

# UNLOCKING THE GENOME: THE LEGAL CASE AGAINST GENETIC DIAGNOSTIC PATENTS

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## I. INTRODUCTION

We are on the leading edge of a true revolution in medicine, one that promises to transform the traditional ‘one size fits all’ approach into a much more powerful strategy that considers each individual as unique and as having special characteristics that should guide an approach to staying healthy. Although the scientific details to back up these broad claims are still evolving, the outline of a dramatic paradigm shift is coming into focus.<sup>1</sup>

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1. FRANCIS S. COLLINS, THE LANGUAGE OF LIFE: DNA AND THE REVOLUTION IN PERSONALIZED MEDICINE xxiii–xxiv (2010).

The growth of personalized medicine, which aims to better customize and target treatments to patients through the use of information about an individual's genes, proteins, and environment, is changing the healthcare industry and holds tremendous potential to improve patients' lives. The medical diagnostics field is a key attribute of personalized medicine, as simple tests measuring levels of proteins, genes, or mutations can be performed on patients to optimize specific therapies for that individual's condition. In many cases, this individualized treatment avoids costly, unnecessary, and potentially dangerous procedures.

Within the medical diagnostics field, genetic diagnostic methods are rapidly changing the way diseases are diagnosed, prevented, and treated. The ability to link genetic mutations to specific diseases can lead to improved diagnostics, higher quality health care and, in some instances, life-saving treatments. Current estimates place the number of inheritable diseases stemming from mutated genes at four thousand.<sup>2</sup> Thus far, genetic information has been used to assist physicians in individualizing treatments for their patients in a variety of contexts. And, "most of the promise offered by the sequencing of the human genome still lies ahead."<sup>3</sup>

Although personalized medicine remains in its early stages, its potential to improve patients' lives cannot be overstated. However, translating this seemingly limitless scientific revolution into tangible benefits for patients and ensuring that these discoveries are accessible on reasonable and fair terms to patients promises to be a difficult challenge. As our understanding of the linkages between genetic mutations and diseases has grown, so has a heated debate over whether patents on genes are deserving of patent protection. Currently, genetic diagnostic methods can be broadly claimed in a patent.<sup>4</sup> These diagnostic gene patents typically involve the process of comparing a particular portion of a patient's genetic sequence to a wild-type or mutation sequence in order to diagnose a genetic predisposition or disease. These patents oftentimes claim every single known and possible method for looking at the DNA sequence, including many of

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2. Biotechnology Industry Organization, National Issues, Intellectual Property, available at <http://web.archive.org/web/20101119211310/http://bio.org/ip/primer/genehelps.asp> (last visited Sept. 7, 2011).

3. COLLINS, *supra* note 1, at 3.

4. *Metabolite Labs. Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1361–66 (Fed. Cir. 2004).

the standard processes regularly employed in the field. Over the past few decades, the U.S. Patent and Trademark Office (PTO) has granted thousands of patents on human genes, many of these directed towards diagnostic methods. Presently, patents are held on diagnostic tests tied to a wide array of diseases including prostate cancer,<sup>5</sup> HIV/AIDS,<sup>6</sup> breast cancer,<sup>7</sup> ovarian cancer,<sup>8</sup> and vitamin B deficiencies.<sup>9</sup> Half of the genes known to be connected to cancer are already patented, and one company alone holds patents on approximately ten percent of the human genome. Whether such advanced diagnostic methods should be afforded patent protection is of increasing significance as our understanding of the makeup of the human genome grows.

The wisdom of patenting genetic diagnostic methods, particularly whether or not such patents promote or prevent medical and scientific advancements, is a hotly debated issue. Supporters of such patents argue that they are deserving of patent protection because they accelerate scientific discoveries and improve medical care by incentivizing investment into research. Critics of patents held on diagnostic methods argue that many of these patents actually fall within the judicial exceptions to patentable subject matter because they claim such patents are laws of nature, natural phenomena, or abstract ideas. They advance numerous policy arguments against them as well, namely that they are unnecessary to motivate innovation and commercialization, that they have a chilling effect on medical and scientific research, and that they result in a lower standard of medical care. Because patents provide the ability to extract monopoly rent, in cases where those rents are beyond what is necessary to encourage innovation, overbroad patent protection comes with very real costs both to consumers and innovation.

This paper examines whether genetic diagnostic patents constitute patentable subject matter under 35 U.S.C. § 101. Part II examines the jurisprudence surrounding the boundaries of patentable subject matter. Part III presents a brief background on the science of genetics and the history of gene patents. Part III also traces the litigation in *Association for Molecular Pathology v. United States Patent and Trademark Office*, and concludes by arguing that diagnostic genetic patents, as well as

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5. U.S. Patent No. 5,840,501 (filed July 31, 1997).

6. U.S. Patent No. 5,838,352 (filed Dec. 16, 2003).

7. U.S. Patent No. 5,709,999 (filed June 7, 1995).

8. U.S. Patent No. 4,968,603 (filed Dec. 31, 1986).

9. U.S. Patent No. 4,940,658 (filed Nov. 20, 1986).

other advanced diagnostic method patents, constitute non-patentable subject matter under 35 U.S.C. § 101. Part IV presents several policy arguments against granting patents on diagnostic methods.

## II. PATENTING PROCESSES

The courts have struggled in determining the proper boundaries for patentable subject matter, particularly when applied to process patents. The Constitution grants Congress broad power to legislate to “promote the [p]rogress of [s]cience and useful [a]rts, by securing for limited [t]imes to [a]uthors and [i]nventors the exclusive [r]ight to their respective [w]ritings and [d]iscoveries.”<sup>10</sup> Patents promote scientific progress by offering inventors a monopoly for a limited period of time in order to incentivize innovation.<sup>11</sup> Patents can be obtained for several types of inventions, including a process, machine, manufacture, or composition of matter.<sup>12</sup> Patent-holders have the absolute right to exclude others from making, using, or selling their invention for twenty years after the application for the patent is filed.<sup>13</sup> Properly employed, patents incentivize innovation, promote the disclosure of information, and offer protection for commercialization. However, patent law necessitates a careful balancing between promoting innovation while not stifling scientific research and development. In some cases, “*too much* patent protection can impede rather than ‘promote the Progress of Science and useful Arts,’ the constitutional objective of patent and copyright protection.”<sup>14</sup>

Thus, in order to receive the Patent Act’s protection, a claimed invention must be novel,<sup>15</sup> nonobvious,<sup>16</sup> and fully and particularly described.<sup>17</sup> However, before a court may even turn to these requirements, it must first determine the threshold issue of whether the invention for which patent protection is sought is patentable subject matter under 35 U.S.C. § 101.<sup>18</sup> While patent protection may be applied

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10. U.S. CONST., art.1, § 8, cl. 8.

11. *Diamond v. Chakrabarty*, 447 U.S. 303, 307 (1980).

12. 35 U.S.C. § 101 (2006).

13. 35 U.S.C. § 154 (2006).

14. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 126–27 (2006) (Breyer, J., dissenting) (quoting U.S. CONST., art. 1, § 8, cl. 8).

15. 35 U.S.C. § 102 (2006).

16. 35 U.S.C. § 103 (2006).

17. 35 U.S.C. § 112 (2006).

18. The inquiry into an invention’s patent eligibility is a fundamental one, and as such, “[t]he obligation to determine what type of discovery is sought to be patented must precede the determination of whether that discovery is, in fact, new or obvious.” *Parker v. Flook*, 437

to “anything under the sun that is made by man,”<sup>19</sup> this expansive reading is not without its limits. The Supreme Court has recognized three categories of subject matter that fall outside of § 101 and are not patentable: the laws of nature, physical phenomena, and abstract ideas.<sup>20</sup> In explaining the reasoning behind these exceptions, the Supreme Court has noted as follows:

[A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that  $E=mc^2$ ; nor could Newton have patented the law of gravity. Such discoveries are “manifestations of . . . nature, free to all men and reserved exclusively to none.”<sup>21</sup>

The rule that the discovery of a law of nature is unpatentable rests on the understanding that they are not the type of discovery that the patent laws were enacted to protect.<sup>22</sup> These fundamental principles “even when for the first time discovered, have existed throughout time, define the relationship of man to his environment, and, as a consequence, ought not to be the subject of exclusive rights to any one person.”<sup>23</sup> They “are part of the storehouse of knowledge of all men . . . free to all men and reserved exclusively to none.”<sup>24</sup> As Justice Breyer eloquently observed the reasoning behind these exceptions:

The justification for the principle does not lie in any claim that ‘laws of nature’ are obvious, or that their discovery is easy, or that they are not useful. To the contrary, research into such

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U.S. 584, 593 (1978).

19. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (quoting S. Rep. No. 1979, at 6 (1952), *reprinted in* 1952 U.S.C.C.A.N. 2394, 2398, 2409–10). Although often cited, this phrase is somewhat misleading as the full quote, which originally appeared in the legislative history of the Patent Act of 1952, reads “[a] person may have ‘invented’ a machine or a manufacture, which may include anything under the sun made by man, but it is not necessarily patentable under section 101 unless the conditions of [this] title are fulfilled.” S. Rep. No. 1979, at 6 (1952), *reprinted in* 1952 U.S.C.C.A.N. 2394, 2398, 2409–10. In *Bilski v. Kappos*, Justice Stevens reiterated the point that just because a person may have “‘invented’ . . . anything under the sun,” that thing is not necessarily patentable under § 101. 130 S. Ct. 3218, 3249 (2010) (Stevens, J., concurring).

20. *Chakrabarty*, 447 U.S. at 309.

21. *Id.* (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)).

22. *Parker v. Flook*, 437 U.S. 584, 593 (1978).

23. *In re Meyer*, 688 F.2d 789, 795 (C.C.P.A. 1982) (citing *Le Roy v. Tatham*, 55 U.S. 156, 175 (1852)).

24. *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948).

matters may be costly and time consuming; monetary incentives may matter; and the fruits of those incentives and that research may prove of great benefit to the human race. Rather, the reason for this exclusion is that sometimes too much patent protection can impede rather than ‘promote the Progress of Science and useful Arts,’ the constitutional objective of patent and copyright protection.<sup>25</sup>

Unfortunately, the fundamental principles exception can be a difficult standard to apply particularly when assessing the patentability of process claims. A process claim involves any series of steps “to produce a given result.”<sup>26</sup> The prohibition against patenting fundamental principles does not necessitate that all processes which incorporate fundamental principles necessarily fall outside the scope of patent protection.<sup>27</sup> The application of a law of nature in a new and useful way may very well be deserving of patent protection. To find otherwise would, “if carried to its extreme, make all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious.”<sup>28</sup> Rather, whether a method patent constitutes patentable subject matter turns upon whether the patent application attempts to patent a fundamental principle, i.e. a natural correlation, or simply incorporates it into a new and useful process. Unfortunately, determining whether a patent application seeks to incorporate a law of nature into a new and useful series of steps or is an attempt to circumvent the fundamental principles exception through crafty draftsmanship can be a challenging task.

Over the past few decades, the Supreme Court has offered minimal guidance as to how to best determine whether a process patent is drawn to statutory subject matter. Given the Supreme Court’s reticence in this area, the Federal Circuit has been left to wrestle with this issue over the past several decades. In 1998, the Federal Circuit addressed this issue in a case involving business patents—*State Street Bank & Trust Co. v. Signature Financial Group, Inc.*—which held that a “process” claim would be patentable subject matter so long as it provided “a useful,

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25. *Lab. Corp. of Am. Holdings*, 548 U.S. at 126–27 (2006) (Breyer, J., dissenting) (quoting U.S. CONST., art. 1, § 8, cl. 8).

26. *Cochrane v. Deener*, 94 U.S. 780, 788 (1877).

27. *In re Bilski*, 545 F.3d 943, 958 (Fed. Cir. 2008) (citations omitted).

28. *Diamond v. Diehr*, 450 U.S. 175, 189 n.12 (1981).

concrete, and tangible result.”<sup>29</sup> However, this test was later thrown into doubt in dicta penned by Justice Breyer in *Metabolite Labs. Inc. v. Lab. Corp. of Am. Holdings*, when he pointedly critiqued the *State Street* decision, by noting that the Supreme Court “never made such a statement and, if taken literally, the statement would cover instances where this Court has held the contrary.”<sup>30</sup> The Federal Circuit later revisited the issue in *In re Bilski*, and perhaps in an attempt to correct the overly broad standard of *State Street*, articulated a bright-line rule for determining whether a method patent is patent-eligible. In *Bilski*, the Federal Circuit examined whether a business method for using commodity exchange transactions to hedge risks was patentable subject matter.<sup>31</sup> In its decision, the Federal Circuit struggled to outline more definitive guidelines as to what constitutes a patentable process. Acknowledging the inherent tension in applying the fundamental principles exception to process patents, the Federal Circuit stated that any inquiry as to whether a process is patent eligible should seek to “determine whether [the] process claim is tailored narrowly enough to encompass only a particular application of a fundamental principle rather than to pre-empt the principle itself.”<sup>32</sup>

In *Bilski*, the Federal Circuit ultimately adopted the “machine-or-transformation” test as the exclusive test for making this pre-emption decision.<sup>33</sup> Under this test, a claimed process is patent eligible if “(1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.”<sup>34</sup> Furthermore, the transformation “must be central to the purpose of the claimed process”<sup>35</sup> and must not be “insignificant extra-solution activity” or merely a “data-

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29. See *State Street Bank & Trust Co. v. Signature Fin. Group*, 149 F.3d 1368, 1375 (Fed. Cir. 1998) (quoting *In re Alappat*, 33 F.3d 1526, 1544 (Fed. Cir. 1994)).

30. *Lab. Corp. of Am. Holdings*, 548 U.S. at 136.

31. *In re Bilski*, 545 F.3d at 949–51. Claim 1 of the petitioner’s application stated as follows:

A method for managing the consumption of risk costs of a commodity [,] comprising the steps of: (a) initiating a series of transactions between [a] commodity provider and consumers of said commodity . . . ; (b) identifying market participants for said commodity . . . ; (c) initiating a series of transactions between said commodity provider and said market participants . . . such that said series of market participant transactions balances the risk position of said series of consumer transactions.

*Id.* at 949.

32. *Id.* at 954.

33. *Id.* at 966.

34. *Id.* at 954.

35. *Id.* at 962.

gathering step.”<sup>36</sup> Phrased differently, a patentee “cannot rely on the data-gathering steps to prove that the claimed process is transformative and thus drawn to patentable subject matter.”<sup>37</sup>

Last year, the Supreme Court took the case up on appeal, and for the first time since its decision in *Diamond v. Diehr* in 1981, the Supreme Court addressed the boundaries of patentable subject matter in *Bilski v. Kappos*. In an eagerly awaited decision, the Court upheld the Federal Circuit’s decision to strike down the business method patents on the basis that they were attempts to patent abstract ideas while simultaneously overturning the “machine-or-transformation” test as the exclusive means for determining the patent eligibility of processes.<sup>38</sup> Rejecting the Federal Circuit’s exclusive reliance on the “machine-or-transformation” test, the Supreme Court acknowledged that “new technologies may call for new inquiries.”<sup>39</sup> Thus, the machine-or-transformation test, which had been relied upon in numerous cases during the interim, including several cases involving patents on diagnostic methods, is no longer the sole test for determining whether an invention is patentable subject matter under 35 U.S.C. § 101.<sup>40</sup>

The Court did not, however, formulate a new test for determining what constitutes patentable subject matter and chose instead to reiterate the long-standing rule that bars patents for laws of nature, physical phenomena, or abstract ideas. Although some hoped *Bilski* would provide concrete guidance as to when process claims constitute patentable subject matter, the Court ultimately opted for a narrow ruling. Offering minimal guidance as to what other considerations or tests might apply in determining what constitutes a patentable “process,” the Court instead referred back to the language of § 100(b)<sup>41</sup> and its earlier decisions in *Gottschalk v. Benson*, *Parker v. Flook*, and

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36. *Id.* at 963 (providing that “[f]urther, the inherent step of gathering data can also fairly be characterized as insignificant extra-solution activity.”).

37. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1343 (Fed. Cir. 2009), *vacated sub nom.*, *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 130 S. Ct. 3543 (2010) (“stating that mere data-gathering will not ‘at least in most cases, . . . constitute a transformation of any article.’”).

38. *Bilski v. Kappos*, 130 S. Ct. 3218, 3227, 3229 (2010).

39. *Id.* at 3228.

40. *See generally id.*

41. 35 U.S.C. § 100(b) (2006) (Section 100(b) defines a process, in a somewhat circular fashion, as a “process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter or material.”).



