a “working solution” to the threat of patent holdup.⁸⁶ Notably, this norm was largely undisturbed by *Madey v. Duke*, which articulated a very narrow formal experimental use exception.⁸⁷ The combined effect of most patentees and scientists ignoring patents in the research context means that the vast majority of university research proceeds unfettered by direct threat of patent enforcement. Some commentators, however, have questioned whether patentees will continue to tolerate infringement and scientists will continue to ignore patents.⁸⁸ Concerned by the fragility of these “working solutions,” they have argued for a more robust, legally grounded experimental use exception.⁸⁹ And it is important to also keep in mind that “academic” uses of research inputs are not the only uses that have research and scientific importance. As discussed above, commercial diagnostic testing—which is not subject to the informal experimental use exception—yields significant research insights as well.⁹⁰

Having discussed the inhibitory potential of patents in general, then in the context of biomedical science, it is now instructive to drill down even further to explore this phenomenon in the specific context of “gene patents.”⁹¹ It has been estimated that 20% of human genes are patented,⁹² although that figure has been seriously questioned.⁹³ The prevalence and fundamentality of gene patents has fueled concerns that exclusive rights may inhibit both patient access to diagnostic tests as well as basic research.⁹⁴ Notably, much of this attention has focused on the controversy surrounding Myriad Genetics and its isolated DNA and cDNA patents.⁹⁵ Here again, however, empirical studies focusing

⁸⁵ Walsh et al., Effects, *supra* note , at 324; Walsh et al., Patents, Material Transfers, and Access, *supra* note , at 3; John P. Walsh et al., View from the Bench: Patents and Material Transfers, 308 Science 2002, 2002 (2005) [hereinafter Walsh et al., View from the Bench].

⁸⁶ See David E. Adelman, A Fallacy of the Commons in Biotech Patent Policy, 20 Berkeley Tech. L.J. 985, 1000 (2005).

⁸⁷ Walsh et al., Patents, Material Transfers, and Access, *supra* note , at 15.

⁸⁸ Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 HOUS. L. REV. 1059, 1097 (2008) [hereinafter Eisenberg, Noncompliance].

⁸⁹ Eisenberg, Noncompliance, *supra* note , at 1097.

⁹⁰ See *supra* notes – and accompanying text.

⁹¹ The term “gene patents” is itself highly contested. In one view, it encompasses a wide range of composition of matter patents on various forms of isolated DNA as well as patents on processes that involve isolated DNA. Kenneth Offit et al., Gene Patents and Personalized Cancer Care: Impact of the Myriad Case on Clinical Oncology, 31 J. Clinical Oncology 2743, 2744 (2013); but see Holman, Impact, *supra* note , at 315-19 (critiquing prevailing definitions of gene patents).

⁹² Kyle Jensen & Fiona Murray, Intellectual Property Landscape of the Human Genome, 310 Science 239, 239 (2005).

⁹³ See, e.g., Christopher M. Holman, Debunking the Myth that Whole-Genome Sequencing Infringes Thousands of Gene Patents, 30 Nature Biotechnology 240, 240-41 (2012) [hereinafter Holman, Debunking].

⁹⁴ Timothy Caulfield et al., *Evidence and Anecdote: An Analysis of Human Gene Patenting Controversies*, 24 NATURE BIOTECH. 1091, 1091 (2006) [hereinafter Caulfield et al., Evidence and Anecdote]; Lori B. Andrews, Genes and Patent Policy, Rethinking Intellectual Property Rights, 3 Nature Reviews Genetics, 803, 803 (2002); Susanne B. Haga & Huntington F. Willard, Defining the Spectrum of Genome Policy, 7 Nature Reviews Genetics 966, 968 (2006).

⁹⁵ Caulfield et al., Evidence and Anecdotes, *supra* note , at 1091; Holman, Impact, *supra* note , at 299.

specifically on gene patents have found little inhibitory effect.⁹⁶ A meta-study of studies focused on gene patents concludes that “the effects predicted by the anticommons problem are not borne out in the available data.”⁹⁷ Similarly, Timothy Caulfield notes that “despite all the noise, there is still no solid evidence that gene patents hurt basic research.”⁹⁸ Rebecca Eisenberg, revisiting the anticommons thesis a decade after her seminal co-authored article, observes that “patents appear to have a greater impact on downstream product development than on upstream academic research.”⁹⁹

Commentators have particularly focused on the potential for gene patents to chill whole genome sequencing. Such sequencing has significant clinical and research value, but some worry that sequencing a person’s entire genome may infringe thousands of isolated DNA patents. Notably, fears that isolated DNA patents would inhibit whole genome sequencing arose in the *Myriad* litigation itself. At the Federal Circuit, Judge Bryson argued in his partial concurrence that isolated DNA patents might inhibit this valuable activity.¹⁰⁰ These concerns, however, appear largely to be unfounded.¹⁰¹ Both existing methods for “whole genome shotgun sequencing” as well as next generation nanopore sequencing¹⁰² do not involve creating significant numbers of gene fragments that are likely to infringe isolated DNA patents. This technological state of affairs largely mitigates potential inhibitory effects of *Myriad*-style patents.¹⁰³

Similarly, it is unlikely that gene patents significantly impede efforts to express therapeutic proteins. In addition to diagnostic tests, one of the most important practical applications of human DNA is the mass production of biologically beneficial proteins. There are concerns that isolated DNA may inhibit such activity, but these concerns are also largely unfounded. It may not be necessary to isolate DNA (and thus run afoul of isolated DNA patents) to express a protein, particularly based on new techniques of gene activation.¹⁰⁴ Furthermore, the trend in biotechnology is to move toward synthetic varieties of therapeutic proteins featuring structural changes relative to naturally-occurring proteins. Scientists create such proteins by modifying the sequence of genomic

⁹⁶ See Subhashini Chandrasekharan & Robert Cook-Deegan, Gene Patents and Personalized Medicine – What Lies Ahead? 92 *Genome Medicine* x.1, x.1 (2009) (“Gene patents have generally not impeded biomedical research.”); Nicol, *supra* note , at 35 (“On the available evidence, the detrimental impact of DNA patents appears to be considerably lower than anticipated by many commentators, even in the contexts of research and consumer access to healthcare.”).

⁹⁷ Caulfield et al., *supra* note , at 1092.

⁹⁸ Timothy Caulfield, Do Gene Patents Hurt Research? The Data Say They Don’t, *Science Progress*, Oct. 29, 2009, at <http://scienceprogress.org/2009/10/do-gene-patents-hurt-research/>.

⁹⁹ Eisenberg, *Noncompliance*, *supra* note , at 1062.

¹⁰⁰ See, e.g., *Ass’n for Molecular Pathology v. United States Patent & Trademark Office*, 653 F.3d at 119-20 (Bryson, J., concurring in part and dissenting in part) (“[S]ome of *Myriad*’s challenged composition claims effectively preempt any attempt to sequence the BRCA genes, including whole-genome sequencing.”).

¹⁰¹ W. Nicholson Price II, Unblocked Future: Why Gene Patents Won’t Hinder Whole Genome Sequencing and Personalized Medicine, 33 *Cardozo L. Rev.* 1601, 1606 (2012).

¹⁰² Price, *supra* note , at 1606.

¹⁰³ Conley, *supra* note ; Offit et al., *supra* note , at 2746; Holman, *Impact*, *supra* note , at 326; Holman, *Debunking*, *supra* note , at 242.

¹⁰⁴ Holman, *Impact*, *supra* note , at 327.