*Diamond v. Diehr*.<sup>42</sup> Because, as Justice Stevens pointed out in his concurrence in *Bilski v. Kappos*, the Court “never provides a satisfying account of what constitutes an unpatentable abstract idea,”<sup>43</sup> practitioners and academics are left struggling to define the implications the decision holds. In order to unpack the potential implications *Bilski v. Kappos* may hold for process patents and specifically diagnostic process patents, an overview of the three cases *Bilski* cites is instructive. All three struggle to distinguish between instances when a patent application seeks to patent a fundamental principle and when it simply seeks to incorporate a fundamental principle into a series of steps deserving of patent protection. Indeed, they all struggle with the challenge that “[w]hen a claim contains a natural phenomenon, the court must determine whether the claim is merely seeking to patent the phenomenon itself by describing it in abstract process terms.”<sup>44</sup>

*Gottschalk v. Benson* involved a patent application claiming an algorithm that converted binary-coded decimal numerals into pure binary code.<sup>45</sup> In holding that the application embodied an unpatentable abstract idea, the Court reiterated the fact that patent-eligible processes must include “the application of the law of nature to a new and useful end.”<sup>46</sup> The Court emphasized the fact that the patent application would “wholly pre-empt” the fundamental principle, and in all practicality, would be a patent on the fundamental principle itself.<sup>47</sup>

The theory of preemption is of critical importance in determining the patentability of a process incorporating a fundamental principle and is returned to in the Court’s later decisions. In *Parker v. Flook*, the Court further refined the theory of preemption by holding that a process need not preempt all uses of a fundamental principle in order to fall within the fundamental principles exception. There, the patent at issue was for a method to update an “alarm limit.” The method consisted of three steps: (1) a measurement of a given variable followed by (2) a mathematical calculation to arrive at a new alarm limit value ending with (3) adjustment of the limit to correspond to that new value. The Court further refined the theory of preemption in rejecting the

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42. *Bilski*, 130 S. Ct. at 3222.

43. *Id.* at 3236 (Stevens, J., concurring).

44. *Classen Immunotherapies, Inc. v. Biogen Idec*, 2006 WL 6161856, at \*4 (D. Md.) (citing *Diamond v. Diehr*, 450 U.S. 175, 192 (1981)).

45. *Gottschalk v. Benson*, 409 U.S. 63, 64–71 (1972).

46. *Id.* at 67 (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)).

47. *Id.* at 72.

argument that simply because “all possible uses of the mathematical formula were not pre-empted, the claim should be eligible for patent protection,”<sup>48</sup> noting that, “[a] mathematical formula does not suddenly become patentable subject matter simply by having the applicant acquiesce to limiting the reach of the patent for the formula to a particular technological use. A mathematical formula in the abstract is non-statutory subject matter regardless of whether the patent is intended to cover all uses of the formula or only limited uses.”<sup>49</sup> Furthermore, the Court held that the fact that the mathematical algorithm was followed by the “‘post-solution’ activity” of an adjustment of the limit was not enough to transform an unpatentable principle into a patentable method.<sup>50</sup> Stripped of the post solution activity, the method consisted of little more than plugging a variable into a formula. The Court thus further refined the theory of preemption by rejecting “[t]he notion that post-solution activity, no matter how conventional or obvious in itself, can transform an unpatentable principle into a patentable process.”<sup>51</sup> *Flook* stands for the principle that the prohibition against patenting abstract ideas “cannot be circumvented by attempting to limit the use of the formula to a particular technological environment” or adding “insignificant post-solution activity.”<sup>52</sup> The Court concluded that the process at issue there was “unpatentable under § 101, not because it contain[ed] a mathematical algorithm as one component, but because once that algorithm [wa]s assumed to be within the prior art, the application, considered as a whole, contain[ed] no patentable invention.”<sup>53</sup> If the claim does not disclose another inventive concept, apart from the fundamental principle, it is unpatentable under § 101.<sup>54</sup>

Of the three cases, *Diamond v. Diehr* was the only process patent the Court found eligible. That case involved a previously unknown method for molding raw synthetic rubber into cured precision products using a mathematical formula to complete some of its several steps with the use of a computer.<sup>55</sup> The Court held that a process claim involving a physical transformation of matter is patentable subject matter but

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48. *Diehr*, 450 U.S. at 192 n.14 (1981).

49. *Id.*

50. *Parker v. Flook*, 437 U.S. 584, 590 (1978).

51. *Id.*

52. *Diehr*, 450 U.S. at 191–92.

53. *Flook*, 437 U.S. at 594.

54. *Id.* at 591–95.

55. *Diehr*, 450 U.S. at 177.

indicated that a process claim not involving a particular machine may still be patentable.<sup>56</sup> *Diehr* affirmed that “an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.”<sup>57</sup> However, when a claim recites a fundamental principle, “an inquiry must be made into whether the claim is seeking patent protection for that formula in the abstract.”<sup>58</sup> Thus, while the claimed process must be considered as a whole, the inventive concept cannot derive solely from the fundamental principle.

In summation, *Bilski* reaffirmed that preemption is the controlling standard for § 101 under the Court’s *Benson*, *Flook*, and *Diehr* precedents and that while the machine-or-transformation test may inform the analysis, that test is not outcome determinative.<sup>59</sup> A careful reading of *Bilski v. Kappos* and these three decisions affirms that a patent cannot preempt, that is to say, foreclose all “practical application” of a fundamental principle.<sup>60</sup> Thus the key consideration is whether the patent threatens to (a) wholly preempt the fundamental principle or (b) be the only practical and useful application of the principle. This approach analyzes the extent to which a patent operates as a roadblock to other useful applications of the fundamental principle. Furthermore, limiting a fundamental principle to a particular industry or technological environment is not sufficient to make said claim patent eligible. Simply because a correlation is a narrowly drawn one does not make it any less of a fundamental principle. Placing insignificant limitations on a fundamental principle will not transform it into a patentable process, and neither will post-solution activity transform an unpatentable principle into a patentable process—this is especially true where the application considered as a whole contains no patentable invention. Rather, there must be a significant application of the principle to what is, when reading the claim as a whole, a new and useful process. Although the claimed process must be considered as a whole, the inventiveness and novelty of the process should not derive solely from the fundamental principle. Finally, although the Supreme Court rejected the “machine-or-transformation” test as a categorical rule, it remains “an important and useful clue” and helpful “investigative tool”

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56. *Id.* at 184.

57. *Id.* at 187.

58. *Id.* at 191.

59. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347, 1354 (Fed. Cir. 2010).

60. *See Diehr*, 450 U.S. at 185–86 (citing *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)); *see generally Bilski v. Kappos*, 130 S. Ct. 3218 (2010).

in determining whether some claimed processes are patent eligible under § 101.<sup>61</sup> In short, the machine-or-transformation remains a helpful, but at times inaccurate, proxy for assessing the more important challenge of “securing patents for valuable inventions without transgressing the public domain.”<sup>62</sup>

### III. PATENTS ON GENETIC DIAGNOSTIC METHODS

*Bilski v. Kappos* may hold potential implications for the patenting of genetic diagnostic methods and other advanced diagnostic methods. Genetic diagnostic patents claim the process of comparing a wild-type DNA sequence against an individual’s DNA, in order to diagnose either the existence of or a predisposition to a particular disease. These patents often claim all methods of comparing genetic sequences in a human subject to the genetic sequence in a control group<sup>63</sup> and do not link the diagnoses to any particular equipment or machine.<sup>64</sup> Genetic diagnostic patents currently exist for genes linked to breast cancer,<sup>65</sup> ovarian cancer,<sup>66</sup> and Canavan Disease,<sup>67</sup> to name just a few. Whether such advanced diagnostic methods should be afforded patent protection is of increasing significance due to the advent of personalized medicine.

Advanced diagnostic patents, particularly diagnostic genetic patents, highlight the inherent difficulties of assessing whether a claimed method seeks to patent a fundamental principle or simply incorporate it into a series of steps. The Court explicitly acknowledged the challenging issues raised by diagnostic methods in *Bilski* when rejecting the machine-or-transformation test, by noting that “there are reasons to doubt whether the test should be the sole criterion for determining the patentability of inventions in the Information Age. As numerous *amicus* briefs argue, the machine-or-transformation test would create uncertainty as to the patentability of . . . advanced diagnostic medicine techniques.”<sup>68</sup> In short, the decision suggests that the Court believes the machine-or-transformation test was not up to the task of establishing the patentability of advanced diagnostic methods. Unfortunately, the Court provided little further guidance as to what other tests or

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61. *Bilski*, 130 S. Ct. at 3226–27.

62. *Id.* at 3227.

63. U.S. Patent No. 5,753,441 claim 1 (filed Jan. 5, 1996).

64. *Id.*

65. U.S. Patent No. 5,709,999 (filed June 7, 1995).

66. U.S. Patent No. 4,968,603 (filed Dec. 31, 1986).

67. U.S. Patent No. 5,679,635 (issued Oct. 21, 1997).

68. *Bilski v. Kappos*, 130 S. Ct. 3218, 3227 (2010).

considerations may apply for these discoveries, choosing instead to adopt a wait-and-see approach.

The Supreme Court has been similarly reluctant to address the issue of diagnostic patents in the past. In 2006, the Supreme Court granted certiorari in *Metabolite Laboratories Inc. v. Laboratory Corporation of America Holdings* to decide whether a method-of-diagnosis claim constituted patentable subject matter;<sup>69</sup> however, the Court later dismissed certiorari as improvidently granted because the issue had not been argued in the lower courts.<sup>70</sup> At that time, the Court opted to not rule on whether medical diagnostics were patentable and chose instead to allow the issue to percolate through the lower courts. And so, over the past few years, several cases involving diagnostic methods have been raised to the Federal Circuit. The Court's ruling in *Bilski v. Kappos* may hold important implications for the patenting of genetic diagnostic methods as well as for other advanced medical diagnostic methods. Signaling its interest in the patentability of advanced diagnostic methods, the Supreme Court vacated and remanded two Federal Circuit opinions involving diagnostic patents the day after its ruling in *Bilski v. Kappos*, *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*,<sup>71</sup> and *Classen Immunotherapies, Inc. v. Biogen IDEC*.<sup>72</sup> Both cases involved patents on medical diagnostic processes and relied on the "machine-or-transformation" test in assessing the validity of the diagnostic patents—this test has now been thrown into question.<sup>73</sup> In December 2010, the Federal Circuit reconsidered *Prometheus* and reached the same result it had originally, upholding the patents as valid under Section 101.<sup>74</sup> Of particular interest to this issue is the case *Association of Molecular Pathologists v. USPTO*, which was recently ruled on by the Federal Circuit and was originally decided using the

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69. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 125 (2006).

70. *Id.*

71. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1343 (Fed. Cir. 2009), *vacated sub nom*, *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 130 S. Ct. 3543 (2010).

72. *Classen Immunotherapies, Inc. v. Biogen IDEC*, 304 F. App'x 866 (Fed. Cir. 2008) (holding that patents on the correlation between vaccination schedules and the risk of developing chronic immune mediated disorders were attempt to patent an unpatentable natural phenomenon).

73. The simultaneous remand of these two cases is interesting because in *Prometheus* the Federal Circuit held that the medical diagnostic claims at issue were valid while the *Classen* court upheld the district court's holding of invalidity.

74. *Prometheus Labs. v. Mayo Collaborative Servs.*, 628 F.3d 1347 (Fed. Cir. 2010), *cert. granted*, 131 S. Ct. 3027.

machine-or-transformation test. In the district court case, the court invalidated fifteen claims drawn from seven patents tied to the breast cancer genes by finding that the diagnostic gene patents held on the breast cancer genes did not encompass patentable subject matter under 35 U.S.C. § 101.<sup>75</sup> This decision marked the first time a court had ruled on whether genetic diagnostic methods constitute patentable subject matter.<sup>76</sup> While overturning much of the district court's decision, the Federal Circuit Court of Appeals did uphold the lower court's decision that several of the diagnostic gene patents were invalid. The case may eventually reach the Supreme Court and their decision could reshape both the biotechnology industry and the law of intellectual property.

### A. Science of Genes

Before turning to the legal issues surrounding genetic diagnostic patents, a brief summary of relevant basic principles of molecular biology and genetics is helpful. DNA is a chemical molecule composed of repeating chemical units known as nucleotides or bases.<sup>77</sup> DNA is composed of four nucleotides<sup>78</sup> and typically exists as a double helix consisting of two intertwined strands of DNA that are chemically bound to each other through base pairing.<sup>79</sup> Genes are the basic units of heredity and are responsible for the inheritance of discrete traits.<sup>80</sup> Each gene is typically thousands of nucleotides long and contains the information used by the body to produce proteins.<sup>81</sup> Genes contain both exons and introns: exons are the coding sequences necessary for the creation of proteins, and introns contain regulatory sequences that affect the body's rate of production of the protein encoded by a gene.<sup>82</sup> The human genome, which is comprised of approximately 25,000 genes, is contained within almost every cell in the human body and defines

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75. See *Ass'n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 702 F. Supp. 2d 181, 185 (S.D.N.Y. 2010), *aff'd in part*, No. 2010-1406, 2011 WL 3211513 (Fed. Cir. July 29, 2011).

76. Cf. *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1293 (Fed. Cir. 2010) (Dyk, J., concurring) (observing that "thus far the question has evaded judicial review").

77. See *Ass'n of Molecular Pathology*, 702 F. Supp. 2d at 193-94.

78. *Id.*

79. *Id.* at 194. The four nucleotides that comprise DNA are adenine, thymine, cytosine and guanine. Adenine always binds to thymine, and cytosine will always bind to guanine.

80. *Id.*

81. *Id.*

82. *Id.*

physical traits as well as influences the development of certain diseases.<sup>83</sup>

DNA as it is found in the human body is sometimes referred to as “native DNA.”<sup>84</sup> Native DNA can be extracted from its natural cellular environment through established laboratory techniques, and a particular segment of that DNA, such as a gene, can then be excised from the extracted material. Such a segment of DNA nucleotides existing distinctly from the cellular components normally associated with native DNA is referred to as “isolated DNA.”<sup>85</sup> The term isolated DNA can refer both to DNA originating from a cell and DNA which has been synthesized through chemical or biological means.<sup>86</sup>

Scientists use the term “wild-type” to refer to the “normal” human gene sequence, i.e., the sequence of a gene without any variations.<sup>87</sup> Variations or “mutations” in the human genome can occur at different magnitudes. Small scale mutations can manifest as slight sequence differences between the same genes in different individuals<sup>88</sup> while large scale variations can include the addition or deletion of substantial chromosomal regions.<sup>89</sup> While many mutations may have little to no effect on the body’s processes, others can interfere with the body’s processes and may correlate with an increased risk, or in some cases, near certainty, of developing a particular disease.<sup>90</sup> There are also mutations, or variants, of uncertain significance (VUS), whose affect on the body is unknown.

DNA sequencing involves determining the order of nucleotides within a DNA molecule.<sup>91</sup> Once a gene has been sequenced, the information can be used in diagnostic testing to determine whether an individual’s gene contains mutations that have been associated with a particular disease or condition.<sup>92</sup> Once the location of a gene is found, it is relatively simple to directly analyze the sequence of the DNA and identify the nucleotides comprising the gene.<sup>93</sup> However, locating genes tied to various conditions is a much more difficult process. In order to

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83. *Id.*

84. *Id.* at 195.

85. *Id.* at 196.

86. *Id.* at 217.

87. *Id.* at 195.

88. *Id.*

89. *Id.*

90. *Id.*

91. *Id.* at 199.

92. *Id.*

93. *Id.* at 201.

locate genes tied to various conditions, scientists often use linkage analysis. Linkage analysis uses correlations between the occurrence of cancer and the inheritance of certain DNA markers among family members to map the physical location of a particular gene.<sup>94</sup> Successful linkage analysis requires large and genetically informative families, or kindreds, and detailed family information and can be a burdensome and time-consuming process.

### *B. The History of Gene Patents*

The explosion of patents within the biotechnology industry, including genetic patents, can trace itself back to the convergence of two significant events in 1980. That year, Congress passed the Bayh-Dole Act and the Supreme Court decided *Diamond v. Chakrabarty*.<sup>95</sup> The Bayh-Dole Act allowed universities, research institutions, and other non-profit organizations to seek patent protection for inventions made with government funding and to retain the royalties on those patents for the first time.<sup>96</sup> The ability to retain and license the patents from academic research led to significant monetary gains for many universities. That same year, the Supreme Court decided *Diamond v. Chakrabarty*, a case involving a patent application for a genetically engineered bacterium capable of “digesting” multiple components of crude oil.<sup>97</sup> The original patent application for the bacterium had been denied based on the argument that living organisms constitute unpatentable subject matter. On appeal, the Supreme Court held for the first time that a living organism could constitute patentable subject matter under § 101. In its oft-quoted opinion, the Court stated that patent protection “includes[s] anything under the sun that is made by man.”<sup>98</sup>

*Chakrabarty* opened the door to gene patenting by holding that

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94. *Id.*

95. *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

96. Bayh-Dole Act, 35 U.S.C. § 202 (2006).

97. *Chakrabarty*, 447 U.S. at 305.

98. *Id.* at 309 (quoting S. Rep. No. 1979, at 6 (1952), *reprinted in* 1952 U.S.C.C.A.N. 2394, 2398, 2409–10). Although often cited, this phrase is somewhat misleading as it first originally appeared in the legislative history of the Patent Act of 1952. The full quote states “A person may have ‘invented’ a machine or a manufacture, which may include anything under the sun made by man, but it is not necessarily patentable under § 101 unless the conditions of the title are fulfilled.” S. Rep. No. 1979, at 6 (1952), *reprinted in* 1952 U.S.C.C.A.N. 2394, 2398, 2409–10. In *Bilski v. Kappos*, Justice Stevens reiterated the point that just because a person may have ‘invented’ . . . anything under the sun,” that thing is not necessarily patentable under § 101. 130 S. Ct. 3218, 3249 (Stevens, J., concurring).



biological materials were patentable subject matter under 35 U.S.C. § 101. Relatively soon after the decision in *Chakrabarty*, the first United States patents relating to “isolated DNA” were issued.<sup>99</sup> Four years later, in 1991, the Federal Circuit held that “isolated and purified” DNA sequences constitute patentable subject matter.<sup>100</sup> Since the Federal Circuit’s decision to permit the patenting of genes in 1991, the number of patent applications for genes has exploded. A 2005 study published in *Science* found that approximately 20 percent of human genes are currently patented.<sup>101</sup> According to another study, 4,382 of the 23,688 genes listed in the database of the National Center for Biotechnology Information (“NCBI”) are explicitly claimed as intellectual property.<sup>102</sup>

In 2001, the United States Patent and Trademark Office (PTO) published revised examination guidelines for the “utility” requirement of § 101.<sup>103</sup> The guidelines attracted a large number of public comments regarding the patent eligibility of human genes given the astounding increase in these types of patent applications. The agency’s response constitutes the only written expression of its views on the issue of genetic patents. The PTO indicated that genetic sequences that have been “isolated and purified” do constitute patent-eligible matter.<sup>104</sup> They stated that, as long as the specification of a patent discloses a particular use for a gene, the “inventor’s discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it.”<sup>105</sup> Their rationale was that a DNA molecule that has been “isolated” is not a product of nature, and

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99. See U.S. Patent No. 4,680,264 claim 27 (filed July 1, 1983) (claiming a recombinant vector rather than genomic DNA).