DNA, thus offering another route to design around isolated DNA patents.¹⁰⁵ As Christopher Holman observes, “as the chemical structure of therapeutic proteins continue to diverge farther from naturally-occurring human proteins, human gene patents will probably play a diminishingly important role in providing market exclusivity for these important products.”¹⁰⁶

Diagnostics, however, are a different story. While gene patents do not seriously threaten whole genome sequencing and protein expression, they have played an important role in curtailing diagnostic testing.¹⁰⁷ In this context, voluntary forbearance on the part of patentees can quickly come to an end,¹⁰⁸ and they have even asserted their rights against university researchers.¹⁰⁹ One survey found that 25% of clinical laboratories stopped performing a clinical genetic test because of patent concerns, and 53% did not develop a new clinical genetic test because of such concerns.¹¹⁰ Empirical studies show that “research on clinical diagnostic testing suggest that when the research is itself a commercial activity, patent holders are more likely to assert and clinical researchers more likely to abandon infringing activities.”¹¹¹ Of course, this type of behavior is illustrated by Myriad Genetics itself,¹¹² which asserted its patents to curtail clinical genetic diagnostic testing at the University of Pennsylvania GDL.¹¹³ Another biotechnology firm, Chiron, has also developed a reputation for aggressively enforcing patents.¹¹⁴ Patentees have also enforced intellectual property rights to threaten testing on genes related to Alzheimer’s disease, cystic fibrosis, spinocerebellar ataxia type 1, hemochromatosis, and Canavan disease, among other conditions.¹¹⁵

Because diagnostic testing often generates fundamental biological knowledge, patent-based chilling of such testing has real implications for research. As mentioned above, widespread clinical testing can reveal previously unrecognized mutations that may contribute to disease.¹¹⁶ In general, significant clinical study is necessary to understand a newly-discovered gene, and patent enforcement produces “fear that limiting clinical testing will inhibit further discovery as well as the understanding that emerges naturally from broad medical adoption.”¹¹⁷ For instance, although many laboratories routinely offered genetic tests for haemochromatosis, 30% of surveyed labs discontinued services

¹⁰⁵ Holman, Impact, supra note , at 339.

¹⁰⁶ Holman, Impact, supra note , at 356-57.

¹⁰⁷ Caulfield et al., Evidence and Anecdotes, supra note , at 1092; see Chandrasekharan & Cook-Deegan, supra note , at x.2 (“Multi-gene diagnostic tests may infringe existing DNA-sequence or method claims.”).

¹⁰⁸ Dreyfuss, supra note , at 8; see also John F. Merz, Are there Limits on What May Be Patented?, in *Who Owns Life?* (David Magnus et al. eds. 2002), at 99, 101 (arguing that disease gene patents and exclusive licenses “restrict clinical observation and formal research”).

¹⁰⁹ Walsh et al., Effects, supra note , at 317-18; Eisenberg, Noncompliance, supra note , at 1071-72.

¹¹⁰ Mildred K. Cho et al., Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services, 5 J. Mol. Diag. 3, 3 (2003).

¹¹¹ Walsh et al., View from the Bench, supra note , at 2002.

¹¹² See Eisenberg, Noncompliance, supra note , at 1081.

¹¹³ See Walsh et al., Effects, supra note , at 312; Offit et al., supra note , at 2746; supra Part I.

¹¹⁴ Walsh et al., Effects, supra note , at 312.

¹¹⁵ Blanton, supra note , at .

¹¹⁶ Andrews, supra note , at 804; see supra notes – and accompanying text.

¹¹⁷ John F. Merz et al., Diagnostic Testing Fails the Test, 415 Nature 577, 577 (2002).

or did not develop tests in light of patent concerns.¹¹⁸ In countries where isolated DNA associated with haemochromatosis and Alzheimer's disease is not patented, researchers have found new disease-contributing mutations that were previously undiscovered.¹¹⁹ A study found that 14 of 27 owners of patents on genetic tests would require a license for a researcher to study the "penetrance and prevalence of the genetic mutation covered by their patent."¹²⁰ Viewed in this light, the Supreme Court's holding that isolated DNA is not patentable subject matter may accelerate genetic diagnostic testing more generally, thus promoting valuable research. This is especially the case because other genes may not necessarily be subject to the same kind of patent thickets as BRCA 1 and BRCA 2.¹²¹ In such cases, isolated DNA patents may represent the primary barrier to wide diagnostic testing, and thus rendering elimination of such patents particularly impactful.

Of course, an opposing narrative can be advanced in which the patent eligibility of isolated DNA would actually lead to a net gain in scientific research, or at least promote a form of scientific research with high social value. Based on the traditional theory of patent protection, exclusive rights may encourage parties to invest the time, energy, and resources to "invent" isolated DNA sequences as well as develop them into useful applications like diagnostic tests and therapeutic proteins. In some cases, "companies have invested heavily in developing the clinical evidence base for diagnostics to exploit a strong IP position based on exclusive licenses to DNA patents."¹²² In particular, biomarker patents may support "virtuous corporate behavior," motivating significant private investment in researching and developing promising diagnostics.¹²³ Along these lines, it is possible that the absence of patent protection on isolated DNA following *Myriad Genetics* will *harm* research.

The argument that maintaining the patent eligibility of isolated DNA would significantly enhance research, however, is questionable on several fronts. First, a substantial amount of (patented) genetic discoveries arise from academic science.¹²⁴ In such cases, public funding, professional rewards, and scientific norms of discovery already provide robust support for invention, thus undermining the justification for exclusive rights.¹²⁵ One might surmise that patents would be most useful not to spur initial invention, but to motivate private firms to develop inventions into diagnostic tests, commercial therapeutics, and other practical products. In this sense, the presence or absence of isolated DNA patents may affect not just the *amount* of genetic research conducted but the *kind* of research performed: patent eligibility may encourage more

¹¹⁸ Merz et al., *supra* note , at 577.

¹¹⁹ Andrews, *supra* note , at 804.

¹²⁰ Caulfield et al., Patenting Human Genetic Material, *supra* note , at 230; Anna Schissel et al., Survey Confirms Fears About Licensing of Genetic Tests, 402 *Nature* 118, 118 (1999).

¹²¹ See *supra* note s – and accompanying text.

¹²² Michael M. Hopkins & Stuart Hogarth, Biomarker Patents for Diagnostics: Problem or Solution?, 30 *Nature Biotechnology* 498, 499 (2012).

¹²³ Hopkins & Hogarth, *supra* note , at 499.

¹²⁴ Offit et al., *supra* note , at 2745; cf. 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, 1374 (2011) ("[T]he genetics case studies show that associations between genotypes and specific diseases are most often identified by academics.").

¹²⁵ See generally Lee, Open Science, *supra* note .

applied research by the patentee to develop a diagnostic test from an initial genetic discovery, but perhaps at the cost of more upstream, basic research by the scientific community more generally.¹²⁶ However, commentators have suggested that patents are not an effective incentive for developing clinical genetic diagnostic tests.¹²⁷ The Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) similarly concluded that patent exclusivity was not necessary to ensure that several diagnostic tests were developed and made available to patients.¹²⁸ Additionally, as mentioned above, therapeutic expression of important genes is not likely covered by (or facilitated by) isolated DNA patents.

Ultimately, the question of whether isolated DNA patents promote more research (by the patentee) or less research (by stymying uses by others) is a complicated inquiry. However, from a theoretical standpoint, it seems that more aggregate research would be performed by a broad scientific community unconstrained by patents than by a single patentee seeking to commercialize a discovery. Furthermore, available evidence suggests that these patents may not be necessary to spur initial investigations, they are not enforced particularly stringently (outside of the diagnostics context), and they are not necessary to develop practical applications.