100. See *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991) (holding that a “gene is a chemical compound” and affirming patentability of claims directed to a “purified and isolated DNA sequence.”).

101. Kyle Jenson & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, 310 *SCI.* 239, 239 (2005).

102. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 702 F. Supp. 2d 181, 185 (S.D.N.Y. 2010).

103. USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001), available at <http://www.uspto.gov/web/offices/com/sol/notices/utilexmguide.pdf>.

104. *Id.* (“An inventor’s discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it.”); see also Secretary’s Advisory Committee on Genetics, Health and Society, 110 Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests 24 (Mar. 9, 2009).

105. USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001), available at <http://www.uspto.gov/web/offices/com/sol/notices/utilexmguide.pdf>.

therefore unpatentable, because (1) “that DNA molecule does not occur in that isolated form in nature;” and (2) the purified state of synthetic DNA preparations “is different from the naturally occurring compound.”<sup>106</sup>

The PTO stopped short of allowing patents on gene sequences as they exist in a person’s body. Thus, today the term “gene patent” is more commonly used to refer to a wide variety of patents relating to genes but not on patents directed towards genes as they exist in the human body. There are several different categories of patents tied to genetics, including composition-of-matter patents on isolated nucleic acid molecules and diagnostic genetic patents. Composition-of-matter gene patents claim the “isolated and purified” DNA or cDNA sequences as explained above. These isolated DNA sequences are often used as probes, which molecular biologists use to target and bind to particular portions of a patient’s DNA thereby allowing it to be detectable using laboratory machinery.<sup>107</sup> Diagnostic genetic patents involve patent claims to processes for the detection of particular nucleic acid sequences or mutations using probes, primers, or some other method. In short, these patents claim the process of comparing a wild-type DNA sequence against an individual’s DNA, in order to diagnose either the existence of or a predisposition to a particular disease.

### C. *Association for Molecular Pathology v. USPTO*

The debate over diagnostic patents recently came to a head in litigation surrounding two genes linked to breast and ovarian cancer.<sup>108</sup> In March of 2010, the Southern District of New York addressed the validity of genetic diagnostic patents in *Association for Molecular Pathology v. United States Patent and Trademark Office*.<sup>109</sup> The highly-watched case involved patents held on the BRCA1 and BRCA2 genes or, as they are more commonly known, the breast cancer genes. Certain mutations in these two genes are associated with a highly increased risk of breast and ovarian cancer, and genetic testing for these mutations can

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106. *Id.*

107. Defendant’s Memorandum of Law In Support of their Motion for Summary Judgment and in Opposition to Plaintiffs’ Motion for Summary Judgment, at \*1, *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 702 F. Supp. 2d 181, 185 (S.D.N.Y. 2010), *aff’d in part*, No. 2010–1406, 2011 WL 3211513 (Fed. Cir. July 29, 2011).

108. The names BRCA1 and BRCA2 stand for Breast Cancer Susceptibility Gene 1 and Breast Cancer Susceptibility Gene 2.

109. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 702 F. Supp. 2d 181, 185 (S.D.N.Y. 2010), *aff’d in part*, No. 2010–1406, 2011 WL 3211513 (Fed. Cir. July 29, 2011).

inform women as to whether they are at a heightened risk of developing these cancers. In March of 2010, the Southern District of New York addressed the validity of composition-of-matter and method patents relating to these genes in *Association for Molecular Pathology v. United States Patent and Trademark Office*<sup>110</sup> and invalidated fifteen patents associated with the BRCA1 and BRCA2 genes. On July 29, 2011, the Federal Circuit Court of Appeals ruled on the case, overturning much of the lower court's decision. The Federal Circuit reversed the lower court's decision as to Myriad's patents on the isolated BRCA1 and BRCA2 genes, but affirmed the lower court's finding that all but one of the method patents tied to BRCA1 and BRCA2 were invalid.<sup>111</sup>

Breast cancer is currently the most frequently diagnosed cancer worldwide and the second leading cause of cancer deaths for women in the United States.<sup>112</sup> In the 1990s, a group of researchers discovered that the BRCA1 and BRCA2 genes correlated with an increased risk of breast and ovarian cancer.<sup>113</sup> A woman's risk of developing breast or ovarian cancer dramatically rises if she has inherited a deleterious BRCA1 or BRCA2 mutation. Women carrying inherited mutations on their BRCA1 and BRCA2 genes can face up to an 85% cumulative risk of breast cancer and up to a 50% cumulative risk of ovarian cancer.<sup>114</sup> Harmful BRCA1 mutations may also increase a patient's risk of developing cervical, uterine, pancreatic, and colon cancer,<sup>115</sup> while harmful BRCA2 mutations have been linked to an increased risk of pancreatic cancer, stomach cancer, and melanoma.<sup>116</sup> Based on these findings, Myriad Genetics, a company which had participated in the research to isolate and sequence the genes, developed a diagnostic test to detect the presence of mutations on the BRCA1 and BRCA2 genes in order to aid women and physicians when making prognostic decisions. The University of Utah and Myriad Genetics obtained the patents to the BRCA1 and BRCA2 genes between 1995 and 1998.<sup>117</sup>

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110. *Id.* at 200.

111. *Ass'n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 653 F.3d 1329, 1331 (Fed. Cir. 2011).

112. *Ass'n of Molecular Pathology*, 702 F. Supp. 2d at 200 (citing Parthasarathy Decl. ¶ 8).

113. *Id.* at 201–02.

114. *Id.* at 203 (citing Love Decl. ¶ 10).

115. Luna Kadouri, Ayala Hubert, et al., *Cancer Risks in Carriers of the BRCA1/2 Ashkenazi Founder Mutations*, 44 JOURNAL OF MEDICAL GENETICS 467, 467–71 (2007).

116. The Breast Cancer Linkage Consortium, *Cancer risks in BRCA2 mutation carriers*, 91 JOURNAL OF THE NATIONAL CANCER INSTITUTE 15, 1310 (1999).

117. *Ass'n of Molecular Pathology*, 702 F. Supp. 2d at 202–06.

The ability to determine whether a patient carries inherited mutations of the BRCA1/2 genes offers tremendous benefits in the provision of medical care to them. Determining whether a woman carries inherited mutations of either of these genes can be of critical importance in informing her prognosis and potentially providing her with life-saving preventative measures. Knowing whether a woman is a carrier of BRCA1 or BRCA2 genetic mutations allows her and her physician to make more informed decisions about her health and body. Women who carry a BRCA1/2 genetic mutation have a range of options for managing their risk of cancer, including increased surveillance, prophylactic surgery, chemoprevention, and risk avoidance. Likewise, a woman who has been diagnosed with breast cancer may opt for a more aggressive course of treatment if she carries the BRCA1 and BRCA2 mutations and is therefore at heightened risk of recurrence.

Unfortunately, as the patent-holder and sole provider of the BRCA1/2 tests, Myriad's enforcement of its patents highlighted several of the criticisms commonly leveled against gene patents. Many women were prevented from determining whether they were carriers of the mutations because the genes have been patented by Myriad Genetics. As the monopoly-holder over the diagnostic tests, Myriad Genetics was able to charge upwards of \$3,000 a test, a cost which proved prohibitive for many women. Myriad Genetics also refused to license the diagnostic tests to other laboratories,<sup>118</sup> which in many cases prevented women from obtaining a second opinion in order to confirm or clarify ambiguous test results.

In 2008, several doctors' groups, together with the ACLU and Public Patent Foundation, filed a lawsuit in the Southern District of New York seeking to invalidate Myriad Genetics' patents on BRCA1 and BRCA2. Citing a litany of complaints, the plaintiffs claimed that "Myriad's patents and its position as the sole provider of BRCA1/2 testing has hindered the ability of patients to receive the highest-quality breast cancer genetic testing and has impeded the development of improvements to BRCA1/2 genetic testing."<sup>119</sup> The plaintiffs argued that Myriad's monopoly had resulted in less comprehensive and lower test qualities, and prevented many patients from determining whether they had these mutations before making potentially life-altering medical decisions.<sup>120</sup>

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118. *Id.*

119. *Id.* at 206 (emphasis removed).

120. *Id.*

The plaintiffs challenged the validity of several different types of gene patents owned by Myriad Genetics, arguing that they were invalid under 35 U.S.C. § 101. The patents challenged included both: (1) composition of matter gene patents of “isolated and purified” DNA sequences; and (2) diagnostic gene patents involving methods of analyzing or comparing the DNA sequences of the BRCA1/2 genes to detect mutations. In March 2010, the Southern District of New York ruled in favor of the plaintiffs and invalidated fifteen claims made in the seven patents relating to the BRCA1 and BRCA2 breast cancer genes.<sup>121</sup> In July of 2011, the Federal Circuit reversed the district court’s decision and found that claims covering isolated DNA sequences are patentable subject matter under 35 U.S.C. § 101. However, the Federal Court affirmed the lower court’s ruling with respect to the diagnostic genetic patents, finding all but one of Myriad’s method claims were directed to patent-ineligible, abstract mental process, and fail the machine-or-transformation test.<sup>122</sup>

The challenged diagnostic gene patents claimed the method of diagnosing whether an individual carried the BRCA1/2 genetic mutations and was therefore at a heightened risk of developing breast or ovarian cancer. For example, Claim 1 of the ‘999 patent was directed to the process of “analyzing” a BRCA1 sequence in order to determine whether or not a specified naturally-occurring mutations exists.”<sup>123</sup> The process was not limited to any particular method of analysis and did not specify any further action beyond the act of “analyzing.”<sup>124</sup> Likewise, other claims, such as claims 1 of the ‘001, ‘441, and ‘857 patents, were directed to “comparing” two gene sequences to determine whether any differences existed and failed to specify any limitations on the method of comparison.<sup>125</sup> Following is a brief excerpt of the language from one of the contested patents, claim 1 of ‘857:

A method for identifying a mutant BRCA2 nucleotide sequence in a suspected mutant BRCA2 allele which comprises comparing the nucleotide sequence of the suspected mutant BRCA2 allele with the wild-type BRCA2 nucleotide sequence, wherein a difference between the suspected mutant and the wild-type

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121. See generally *id.* at 181.

122. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 653 F.3d 1329, 1356 (Fed. Cir. 2011).

123. *Ass’n of Molecular Pathology*, 702 F. Supp. 2d at 233.

124. *Id.*

125. *Id.*

sequence identifies a mutant BRCA2 nucleotide sequence.<sup>126</sup>

At the time of its decision, the district court relied on the “machine-or-transformation” test in assessing the validity of the diagnostic gene patents at issue.<sup>127</sup> Relying heavily on the Federal Circuit’s analysis in *Bilski* as to what constitutes a transformation, the court held that the diagnostic gene patents at issue did not involve any transformation and therefore were non-patentable subject matter. In particular, the court held that the addition of a data-gathering step was insufficient to convert a series of steps into a patentable process,<sup>128</sup> and emphasized that the “transformation must be central to the purpose of the claimed process.”<sup>129</sup> The court noted that “the inherent step of gathering data can also fairly be characterized as insignificant extra-solution activity.”<sup>130</sup> To hold otherwise, the court reasoned, would place a meaningless limit on patent claims, as “a requirement simply that data input be gathered - without specifying how - is a meaningless limit on a claim to an algorithm because every algorithm inherently requires the gathering of data inputs.”<sup>131</sup> The court concluded that diagnostic gene patents “seek to claim a non-transformative process that encompasses [a fundamental principle] without the aid of . . . any other device.”<sup>132</sup> This past July, the Federal Court affirmed the lower court’s ruling with respect to the diagnostic genetic patents, finding all but one of Myriad’s method claims were directed to patent-ineligible, abstract mental process, and failed the machine-or-transformation test.<sup>133</sup>

The Federal Circuit agreed that “all but one of Myriad’s claims are directed to patent-ineligible abstract mental processes, and fail the machine-or-transformation test.”<sup>134</sup> The court rejected Myriad’s argument that its methods of “comparing” or “analyzing” BRCA sequences satisfy the machine-or-transformation test as outlined in *Prometheus* because each requires extracting and sequencing a human

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126. U.S. Patent No. 6,033,857 claim 1 (filed on Mar. 20, 1998).

127. See generally *Ass’n of Molecular Pathology*, 702 F. Supp. 2d at 181.

128. *Id.* at 233 (“[A]dding a data-gathering step to an algorithm is insufficient to convert that algorithm into a patent-eligible process.”) (citing *In re Bilski*, 545 F.3d at 963).

129. *Id.* (citing *In re Bilski*, 545 F.3d at 962).

130. *Id.* (citing *Flook*, 437 U.S. at 590).

131. *Id.* (citing *In re Grams*, 888 F.2d at 839–40 (Fed. Cir. 1989)).

132. *In re Bilski*, 545 F.3d at 965.

133. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 2011 WL 3211513, at \*20 (July 29, 2011).

134. *Id.*

sample before the sequences can be analyzed.<sup>135</sup> The court held that the method claims lacked any “necessarily transformative step” and, in the end, “recite nothing more than the abstract mental steps necessary to compare two different nucleotide sequences.”<sup>136</sup> The court ruled that the claims themselves did not include those steps, and the steps of “comparing” and “analyzing” could not be read to imply that “extracting” or “sequencing” need also be conducted. The Federal Circuit concluded that because the process of comparing and analyzing could be “accomplished by mere inspection alone,”<sup>137</sup> Myriad’s claims failed the machine-or-transformation test, and were directed to patentable abstract mental processes.

The court was right to find diagnostic patents equally undeserving of patent protection under the standards outlined in *Bilski v. Kappos*. As was affirmed by the Supreme Court, a patent cannot foreclose all “practical application” of a fundamental principle.<sup>138</sup> Considered as a whole, diagnostic gene patents cover a phenomenon of nature - whether two genetic sequences are different or the same. The claims exemplify how a patent on a general correlation can monopolize a law of nature. Furthermore, placing insignificant limitations on a fundamental principle will not transform it into a patentable process, and neither will post-solution activity transform an unpatentable principle into a patentable process. In the case of genetic diagnostic tests, the isolation and sequencing of DNA from a human sample, when incorporated into the diagnostic genetic patents, represents nothing more than a data-gathering step. Thus, the sole difference between the claims seeking patent protection and the correlation is the inclusion of this insignificant data-gathering step, and “insignificant extra-solution activity will not transform an unpatentable principle into a patentable process.”<sup>139</sup> Furthermore, although the process must be considered as a whole, the “inventive concept” of the process should not derive solely from the fundamental principle. In the case of genetic diagnostics, the inventive concept derives solely from the natural correlation, whereas the process utilizing it offers no new or useful end.

The problems raised by granting a monopoly over diagnostic

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135. *Prometheus Labs. v. Mayo Collaborative Svcs.*, 628 F.3d 1347 (Fed. Cir. 2010), *cert. granted*, 131 S. Ct. 3027.

136. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 353 F.3d 1329, 1336 (Fed. Cir. 2011).

137. *Id.* at 22.

138. *Diamond v. Diehr*, 450 U.S. 175, 189–86 (1981) (citing *Benson*, 409 U.S. 63).

139. *Id.* at 191–92.

methods were highlighted in the case of *Metabolite Laboratories, Inc. v. Laboratory Corp. of America Holdings*, in which the Federal Circuit upheld the patentability of a diagnostic patent claim for a vitamin B deficiency.<sup>140</sup> The claim in *Metabolite Labs* was directed at correlating elevated levels of total homocysteines in patients' blood to vitamin B deficiencies,<sup>141</sup> which can cause serious illnesses including cognitive dysfunction, birth defects and cancer, and was very similar in form to the claims raised in *Molecular Pathology*.<sup>142</sup> The claim did not specify any particular procedure for performing the measurement,<sup>143</sup> and respondents argued that the patent created a protected monopoly over the process of 'correlating' test results and potential vitamin deficiencies. LabCorp filed a petition for certiorari to the Supreme Court, questioning "[w]hether a method patent . . . directing a party simply to 'correlat[e]' test results can validly claim a monopoly over a basic scientific relationship . . . such that any doctor necessarily infringes the patent merely by thinking about the relationship after looking at a test result."<sup>144</sup>

In a dissenting opinion to the dismissal of certiorari, Breyer cogently outlined the problems raised by diagnostic patents. Discussing the merits of the underlying case, Breyer noted that *Metabolite Laboratories* "cannot avoid the fact that the process is no more than an instruction to read some numbers in light of medical knowledge."<sup>145</sup> Breyer went on to explain that although, "[o]ne might, of course, reduce the 'process' to a series of steps, e.g. Step 1: gather data; Step 2: read a number; Step 3: compare the number with the norm; Step 4: act accordingly. But one can reduce any process to a series of steps. The question is what those steps embody."<sup>146</sup> As Breyer aptly pointed out, "Claim 13's process instructs the user to (1) obtain test results and (2) think about them."<sup>147</sup> Breyer further likened the diagnostic correlation at issue with the unpatentable algorithm in *Flook* because the subject matter at issue in both cases, and as in this case, was a "simple natural

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140. *Metabolite Labs. Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1368 (Fed. Cir. 2004).