Another important consideration is that patents on research inputs (including isolated DNA) have second-order effects aside from directly impeding research activities. Studies show that patenting activities delay publication of new biotechnology discoveries.¹²⁹ Furthermore, researchers are less likely to work in areas after significant findings have been patented, and more researchers enter a field and do more varied work after patents expire.¹³⁰ Furthermore, patents on inputs to scientific experimentation may help create a culture of secrecy within academia or skew university research toward more applied ends.¹³¹ Some, however, have speculated that an “overabundance of research opportunities” in genomics and other fields has “transformed biomedical science into an unbounded resource,” thus mitigating concerns over meaningful patent holdup.¹³² However, given the indispensable and nonsubstitutable nature of some research inputs—such as isolated DNA corresponding to specific genes—this claim seems doubtful.

¹²⁶ See *supra* notes – and accompanying text.

¹²⁷ Heller & Eisenberg, *supra* note , at .

¹²⁸ Secretary's Advisory Committee on Genetics, Health, and Society, *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* (2010).

¹²⁹ David Blumenthal et al., *Data Withholding in Genetics and Other Life Sciences*, 277 JAMA 1224 (1997).

¹³⁰ Kenneth G. Huang & Fiona E. Murray, *Does Patent Strategy Shape the Long-Run Supply of Public Knowledge? Evidence from Human Genetics*, 52 Acad. of Mgmt. J. 1193 (2009).

¹³¹ Caulfield et al., *Patenting Human Genetic Material*, *supra* note , at 230; cf. Nicol, *supra* note , at 16 (describing commentary suggesting that patenting may alter “fundamental scientific norms at the upstream end of the research-development continuum”); but see Caulfield et al., *Evidence and Anecdotes*, *supra* note , at 1093 (questioning whether an increase in academic secrecy is attributable to patents); Walsh et al., *Effects*, *supra* note , at 305 (suggesting that redirecting scientific efforts toward more practical ends may be socially beneficial).

¹³² Adelman, *supra* note , at 986.

Although this Article has focused on the Supreme Court’s invalidation of Myriad Genetics’ isolated DNA patents, it will briefly consider the research implications of the Court’s additional holding that cDNA remains eligible for patenting. In a somewhat simplified dichotomy, commentators tend to associate isolated DNA with diagnostics and research while viewing cDNA, which has noncoding nucleotides synthetically removed, as less important for research purposes but more important for commercially expressing therapeutic proteins.¹³³ However, cDNA also has significant research uses, and the affirmation that cDNA is patentable subject matter may have “important consequences for research, including research to discover new disease treatments and create new genetic tests.”¹³⁴ For example, scientists often utilize cDNA to create animal models of disease.¹³⁵ For instance, researchers have created fruit flies with cDNA disease genes to study how neurodegenerative diseases kill neurons.¹³⁶ The Court’s ruling affirms that the cDNA underlying these research inputs are eligible for exclusive rights. The Court’s ruling also suggests that other forms of artificially synthesized DNA may comprise patentable subject matter. It also gives rise to some quandaries that the Court does not address. For instance, “[i]f a machine synthesizes a segment of DNA, but it’s the same sequence as [a] gene found in nature, would that be patentable?”¹³⁷ Although it has attracted less attention than isolated DNA, cDNA is also a potentially important research resource. Of course, for the reasons described above, it is debatable whether patentees of cDNA actively enforce their rights against researchers in a purely academic or noncommercial context. Furthermore, given that the Court’s holding that cDNA comprises patentable subject matter merely maintained the status quo, it is difficult to ascertain much direct impact from this particular holding.¹³⁸

In sum, the Court’s ruling that isolated DNA is not patentable subject matter may have important implications beyond BRCA research to genetic research more generally. Empirical studies indicate that concerns over chilling and anticommons effects from patents are generally unfounded in the research context. This in turn suggests that the patent status of a research input—and the patent eligibility of isolated DNA—has little impact on scientific inquiry. One of the consistent themes of this study, however, is that even commercial, diagnostic uses of genetic resources can have significant research implications. One area where holders of gene patents have not been shy in asserting their exclusive rights is in diagnostic testing. Such testing, however, does not simply help individual patients, it also generates general knowledge about genes and disease-causing

¹³³ Briefs from the Solicitor General as well as Eric Lander, co-chair of the President’s Council of Advisors on Science and Technology, argued that cDNA claims can be worked around for research purposes. Rai & Cook-Deegan, *supra* note , at 137.

¹³⁴ Megan Krench, New Supreme Court Decision Rules That cDNA is Patentable—What It Means for Research and Genetic Testing, *Scientific American*, July 9, 2013, at <http://blogs.scientificamerican.com/guest-blog/2013/07/09/new-supreme-court-decision-rules-that-cdna-is-patentable-what-it-means-for-research-and-genetic-testing/>.

¹³⁵ Krench, *supra* note .

¹³⁶ Krench, *supra* note .

¹³⁷ Krench, *supra* note ; see also Seidenberg, *supra* note , at (“The patent-eligibility of synthetic molecules will be an issue in the future.”) (quoting Professor Rochelle Dreyfuss, NYU School of Law).

¹³⁸ Some have speculated, however, that formal validation of the patent eligibility of cDNA may encourage greater patenting, particularly on the part of laboratories seeking to maintain freedom to operate. See Krench, *supra* note (suggesting greater laboratory patenting of cDNA following the

mutations. To the extent that isolated DNA patents were the primary barrier to such tests, the Court's ruling may accelerate genetic research.

PART III. BROADER DOCTRINAL IMPLICATIONS

Beyond its immediate impacts on BRCA testing and genetic research more generally, *Myriad* represents an important doctrinal development with several long-term implications for the intersection of patents and research. First, the opinion helps solidify patentable subject matter doctrine as a policy lever¹³⁹ for policing the boundaries of exclusive rights. Second, within the context of several recent patentable subject matter decisions, *Myriad* reflects the Supreme Court's strong prudential interest in carving out a zone of nonpatentability for natural phenomena. Here again, definitional fluidity plays an important role, for the Court also exhibits significant discretion in determining what constitutes nature and thus qualifies for this exception. Such a policy-oriented approach to patent eligibility may create significant flexibility to challenge patents in research contexts going forward.

A. Elevating Patentable Subject Matter Doctrine to Police Patentability

One of the significant implications of *Myriad* is that it helps galvanize § 101 as a robust doctrinal lever for filtering out patents.¹⁴⁰ From a policy perspective, it is not clear that subject matter exclusions—which are rather blunt instruments—are the optimal mechanism for policing the boundaries of patent exclusivity. Among other considerations, such categorical exclusions are difficult to define, a matter discussed more fully below.¹⁴¹ Along these lines, other patentability doctrines may offer more nuanced, effective means for regulating patentability. For instance, courts have used the written description requirement to invalidate specific gene patent claims that did not find adequate support in a patent disclosure.¹⁴² Although not raised in the litigation, another potential approach for invalidating *Myriad*'s isolated DNA patents is nonobviousness analysis. The now-routine nature of DNA isolation and sequencing, as well as translating protein sequences to nucleotide sequences, is likely to render “mere” isolated DNA obvious under 35 U.S.C. § 103.¹⁴³

¹³⁹ See Dan L. Burk, & Mark A. Lemley, Policy Levers in Patent Law, 89 Va. L. Rev. 1575 (2003).

¹⁴⁰ See *supra* note .

¹⁴¹ See *infra* Part III.B.

¹⁴² See, e.g., *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) (holding that claims covering cDNA that produced insulin in all vertebrates and mammals were invalid in light of written description that only described cDNA that produced insulin in rats).

¹⁴³ *Dreyfuss*, *supra* note , at 3; see 35 U.S.C. § 103. Because *Myriad* filed for its patents before March 16, 2013, it was subject to the nonobvious requirements prior to the America Invents Act. Arguably, the nonobvious hurdle is even slightly higher under the AIA, as the date of prior art is pushed up to the date of filing a patent application rather than the earlier date of invention. Additional developments in nonobviousness doctrine have also raised this bar to patentability. See *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007); *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009) (holding that obvious to try may, in some circumstances, indicate obviousness).

Some authorities, including Federal Circuit opinions, suggest that § 101 should operate as a “coarse eligibility filter,”¹⁴⁴ leaving more nuanced analyses of patentability to other patentability doctrines. There have even been suggestions for courts to scrutinize other requirements of patentability first, analyzing patentable subject matter only later if necessary.¹⁴⁵ Although the *Myriad* court considered patent eligibility to be simply a “threshold test,”¹⁴⁶ it elevated its importance in terms of functioning as a substantive filter for patent law. Of course, the Court cannot decide how litigants frame issues before them; it agreed to adjudicate a patentable subject matter dispute, and it decided it. However, the Court’s emphasis on §101 opens the possibility for other patent eligibility challenges in realms related to research science. The blunt and unwieldy nature of patent eligibility doctrine, however, may translate to a high degree of judicial discretion to determine the patentability of research assets, a phenomenon more fully explored below.

B. Creating a Strong and Flexible Exception for Nature from Patent Eligibility

In addition to elevating the effectiveness and visibility of patentable subject matter doctrine as a mechanism for challenging patents, *Myriad* helped expand its power. As we will see, *Myriad* helps solidify both a strong exclusion for nature from patentable subject matter as well as significant discretion in identifying natural phenomena for this purpose. To understand this development—as well as its potential impact on scientific research—it is necessary to place *Myriad* within the context of several recent Supreme Court decisions on patentable subject matter.

Some of the foundations of *Myriad*’s invalidation of isolated DNA patents are evident in *Bilski v. Kappos*, a 2010 case addressing the patent eligibility of a business method of hedging risks in commodities trading.¹⁴⁷ The Supreme Court invalidated the claims at issue because they covered patent-ineligible “abstract ideas.”¹⁴⁸ On its face, this has little to do with *Myriad*’s holding regarding isolated DNA. However, *Bilski*’s concern with abstract ideas stemmed from a broader desire to prevent patents from “preempting”¹⁴⁹ wide access to foundational, productivity-enhancing assets,¹⁵⁰ a

¹⁴⁴ See *Research Corp. Tech., Inc. v. Microsoft Corp.* 627 F.3d 859, 869 (Fed. Cir. 2010).

¹⁴⁵ See Dennis Crouch & Robert P. Merges, *Operating Efficiently Post-Bilski by Ordering Patent Doctrine Decision-Making*, 25 *Berkeley Tech. L.J.* 1673 (2010).

¹⁴⁶ *Bilski v. Kappos*, 130 S.Ct. 3218, 3225 (2010).

¹⁴⁷ 130 S.Ct. 3218 (2010).

¹⁴⁸ See 130 S.Ct. 3229-31. The Federal Circuit had invalidated the patents as failing the machine-or-transformation test by which a process is only eligible for patenting if it meaningfully involves a machine or effectuates a transformation of one thing or state to another. *In re Bilski*, 545 F.3d 943, 954, 961 (Fed. Cir. 2008). The Supreme Court, however, rejected the machine-or-transformation test as the sole test of process patentability. 130 S.Ct. 3229-31.

¹⁴⁹ See Dreyfuss & Evans, *supra* note , at 1351. The issue of preemption originally arose in *Gottschalk v. Benson*, a 1972 case in which the Supreme Court held that a process of converting numbers from one numerical system to another was not patentable subject matter. 409 U.S. 63, 71-72; see Dreyfuss & Evans, *supra* note , at 1351-52.

¹⁵⁰ See John Thomas, *Mayo v. Prometheus: Implications for Patents, Biotechnology, and Personalized Medicine* 6 (2012).

sentiment that applies as well to laws of nature and physical phenomena.¹⁵¹ Indeed, the Court situated its preemption analysis within traditional doctrine grouping together abstract ideas, laws of nature, and physical phenomena as nonpatentable subject matter.¹⁵² In surprising ways, *Bilski*, a case about hedging risks in financial transactions, also had important implications for the Court's treatment of nature. As Rochelle Dreyfuss and James Evans observe, "since science must deal with the natural world, the inability to invent around is also a clue to *Bilski*'s other exclusions: laws of nature and natural phenomena."¹⁵³

In addition to articulating deep concerns with preempting abstract ideas, laws of nature, and natural phenomena, *Bilski* left significant discretion in how to define these categories. This is a difficult task, for these entities do not have clear, a priori meanings. At points, the Court suggests a purposive approach to identifying these entities through the overarching aim of subject matter exclusions, noting that these entities represent the "storehouse of knowledge of all men."¹⁵⁴ Drawing on *Bilski*, commentators have suggested that courts, both as descriptive and normative matters, define these categories *functionally* based on the purpose of subject matter exclusions.¹⁵⁵ According to Mark Lemley and colleagues, these exclusions are really "about encouraging cumulative innovation and furthering societal norms regarding access to knowledge by preventing patentees from claiming broad ownership over fields of exploration rather than specific applications of those fields."¹⁵⁶ In other words, courts should consider the "generative nature of the new technology" to help determine whether it comprises an abstract idea.¹⁵⁷ Such assets are *infrastructural* and thus ideally open to all. This sentiment applies to the other common law exclusions from patentable subject matter as well: laws of nature and physical phenomena.¹⁵⁸ In other words, the lack of guidance in *Bilski* as well as overarching principles of patent eligibility enable the possibility of identifying some asset as an abstract idea, law of nature, or physical phenomenon precisely *because* exclusive rights over it would foreclose much productive activity.¹⁵⁹ This of course creates a significant amount of judicial discretion in determining what qualifies as nonpatentable subject matter.

¹⁵¹ The relationship between *Bilski* and laws of nature is even more evident given that the Supreme Court remanded *Mayo v. Prometheus* to the Federal Circuit to rehear in light of the Court's decision in *Bilski*. 130 S.Ct. 3543 (2010).

¹⁵² See *Diamond v. Diehr*, 450 U.S. 175, 177 (1981).

¹⁵³ Dreyfuss & Evans, *supra* note , at 1361. This sentiment is also evident in the Federal Circuit's earlier adjudication of *Bilski*, in which Judge Rader stated, "Natural laws and phenomena can never qualify for patent protection because they cannot be invented at all." In re *Bilski*, 545 F.3d 943, 1013 (Rader, J., dissenting).

¹⁵⁴ 130 S.Ct. at 3225 (citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 130 (1948)).

¹⁵⁵ Mark A. Lemley et al., *Life After Bilski*, 63 Stan. L. Rev. 1315 (2010).

¹⁵⁶ Lemley et al., *supra* note , at 1329; but see Eileen M. Kane, *Patent Ineligibility: Maintaining a Scientific Public Domain*, 80 St. John's L. Rev. 519, 545 (2006) ("Rationales for the exclusion of laws of nature, natural phenomena, and abstract ideas cannot be described with precision.").

¹⁵⁷ Lemley et al., *supra* note , at 1339.

¹⁵⁸ See, e.g., Peter Lee, *The Evolution of Intellectual Infrastructure*, 83 Wash. L. Rev. 39, 62-67 (2008) [hereinafter Lee, *Infrastructure*].

¹⁵⁹ An analogous dynamic applies to the idea-expression dichotomy in copyright. In some ways, courts identify an asset as an idea precisely because it facilitates wide downstream productivity. See Lee, *Infrastructure*, *supra* note .