141. *Id.* at 1358–59.

142. *Id.* at 1358.

143. *Id.* at 1358–59.

144. Petition for a Writ of Certiorari, *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 370 F.3d 1354 (2004) (No. 04-607), 2004 WL 2505526 (limiting grant of certiorari to issue three only).

145. *Lab. Corp. of Am. Holdings*, 548 U.S. at 137 (Breyer, J., dissenting).

146. *Id.* at 137 (Breyer, J., dissenting).

147. *Id.* at 136 (Breyer, J., dissenting).



correlation, i.e. a ‘natural phenomenon.’”<sup>148</sup> Similarly, the claims in *Molecular Pathology* were directed to correlating two gene sequences to determine whether any differences existed and failed to identify any limitations on the method of comparison.<sup>149</sup> Diagnostic methods consist of little more than plugging a variable into a formula.

#### D. Patents on Mixed Diagnostic-Therapeutic

A more difficult issue is raised by patents on diagnostic methods that also potentially involve therapeutic applications. In *Association for Molecular Pathology*, the only method claim that the Federal Circuit found to be patentable subject matter was a method claim for screening potential cancer therapeutics by analyzing growth rates of cells with altered BRCA genes in the presence or absence of the treatments. The court reasoned that Myriad’s method claim was “not so ‘manifestly abstract’ as to claim only a scientific principle.”<sup>150</sup> The court also held that the method claim passed the machine-or-transformation test, since it involved the steps of “growing” transformed cells in the presence or absence of a potential cancer therapeutic, and “determining” the cells’ growth rates. Because the court found these steps to be “inherently transformative,” they found that the claimed process covered patentable subject matter under § 101.

In arguing that the method claim satisfied the “machine-or-transformation” test and constituted patentable subject matter, the Federal Circuit looked at cases involving patents on diagnostic methods that also involve therapeutic applications, such as was the case in *Prometheus Laboratories, Inc., v. Mayo Collaborative Servs.*<sup>151</sup> In arguing that their diagnostic gene patents satisfied the “machine-or-transformation” test, Myriad leaned heavily on an earlier decision of the Federal Circuit involving advanced diagnostic method patents - *Prometheus Labs, Inc., v. Mayo Collaborative Servs.*<sup>152</sup> *Prometheus* involved a patent claim directed to methods for calibrating the proper dosage of a drug by measuring metabolites in subjects having

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148. *Id.* at 137 (Breyer, J., dissenting).

149. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 702 F. Supp. 2d 181, 233 (S.D.N.Y. 2010).

150. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 653 F.3d 1329, 1358 (Fed. Cir. 2011).

151. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336 (Fed. Cir. 2009), *cert. granted, judgment vacated, and remanded*, 130 S. Ct. 3543 (2010).

152. *Id.*

gastrointestinal disorders.<sup>153</sup> Patients battling autoimmune diseases, such as Crohn's disease, can suffer debilitating symptoms. Although there are drugs that treat these diseases by suppressing the body's natural immune system, they can carry serious, potentially fatal, side-effects if the dosage is too high for a given patient. Based on the correlation between metabolite levels in a patient's blood and the therapeutic efficacy of a dose of the drug, the patentees in *Prometheus* claimed the process of optimizing therapeutic efficiency by determining metabolite levels in order to identify a need to adjust drug dosages either upwards or downwards based on those levels.<sup>154</sup> Prometheus is the sole licensee of two methods for calibrating the proper dosage of drugs.

Claim 1 of the 302 patent claims:

A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising: (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder, wherein the levels of 6-thioguanine less than about 230 pmol per 8x10 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and wherein the levels of 6-thioguanin greater than about 400 pmol per 8x10 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.<sup>155</sup>

The issue was whether the claimed methods for individually calibrating the appropriate dosages of synthetic drugs for treatment for patients with various autoimmune diseases constituted unpatentable "natural phenomena."

Prior to *Bilski*, the Federal Circuit held "that the relevant transformation for purposes of the 'machine or transformation' test was the transformation of the human body as well as the chemical and physical changes of the drug's metabolites"<sup>156</sup> and concluded that the process was patentable. On remand, the Federal Circuit reaffirmed its earlier ruling, holding not only that Prometheus's asserted claims recite

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153. *Id.* at 1343–50.

154. *Id.* at 1339–40.

155. U.S. Patent No. 6,680,302 (filed on Dec. 27, 2001).

156. *Prometheus Labs., Inc.*, 581 F.3d at 1346.

transformative “administering” and “determining” steps, but also that Prometheus’s claims are drawn not to a law of nature, but to a particular application of naturally occurring correlations, and accordingly do not preempt all uses of the recited correlations between metabolite levels and drug efficacy or toxicity.<sup>157</sup> As such, the court found that the claims did not preempt all uses of the natural correlations; but rather utilized them in a series of specific steps.<sup>158</sup>

Both *Prometheus* and *Association for Molecular Pathology* misread Supreme Court precedent. The prohibition against patenting abstract ideas “cannot be circumvented by attempting to limit the use of the formula to a particular technological environment” or adding “insignificant post-solution activity.”<sup>159</sup> A patent application cannot immunize a claim merely by tying it to a particular application, if that particular application is obvious and nothing useful or new has been added. To hold otherwise would allow patent holders to appropriate rights to fundamental principles bit by bit. Under the governing preemption standard, both claims are invalid because they preempt all practical use of naturally occurring correlations and any machine or transformation present in the claims is merely insignificant post-solution activity.<sup>160</sup>

This past June, the Supreme Court accepted certiorari in *Prometheus* on the patentable subject matter eligibility of medical diagnostic methods. The issue raised on appeal, which emphasized the preemption standard, stated:

Whether 35 U.S.C. § 101 is satisfied by a patent claim that covers observed correlations between blood test results and patient health, so that the claim effectively preempts all uses of the naturally occurring correlations, simply because well-known methods used to administer prescription drugs and test blood may involve “transformations” of body chemistry.

In both *Prometheus* and *Association for Molecular Pathology*, the

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157. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347, 1355 (Fed. Cir. 2010).

158. *Id.* (citing *Diamond v. Diehr*, 450 U.S. 175, 187 (1981)) (stating that “[t]heir process admittedly employs a well-known mathematical equation, but they do not seek to preempt the use of that equation. Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process.”).

159. *Diehr*, 450 U.S. at 191–92.

160. *Prometheus Labs., Inc.*, 628 F.3d at 1354.

presence of transformations and machines is irrelevant. Rather, patentability under § 101 should instead depend on whether the claims “recite” and “wholly preempt” some natural phenomenon.<sup>161</sup> Dissecting the methods into their component parts, the claimed transformations should be disregarded because they are “conventional method steps” (i.e., not novel) or “merely data-gathering steps,” and the final step can “be ignored because it was ‘only a mental step.’”<sup>162</sup>

The ruling in *Prometheus* and *Association for Molecular Pathology* serves as an invitation to patent lawyers to attempt to bring abstract ideas within the penumbra of patentable subject matter simply by including technical details in the claim themselves. Additionally, attempting to distinguish the claims because they may have therapeutic effects threatens to allow all types of fundamental principles under patent protection provided that the claim language is framed as a “method of treatment.” To find these claims deserving of patent protection based on an admonition to pursue an appropriate course of treatment in light of test results would threaten to protect all diagnostic patents from review by simply appending a similar admonition.

#### IV. POLICY ARGUMENTS AGAINST DIAGNOSTIC GENETIC PATENTS

Finally, in rejecting the machine-or-transformation test, it is important to remember that *Bilski* emphasized that relying on rigid tests risks “obscuring the larger object of securing patents for valuable inventions without transgressing the public domain.”<sup>163</sup> The Court went on to reiterate that “patent law faces a great challenge in striking the balance between protecting inventors and not granting monopolies over procedures that others would discover by independent creative application of general principles.”<sup>164</sup> For that reason, when deciding on what the patent laws should cover, one should balance between over- and under-protection, that is to say, perform a cost-benefit analysis. There are sound policy decisions for excluding advanced diagnostics from patent protection. While, generally, patent protection encourages research and development, several convincing arguments have been advanced that the goals of research and development are undermined in the case of diagnostic patents. In the case of diagnostic genetic patents, the cost-benefit analysis weighs in favor of not granting patent

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161. *Id.* at 1351.