These themes of keeping foundational assets in the public domain as well as a purposive approach to identifying them found greater expression in *Mayo v. Collaborative Servs. v. Prometheus Labs.*¹⁶⁰ Substantively, *Mayo* relates more directly to *Myriad Genetics*, as it addressed the patentability of a method of optimizing the therapeutic efficacy of a drug. The method comprised administering a drug to a patient and determining the amount of metabolite in the patient's blood, wherein various concentration thresholds indicated either the likelihood of deleterious side effects or a lack of therapeutic effectiveness. In describing subject matter exclusions from patent eligibility,¹⁶¹ the Court expressed themes of preemption and fundamentality. Regarding preemption, the inability to invent around claims to gene sequences and associations between sequences and disease heightened prudential interest in keeping these assets in the public domain.¹⁶² Regarding fundamentality, the *Mayo* court reiterates articulates concerns with maintaining wide access to productivity-facilitating assets. It cites precedent characterizing laws of nature as “the basic tools of scientific and technological work”¹⁶³ and cautions that “monopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it.”¹⁶⁴ Underlying the subject matter exclusion for laws of nature is a *functional* concern that considers the amount of future innovation foreclosed in comparison to the contribution of the inventor.¹⁶⁵

In addition to reiterating the importance of excluding laws of nature from patentability, *Mayo* also enables significant flexibility in defining what constitutes a law of nature. A principal challenge is identifying when enough transformation or manipulation has occurred such that an application of a natural law passes the threshold to becoming patent eligible subject matter.¹⁶⁶ Drawing from earlier precedent, the Court identifies that “something more” as an “‘inventive concept,’ sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself.”¹⁶⁷ However, the Court does not define what constitutes “enough,”¹⁶⁸ thus leaving ample room for flexibility and discretion.

Indeed, one of the most important legacies of *Mayo* is the Court's expansive and malleable conception of nature. In the Court's analysis, “Prometheus” patents set forth laws of nature—namely, relationships between concentrations of certain metabolites in

¹⁶⁰ 132 S.Ct. 1289.

¹⁶¹ 132 S.Ct. at 1293 (citing 450 U.S. 175, 185 (1981)).

¹⁶² Dreyfuss & Evans, *supra* note , at 1371.

¹⁶³ 132 S.Ct. at 1301; Benson, 95 S.Ct. at 253.

¹⁶⁴ 132 S.Ct. at 1293; see *id.* at 1301 (“[T]here is a danger that granting patents that tie up their use will inhibit future innovation premised upon them.”); *id.* at 1301 (“The Court has repeatedly emphasized this last mentioned concern, a concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature.”); see also *LabCorp v. Metabolite Labs., Inc.* 548 U.S. 124, 126 (2005) (“[S]ometimes *too much* patent protection can impede rather than ‘promote the Progress of Science and useful Arts’”) (Breyer, J., dissenting from dismissal of writ of certiorari).

¹⁶⁵ 132 S.Ct. at 1303.

¹⁶⁶ 132 S.Ct. at 1294.

¹⁶⁷ 132 S.Ct. at 1294.

¹⁶⁸ Bernard Chao, *Moderating Mayo*, 107 Nw. L. Rev. 423, 424-25 (2012).

the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm.”¹⁶⁹ However, the Court recognizes that this is a very narrow conception of a law of nature.¹⁷⁰ The specific correlation of thiopurine metabolite levels and therapeutic efficacy seems to be a far cry from more conventional, general laws of nature such as $E=MC^2$. Furthermore, the Court makes the rather curious statement that the relationship between thiopurine and either toxic side effects or lack of efficacy “exists in principle apart from any human action.”¹⁷¹ Arguably, however, this relationship is not a natural law at all, given that the starting point of the process is a synthetic drug—thiopurine.¹⁷² Accordingly, one of *Mayo*’s real doctrinal innovations is the expansive manner in which the Court defined nature.¹⁷³ According to Rebecca Eisenberg, “The decision could be read as expanding the scope of what is a natural law or natural phenomenon ... The court’s conception of natural phenomena and natural law is huge.”¹⁷⁴

This strong interest in preventing patents on nature, as well as a proclivity to define nature flexibly and expansively, continued in *Myriad* itself. In a sense, *Myriad* culminates contemporary interpretations of the three traditional categories of nonpatentable subject matter: *Bilski* addresses abstract ideas, *Mayo* addresses laws of nature, and *Myriad Genetics* is (largely) framed in terms of physical phenomena.¹⁷⁵ Curiously, the opinion does not directly address the factual relationship of *Myriad Genetics*’ patents to the facts of *Mayo*.¹⁷⁶ However, the opinion situates its legal analysis firmly within the doctrinal and conceptual framework articulated by *Mayo*, expressing a strong prudential interest in maintaining a zone of nonpatentability for nature. It observes that that “laws of nature, natural phenomena, and abstract ideas” are ineligible for patenting because they comprise “basic tools of scientific and technological work.”¹⁷⁷

¹⁶⁹ 132 S.Ct. at 1296.

¹⁷⁰ 132 S.Ct. at 1302 (“The laws of nature at issue here are narrow laws that may have limited applications, but the patent claims that embody them nonetheless implicate this concern.”).

¹⁷¹ 132 S.Ct. at 1297; cf. Rebecca S. Eisenberg, *Prometheus Rebound: Diagnostics, Nature, and Mathematical Algorithms*, 122 Yale L.J. Online 341, 343 (2013) [hereinafter Eisenberg, *Prometheus Rebound*].

¹⁷² See Christopher Holman, *Preliminary Thoughts on the Implications of Prometheus v. Mayo for Biotechnology*, Genetic Engineering & Biotechnology News, Apr. 3, 2012 (“Of course, the correlation does not exist naturally, but only as a consequence of introducing a non-naturally occurring, man-made molecule into the human body.”).

¹⁷³ Eisenberg, *Prometheus Rebound*, supra note , at 342 (2013).

¹⁷⁴ Steven Seidenberg, *New Laws of Nature Law*, ABA Journal, July 2012, at 21 (quoting Rebecca Eisenberg). Interestingly, the Court briefly addresses the issue of whether the patent eligibility of natural correlations will impact the progress of diagnostic research. 132 S.Ct. at 1304. It recites familiar arguments about both the need to recoup research expenses as well as the dangers of patent thickets. 132 S.Ct. at 1304-05. The Court concludes by saying that it “need not determine here whether, from a policy perspective, increased protection for discoveries of diagnostic laws of nature is desirable.” 132 S.Ct. at 1305. The Court appears to be slightly disingenuous, however, as its analysis suggests that the absence of patent protection over natural correlations may best promote scientific progress.

¹⁷⁵ There is some ambiguity here. At times, the Court characterizes *Myriad*’s claimed isolated DNA as a “product of nature” and “naturally occurring phenomena.” Id. at 2111, 2116. At other times, it characterizes *Myriad*’s invention as encompassing a “law of nature.” Id. at 2117.

¹⁷⁶ As Dan Burk observes, this is particularly odd because the Supreme Court had earlier remanded *Myriad* to the Federal Circuit for reconsideration in light of *Mayo*. See Dan L. Burk, *The Curious Incident of the Supreme Court in Myriad Genetics 3* (2014).

¹⁷⁷ 133 S.Ct. at 2116.

Subjecting these resources to exclusive rights would subvert the goals of the patent system by “inhibit[ing] future innovation premised on them”¹⁷⁸ This is a further articulation of a functional, productivity-based view of subject matter exclusions evident in *Mayo*.

The recognition that natural laws and natural phenomena should not be eligible for patenting still leaves the question of defining what exactly nature comprises. In this regard, the Court notably stretches the definition of Myriad’s invention so that it could qualify for a subject matter exclusion. Describing Myriad’s isolated DNA claims, the Court states, “In this case . . . Myriad did not create anything. To be sure, it found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention.”¹⁷⁹ This characterization, however, flies in the face of decades of granting patents on isolated DNA and centuries of precedent indicating that isolations and purifications of natural products may cross the threshold to become patent eligible. The Court, however, rather cursorily dismisses the importance of PTO practice, citing among other reasons the Solicitor General’s recent change of position on the patent eligibility of isolated DNA.¹⁸⁰ Perhaps more remarkably, the Court does not address longstanding precedent holding that isolations and purifications of natural substances may be eligible for patenting. In the venerable case of *Parke-Davis & Co. v. H.K. Mulford Co.*, Judge Learned Hand ruled that a purified and extracted form of human adrenaline was eligible for patenting.¹⁸¹ This and other cases¹⁸² have provided doctrinal justification for decades of patents on isolated DNA, but the Court does not mention them. The Court simply states that because Myriad did not add “enough” to the discovery of the BRCA 1 and BRCA 2 genes, it could not claim the correlative isolated DNA as patent-eligible inventions.¹⁸³

Indeed, the Court takes great pains to characterize Myriad’s claimed invention as not meaningfully distinguishable from nature itself. Regarding isolated DNA, the Court compares Myriad’s contribution to that of the nominal inventor in *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, in which the court rejected the patentability of a composition of naturally occurring bacteria.¹⁸⁴ The Court noted that the “invention” in *Funk Bros.* fell within the law of nature exception, and so does Myriad’s.¹⁸⁵ From a factual standpoint, however, it is unclear that isolated DNA is more similar to the patent ineligible composition at issue in *Funk Bros.* rather than the patent eligible isolations and purifications of *Parke-Davis*.

The oddity of the Court’s reasoning is even more apparent in light of its discussion of Myriad’s cDNA claims. The Court observes that “the lab technician

¹⁷⁸ 133 S.Ct. at 2116.

¹⁷⁹ 133 S.Ct. at 2117.

¹⁸⁰ 133 S.Ct. at 2118-19.

¹⁸¹ 189 F. 95 (S.D.N.Y. 1911).

¹⁸² See, e.g., *Merck & Co., Inc. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958).

¹⁸³ See 133 S.Ct. at 2117; cf. *Amgen Inc. v. Chugai Pharms. Co. Ltd.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991) (holding that conception of a purified and isolated DNA sequence occurs when the gene is isolated).

¹⁸⁴ 333 U.S. 127 (1948).

¹⁸⁵ 133 S.Ct. at 2117.

unquestionably creates something new when cDNA is made.”¹⁸⁶ This reasoning could apply equally well to isolating DNA from its genomic context, which also involves the breaking of chemical bonds. However, the Court never explains why snipping nucleotides to make cDNA makes “something new” while snipping nucleotides to make isolated DNA does not. Commentators have rightfully criticized the decision as internally inconsistent.¹⁸⁷

Crucial to the Court’s reasoning was its characterization of isolated DNA as an informational rather than chemical entity. The Court states that “Myriad’s claims are simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA.”¹⁸⁸ Rather, the opinion states that Myriad’s “claim is concerned primarily with the information contained in the genetic sequences, not with the specific chemical composition of a particular molecule.”¹⁸⁹ This is a significant (re)characterization of Myriad’s claimed invention. Myriad’s patent clearly claims chemicals, isolated DNA, albeit ones with valuable informational attributes. Nonetheless, the court states that “genes and the information they encode are not patent eligible under § 101 simply because they have been isolated from the surrounding genetic material.”¹⁹⁰ This may be an example of what Christopher Holman describes as “genetic exceptionalism,” in which lay observers (such as Supreme Court justices) view genes in a different light than their chemical nature and apply specialized rules accordingly.¹⁹¹ Furthermore, this emphasis on information would seem to apply equally well to cDNA, which is valuable for its informational properties, yet the Court regards it as patentable subject matter. Ultimately, *Myriad* reflects both a strong emphasis on maintaining the nonpatentability of nature as well as broad judicial discretion in defining what comprises nature.

Before considering the implications of these trends for research, it is interesting to note that these principles continue in the Supreme Court’s most recent patent eligibility case. In *Alice Corp. v. CLS Bank Int’l*, the Court addressed the patent eligibility of method and system claims encompassing a computerized scheme for mitigating “settlement risk” in financial transactions.¹⁹² *Alice* reiterates the familiar preemption

¹⁸⁶ 133 S.Ct. at 2119.

¹⁸⁷ Indeed, AMP argued that “[t]here is no scientific or legal distinction between isolated genomic DNA and cDNA that warrants treating their patent eligibility differently.” AMP Brief, *supra* note , at 50; see also Arti K. Rai & Robert Cook-Deegan, Moving Beyond “Isolated” Gene Patents, 341 Science 137, 137 (2013) (“The Court’s analysis does not connect the dots as to why claims to information in the form of cDNA are less problematic than claims to information in the form of gDNA.”).

¹⁸⁸ 133 S.Ct. at 2118.

¹⁸⁹ 133 S.Ct. at 2118.

¹⁹⁰ 133 S.Ct. at 2120. This view, of course, is not without support. See, e.g., Arti Rai Addressing the Patent Gold Rush: The Role of Deference to PTO Patent Denials, 2 Wash. U. J.L. & Pol’y 199, 204 (2000) (describing genes as “carriers of information”); Justine Pila, Bound Futures: Patent Law and Modern Biotechnology, 9 B.U. J. Sci. & Tech. L. 326, 337 (2003); Jordan Paradise et al., Patents on Human Genes: An Analysis of Scope and Claims, 307 Science 1566, 1566 (2005) (“In the case of a human gene sequence . . . the ‘invention’ is the sequence.”).

¹⁹¹ Holman, Impact, *supra* note , at 360.

¹⁹² 134 S.Ct. 2347, 2351-52 (2014). Settlement risk refers to the risk that a party to a financial transaction will not follow through on its obligations.

rationale for the common law exclusions of laws of nature, natural phenomena, and abstract ideas from patentable subject matter.¹⁹³ Additionally, it acknowledges the difficulty of clearly identifying these entities,¹⁹⁴ and it articulates a two-part framework for patent eligibility analyses based on *Mayo*. First, courts must ascertain whether a patent claim covers one of the three patent-ineligible concepts. Second, it must determine whether there is something more—an inventive concept—that elevates the claim beyond simply a claim on the patent-ineligible concept.¹⁹⁵ Although the Court emphasizes that patentable subject matter analyses are not a “like a nose of wax which may be turned and twisted in any direction,”¹⁹⁶ it provides little concrete guidance for determining when exactly a claim contains “enough” to render it eligible for patenting. The Court’s patentable subject matter jurisprudence ensures that the “nose of wax” remains quite malleable.

These twin principles of excluding nature from patentable subject matter and allowing significant judicial discretion to define nature have significant long-term implications for research. Nature, after all, is the principal object of study for scientific research, and *Myriad* and its related cases create more doctrinal room to challenge patents that approach natural phenomena. First, these cases help affirm that productivity concerns—such as the potential gains of unfettered research—are legitimate factors that can inform the contours of patentable subject matter. Within this narrative of promoting productivity, nature assumes an almost talismanic quality. Nature is both impossible to invent around (thus raising preemption concerns) and generative of significant downstream productivity. *Myriad* and its doctrinal siblings create more opportunity for courts and litigants to challenge patents that they can frame as encompassing nature. Second and relatedly, *Myriad* reflects significant discretion and flexibility in characterizing as natural laws or natural products. The decision draws rather questionable distinctions between nonpatent-eligible natural phenomena and patent-eligible technologies, a practice that litigants may now be emboldened to emulate. Going forward, appeals to nature and the natural may have deep rhetorical force in arguments before the Supreme Court.¹⁹⁷ As one commentator observes, “[T]he Supreme Court positioned medical genetics under the framework of natural resource law and, in effect, recast medical genetics as an extractive, rather than inventive, industry.”¹⁹⁸ The notion that one merely extracts rather than invents isolated DNA helped undergird the Court’s decision that it is not patentable subject matter.¹⁹⁹

In concrete terms, the Court’s reasoning on isolated DNA also casts doubt on the patent eligibility of a host of assets of high research interest. In the pharmaceutical industry, many important drugs (that are currently patented) are derived from molecules

¹⁹³ 134 S.Ct. at 2354.

¹⁹⁴ 134 S.Ct. at 2354.

¹⁹⁵ 134 S.Ct. at 2355.

¹⁹⁶ 134 S.Ct. at 2360.

¹⁹⁷ Cf. Jason Karlawish, *Your Genes Are Not for Sale*, Science Progress, June 24, 2013, at <http://scienceprogress.org/2013/06/your-genes-not-for-sale/>.

¹⁹⁸ Barbara J. Evans, *Mining the Human Genome after Association for Molecular Pathology v. Myriad Genetics*, 16 *Genetics in Medicine* 504, 504 (2014).

¹⁹⁹ 133 S.Ct. at 2117.

isolated from their natural context.²⁰⁰ For example, the immune suppressor rapamycin is isolated from the bacterium *Streptomyces hygroscopicus*.²⁰¹ *Myriad* creates greater opportunity to challenge such patents on the theory that the inventor has not added “enough” to differentiate them from natural products. As another example, many nanotechnology patents cover compositions of matter isolated from natural products.²⁰² For instance, scientists create carbon nanotubes by isolating them from graphite; the Court’s holding raises doubt as to whether such nanotubes are patentable subject matter.²⁰³ Of course, the relevance of *Myriad* to such contexts is mitigated to the extent that it was a relatively narrow case dealing with isolated DNA. The Court emphasized that *Myriad* claimed isolated DNA in the context of their informational content (their sequence) rather than as chemical compositions.²⁰⁴ Nevertheless, this is largely an issue of framing, and patents on assets close to recognizable elements of nature are more vulnerable following *Myriad*.

Of course, as discussed above, it is not immediately clear whether the reduced likelihood of patent eligibility for assets characterized as nature is a net positive or negative development for research. The familiar narrative of patent law applies here as elsewhere, and perhaps patent protection for isolated DNA, medicines derived from natural products, and nanotubes would enhance incentives to conduct research in these areas, particularly for patentees. Alternatively, perhaps the absence of patent protection following *Mayo* will lead to a net gain in research, as scientists have greater freedom to study these resources. As a corollary, perhaps the availability of patent protection for more “downstream” applications closer to the market will preserve adequate commercial incentives for research while still leaving ample room for unfettered upstream scientific inquiry. Of course, determining which of these narratives more closely reflects reality is a complicated empirical question that is likely to be highly contextually sensitive. *Myriad* and its related cases, however, send a consistent message that the Court believes in the latter stories, and it is increasingly sensitive to the threat that patents in certain realms inhibit rather than promote the progress of science and useful arts.²⁰⁵

²⁰⁰ Seidenberg, supra note .

²⁰¹ Seidenberg, supra note . But see Rai & Cook-Deegan, supra note , at 138 (noting that rapamycin was claimed in terms of chemical structure—rather than informational content—and might thus avoid analogy to the isolated DNA claimed in *Myriad*).

²⁰² Seidenberg, supra note .

²⁰³ Seidenberg, supra note .

²⁰⁴ Among other implications, this suggests a more expansive conception of patent eligibility for chemicals claimed qua chemicals. See Seidenberg, supra note (“The Supreme Court seemed to express a more favorable view of patents on ‘specific chemical compositions.’”) (quoting Professor Arti Rai, Duke Law School).

²⁰⁵ In this regard, it is useful to place *Myriad* and other decisions narrowing patentable subject matter within the broader context of patent cases that tend to narrow patentability, or at least push it downstream toward the more commercial end of the R&D spectrum. See, e.g., *KSR v. Teleflex*, 550 U.S. 398 (2007) (raising the nonobvious requirement of patentability); *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009) (applying *KSR* to invalidate a patent on isolated DNA as obvious to try); *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) (holding that claims covering cDNA that produced insulin in all vertebrates and mammals were invalid in light of written description that only described cDNA that produced insulin in rats); *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*, 598 F.3d 1336 (Fed. Cir. 2010) (en banc) (denying the patentability of a foundational molecular pathway on written description grounds); *id.* at 1353 (“Much university research relates to basic research, including research into scientific principles

Ultimately, this analysis reaffirms the importance of definitions in the debate over the impact of patentable subject matter and scientific research. Earlier, we saw how differing and nuanced definitions of “noncommercial research use” complicated the question over whether Myriad’s isolated DNA patents threatened BRCA research. Furthermore, empirical arguments that gene patents and anticommons only chill diagnostic testing of genes obscure the important research value of such testing. In the doctrinal context, courts exercise significant discretion in determining whether certain foundational assets satisfy the definition of natural laws or physical phenomena. Whether and how patent law affects scientific research is largely a question of how one defines the terms of the debate.

PART IV. ONGOING CHALLENGES AND LONG-TERM RAMIFICATIONS

Although *Myriad* has both short-term and long-term implications for the intersection of patents and research, it leaves significant issues unaddressed. From the perspective of plaintiffs seeking wider access to BRCA testing, the Supreme Court’s invalidation of Myriad’s isolated DNA patents was only a partial victory. Although several firms began offering diagnostic testing following the Court’s decision, Myriad promptly sued them for infringement. Although a court is still adjudicating one of these cases,²⁰⁶ the prospect that Myriad still exercises considerable intellectual property over BRCA testing suggests that more widespread testing—and the research gains that it produces—may be more slow in coming. Additionally, Myriad Genetics maintains an extensive database of BRCA mutations including over 300,000 cases.²⁰⁷ Although the Court’s ruling on patentable subject matter does not address the database directly, it became an issue in the litigation. According to plaintiffs, “[b]ecause the patents have authorized Myriad to maintain a monopoly on clinical testing, they have permitted Myriad to control huge amounts of data on the nature and significance of variants in the BRCA 1 and BRCA 2 genes.”²⁰⁸ The inability of outside researchers to access this database prevents them from independently characterizing missense variants. This database, which Myriad developed over the course of its patents, may be its “most valuable asset,” and it represents an important research resource that is not fully open to the scientific community.²⁰⁹ In the short term, there is little that patent doctrine could do

and mechanisms of action, and universities may not have the resources or inclination to work out the practical implications of all such research, i.e., finding and identifying compounds able to affect the mechanism discovered. That is no failure of the law’s interpretation, but its intention.”); *Eli v. Medtronic*, 496 U.S. 661 (1990) (interpreting a statutory exemption from patent infringement to apply to certain research on medical devices); *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 193 (2005) (applying that same statutory exemption from patent infringement to apply to preclinical research reasonably related to information submissions to the Food and Drug Agency).

²⁰⁶ See *supra* notes – and accompanying text.

²⁰⁷ Offit et al., *supra* note , at 2746; Robert Nussbaum, *Corporate Genetics: Even Without Gene Patents, Companies are Monopolizing Genetic Data*, MIT Tech. Rev., Aug 21, 2013.

²⁰⁸ AMP Brief, *supra* note , at 47.

²⁰⁹ Conley, *supra* note ; see Krench, *supra* note (“By sharing the rich dataset Myriad has collected from patients, collaborative research efforts from many labs could lead to better cancer detection and treatments.”); Rai & Cook-Deegan, *supra* note , at 138 (“Keeping data proprietary confers an advantage

to enhance access to this resource. In the long term, however, more widespread BRCA testing would enable the emergence of nonproprietary, open databases which all researchers could access.

From the macroscopic perspective of reconciling patents with research, the Supreme Court's invalidation of Myriad's isolated DNA patents represents just one piece of a very large policy puzzle. As noted, patentable subject matter is but one doctrinal lever among many (and perhaps not even the optimal one) for regulating patents in the context of scientific research. Other policy tools, such as nonobviousness and the written description requirement, may represent more granular regulatory mechanisms.²¹⁰ Additionally, policy levers outside of traditional patent doctrine are also available to forge a better balance between research and exclusive rights. Here, the ecosystem of innovation is highly relevant, as much research that produces gene patents arises from federally-funded, academic research.²¹¹ Indeed, NIH contributed about \$4.6 million to the research leading to the sequencing of BRCA 1 and engaged in an inventorship dispute with the University of Utah and Myriad Genetics.²¹²

Public funding and the Bayh-Dole Act may provide another route to regulate the intersection of patents and research.²¹³ Under the Bayh-Dole Act, which allows recipients of public funds to patent the results of federally-funded research, NIH maintains certain rights in subject inventions.²¹⁴ In theory, government rights in Myriad Genetics' isolated DNA patents as well as other federally-funded inventions provide another route for enhancing access to such resources for research purposes.²¹⁵ Although these rights are difficult to assert,²¹⁶ any macroscopic approach to balancing patents and open science should take them into account. Statutory reforms also a possibility, such as the proposed 2007 Genomic Research and Accessibility Act, which would have prohibited the patenting of any "nucleotide sequence or its functions or correlations, or the naturally occurring products it specifies."²¹⁷ Although this act was overly broad and rightfully rejected, other jurisdictions have devised more measured, targeted approaches. For instance, France, Belgium, and Switzerland authorize compulsory licensing of diagnostic patents.²¹⁸ In sum, legal and regulatory mechanisms beyond traditional patent doctrine may also help reconcile patents and research interests.

Ultimately, perhaps the most enduring legacy of *Myriad* for the intersection of patents and research is a deep policy-oriented pragmatism framed in doctrine and science.

when interpreting the small percentage of *BRCA* test results whose clinical importance cannot be discerned from public data sources.").

²¹⁰ See *supra* note – and accompanying text.

²¹¹ Cf. Hopkins & Hogarth, *supra* note , at 500.

²¹² Robert Dalpe et al., Watching the Race to Find the Breast Cancer Genes, 28 *Sci. Tech. & Human Values* 187, 196 (2003).

²¹³ See Lee, Open Science, *supra* note .

²¹⁴ 35 U.S.C. § 200-212; see Lee, Open Science, *supra* note , at 921-24.

²¹⁵ See Lee, Open Science, *supra* note .

²¹⁶ Rai & Eisenberg, *supra* note , at 310.

²¹⁷ H.R. 977, 110th Cong. (2007).

²¹⁸ Hopkins & Hogarth, *supra* note , at 498.

In addition to desiring to clarify patentable subject matter, the Supreme Court likely granted certiorari in *Myriad* because of the enormous political, social, and economic interests at stake, which spanned women's health, access to diagnostics, breast cancer research, and the business model of the biotechnology industry. The result achieved by the Court is not particularly doctrinally or scientifically rigorous, especially its distinctions between isolated DNA and cDNA. Nonetheless, it reflects a pragmatic middle ground. Isolated DNA, which is most relevant for diagnostic and research purposes, is no longer patentable subject matter, but cDNA, which is more closely tied to commercial therapeutics, remains eligible for patenting. Doctrine and science stand as potential stumbling block to these pragmatic and political compromises, and the Court did its best to reconcile its novel distinctions with these authorities.²¹⁹

This type of pragmatism has a long history in patent law.²²⁰ It even manifested itself in earlier stages of the *Myriad* litigation at the Federal Circuit, when Judge Moore cautioned that patentable subject matter should be sensitive to the “settled expectations of the biotechnology industry.”²²¹ In past generations, pragmatic considerations and the needs of industry contributed to judicial innovations that increased patenting. For example, Judge Learned Hand's epochal holding in *Parke Davis* that purified adrenaline constituted patentable subject matter substantially benefitted the nascent U.S. chemical industry.²²² In the contemporary landscape, the pendulum appears to have swung in the opposite direction. Perhaps attentive to growing concerns over the anticommons and patent holdup, the *Myriad* court consistently emphasized that upstream patents may ultimately subvert rather than promote downstream progress, including scientific research. This is evident in the Court's concern with “the considerable danger that the grant of patents would ‘tie up’ the use of tools and thereby ‘inhibit future innovation premised upon them.’”²²³ After all, “[p]atent protection strikes a delicate balance between creating ‘incentives that lead to creation, invention, and discovery’ and ‘imped[ing] the flow of information that might permit, indeed spur, invention.’”²²⁴ Balancing these interests in light of the circumstances of the case and patent law more generally, the Court narrowed patentable subject matter. Whether or not the Court is ultimately correct in its analysis, its opinion reflects a willingness to frame existing law and science to achieve practical objectives. Ultimately, the longstanding impact of the *Myriad* on research hinges considerably on one's institutional confidence in courts to get the policy balance right.

²¹⁹ However, in his notable concurrence, Justice Scalia refused to join the portions of the majority opinion discussing the details of molecular biology because he was “unable to affirm those details on my own knowledge or even on my own belief.” *Ass'n for Molecular Pathology v. Myriad Genetics*, 133 S.Ct. 2107, 2120 (Scalia, J., concurring in part and concurring in the judgment).

²²⁰ Pila, *supra* note , at 339 (“[T]he success of patent law's accommodation of modern biotechnology ultimately reflects the success of legal expediency over legal reasoning.”).

²²¹ *Ass'n for Molecular Pathology v. United States Patent and Trademark Office*, 653 F.3d 1329, 1368 (Fed. Cir. 2011) (Moore, J., concurring-in-part).

²²² See Graham Dutfield, *Intellectual Property Rights and the Life Sciences Industries* 85-89, 108-09 (World Scientific, 2d. ed. 2000).

²²³ *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, (2013) (quoting *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1301 (2012)).

²²⁴ *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2116 (2013) (quoting *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1305 (2012)).

CONCLUSION

The Supreme Court's decision in *Myriad* has several significant and underappreciated implications for the intersection of patents and research. Part of the complexity of this issue has to do with ambiguous and subjective definitions of the terms of debate. This Article has elucidated the impact of *Myriad* on research on three levels. First, on the immediate level of BRCA research, *Myriad* creates more actual and perceived freedom to operate for scientists working with isolated DNA. Although Myriad Genetics maintains that it always had a permissive policy toward noncommercial research, it defined this policy rather opaquely and did not effectively communicate its stance to the research community. Scientists were chilled in their research pursuits, particularly in light of Myriad's high-profile threats of enforcement against GDL. More importantly, there is no bright line separating diagnostic and research uses of the BRCA gene, for the former substantially inform the latter. To the extent that *Myriad* leads to more diagnostic testing for BRCA mutations, it will generate new research insights.

This phenomenon, moreover, extends beyond BRCA research. Although fears of patent holdup and the tragedy of the anticommons initially attracted significant attention, empirical research has found little direct evidence of inhibitory effects in the research sphere. This further suggests that the invalidation of those patents is not particularly significant for promoting scientific inquiry. An important exception, however, is diagnostics, where patentees have not refrained from enforcing their exclusive rights. In this context, the Court's holding that isolated DNA is not patentable subject matter is likely to increase diagnostic testing for a host of genes related to other conditions. And given that diagnostic testing generates scientific knowledge, such use has meaningful research benefits.

Beyond these effects, *Myriad* reflects a trend in patent doctrine that may have long-term implications for the intersection of patents and research. *Myriad* and its related cases evidence both a strong prudential interest in keeping "nature" outside the domain of patent eligibility as well as a high degree of discretion in defining what comprises nature. The flexible nature of the Court's patentable subject matter test leaves ample room to bend doctrine and science to advance broader policy objectives related to promoting productivity. Such flexibility creates more opportunity to challenge patents in research science going forward. Whether or not this ultimately helps or harms scientific research depends on one's confidence in courts to strike the right policy balances in their patent jurisprudence.