162. *Id.* at 1352.

163. *Bilski v. Kappos*, 130 S. Ct. 3218, 3227, 3228 (2010).

164. *Id.* at 3228.

protection to diagnostic methods.

*A. Advanced Diagnostics Patents Are Unnecessary to Motivate Innovation*

Patent law aims to protect inventors while at the same time not granting monopolies over procedures that others would have been independently discovered through the application of general well-known principles.<sup>165</sup> Thus, one of the central constitutional questions involves determining whether a patent monopoly is in fact necessary to motivate innovation.<sup>166</sup> This question necessitates a nuanced calculus as “[b]oth common sense and recent economic scholarship suggest that the[] dynamics of cost, risk, and reward vary by the type of thing being patented.”<sup>167</sup> Undoubtedly, “[i]f a high enough bar is not set when considering patent applications . . . patent examiners and courts could be flooded with claims that would put a chill on creative endeavor and dynamic change.”<sup>168</sup> Patents provide the ability to extract monopoly rent and, in some cases, those rents may be beyond what is necessary to encourage innovation. Overbroad and unnecessary patent protection comes with very real costs, both to consumers and innovation.

Because the very objective of patent protection is to promote innovation,<sup>169</sup> in assessing the wisdom of patent protections, it is important to question “whether a patent monopoly is necessary to ‘motivate the innovation.’”<sup>170</sup> Patents motivate innovation in two principal ways, by stimulating research and innovative activities, and by stimulating investment to commercially develop promising inventions. Patents on diagnostic methods are largely unnecessary to create incentives either for initial discoveries of diagnostic tests or for the development of commercial applications of diagnostic tests once discovered.<sup>171</sup> Indeed, the Medical Procedure Patent Coalition argues that the patent “incentive” is unnecessary in medical practice, as “the development of new medical procedures often occurs in the normal course of medical practice and generally does not require significant

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165. *Id.*

166. *Id.* at 3253 (citing *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 63 (1998)).

167. *Id.*

168. *Id.* at 3229.

169. See U.S. CONST. art. 1, § 8, cl. 8.

170. *Bilski*, 130 S. Ct. at 3253 (citing *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 63 (1998)).

171. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 702 F. Supp. 2d 181, 210 (S.D.N.Y. 2010) (citing *Cho Decl.* ¶ 25; *Leonard Decl.* ¶¶ 20–21).

capital investment.”<sup>172</sup>

The findings from a Report of the Secretary’s Advisory Committee on Genetics, Health, and Society Draft emphasizes that patents offer minor, if any at all, stimulus to the development of genetic diagnostics. As to incentivizing innovation, the report found that

[T]he prospect of patent protection of a genetic research discovery does not play a significant role in motivating scientists to conduct genetic research. Scientists typically are driven instead by factors such as the desire to advance understanding, the hope of improving patient care through new discoveries, and concerns for their own career advancement.<sup>173</sup>

Thus, patents are not necessary to motivate the innovation of advanced medical diagnostics, as medical practitioners already have sufficient incentives to provide patients with the best possible care. Furthermore, in determining whether a patent monopoly is, in fact, necessary to “motivate the innovation”,<sup>174</sup> courts should consider whether the discovery is one that has historically been afforded patent protection. Diagnoses have not historically been eligible to receive the protection of the patent laws. In fact, the first 150 years of patent jurisprudence in this country did not recognize the patentability of medical procedures, treatments, or methods of diagnosis.<sup>175</sup> Nonetheless, the medical and scientific communities have made great strides in the field of diagnostics in that time. Additionally, the majority of the research tied to genetic diagnostics is funded by the government or universities, not private investors. A study of patents issued for genetic diagnostics in the U.S. revealed that 67% of the patents were issued for discoveries that were in fact funded by the U.S. government, not by private investors.<sup>176</sup>

Patents are also largely unnecessary to stimulate investment to

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172. Jenner & Block, *Patents for Surgical/Medical Procedures: A Call for Legislative Prohibition*, available at <http://www.ascers.org/> (last visited at August 1, 2011).

173. Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests, Rep. of the Secretary’s Advisory Committee on Genetics, Health, and Society, at 1 (Apr. 2010) [hereinafter *SACGHS Report*].

174. *Bilski*, 130 S. Ct. at 3253 (citing *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 63 (1998)).

175. Robert M. Portman, *Legislative Restriction on Medical and Surgical Procedure Patents Removes Impediment to Medical Progress*, 4 U. BALT. INTELL. PROP. L.J. 91, 92 (1996).

176. *Ass’n of Molecular Pathology*, 702 F. Supp. 2d at 210 (citing Cho Decl. ¶ 22).

commercially develop diagnostic tests once discovered. As opposed to many pharmaceutical patents, the benefits of diagnostic discoveries generally require minimal capital expenditures to bring them to market once discovered. These discoveries often entail basic scientific principles that can be immediately applied by laboratories and medical facilities. As opposed to therapeutics, in which bringing products to market may require significant investment in order to obtain FDA approval and navigate the regulatory system, in the case of the diagnostic patents, there are generally minimal costs associated with bringing these discoveries to market. Often all that is required is publication. The SACGHS Report emphasizes that “[d]evelopment barriers generally do not appear to pose a significant barrier for bringing new diagnostic tests on-line. When a gene sequence is reported, diagnostic testing quickly arises regardless of patent status to meet clinical need.”<sup>177</sup> Furthermore, “the fact that unpatented genetic discoveries [are] routinely developed into clinical genetic tests suggests that patents are not needed for development of these tests.”<sup>178</sup> Thus, the need to incentivize commercial development of diagnostic tests is lacking, as genetic diagnoses are easily performed once a gene has been sequenced.<sup>179</sup> “[W]hereas biotechnology patents may well be necessary to ensure the commercial viability of the development of gene therapies (in analogy to pharmaceuticals), molecular diagnostics are more easily developed.”<sup>180</sup>

Thus, patent rights appear largely unnecessary in order to encourage clinicians and scientists to develop new diagnostic methods. Clinical need appears to be a sufficient motivator to incentivize development of new diagnostic tests, and once discovered, the investment to commercially develop these discoveries is minimal.

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177. SACGHS Draft Report, *supra* note 173, at 439.

178. *Id.*

179. Mildred K. Cho, *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3 (2003) (discussing one study that found that many laboratories offered testing for genes based on published sequence data, before any commercial kits were made available).

180. Gregory P. Lekovic, *Genetic Diagnosis and Intellectual Property Rights: A Proposal to Amend “The Physician Immunity Statute”*, 4 YALE J. HEALTH POL’Y, L. & ETHICS 275, 298 (2004) (“The timeline for scientific development and regulatory approval of diagnostics is shorter than for therapeutics and the process, overall, is less expensive. However, the revenue potential is smaller for diagnostics than for therapeutics for several reasons, including greater price sensitivity.” See, e.g., Robert S. Schifreen, *Molecular Diagnostics: The Challenge for the Future*, IVD TECH., Nov. 2003, at 27).

### *B. Upstream and Downstream Effects of Genetic Diagnostic Patents*

Not only are genetic patents unnecessary to motivate innovation, they may actually stymie research and development. Certain types of gene patents threaten to impede scientific progress,<sup>181</sup> as much of the advancement of scientific research into the human genome depends on a free-flow exchange of information. Free access to data is of critical importance to the future of genetic discoveries.<sup>182</sup> Thus, while the goal of patents should be to incentivize and reward the development of new knowledge and techniques, gene patents can paradoxically lead to a decrease in scientific advances.

As has been pointed out, “as patent applicants push the quest for patents further and further upstream, particularly in the biotechnology field, the impact of such patent grants has become increasingly troubling.”<sup>183</sup> Gene patents may contribute to a phenomenon known as the “tragedy of the anti-commons.”<sup>184</sup> In the “tragedy of the anti-commons”, competing patent rights held by independent parties prevent any one party from engaging in productive innovation.<sup>185</sup> In effect, the presence of patents leads to an underutilization of resources because the intellectual property rights

[D]iscourage research by impeding the free exchange of information, for example by forcing researchers to avoid the use of potentially patented ideas, by leading them to conduct costly and time-consuming searches of existing or pending patents, by requiring complex licensing arrangements, and by raising the costs of using the patented information, sometimes prohibitively.<sup>186</sup>

In this way, patent protection may ultimately undermine the very goals it seeks to promote. While the existence of the “anticommons is

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181. *Ass'n for Molecular Pathology*, 702 F. Supp. 2d at 208.

182. *Id.*

183. Harry First, *Controlling the Intellectual Property Grab: Protect Innovation, Not Innovators*, 38 RUTGERS L.J. 365, 381 (2007).

184. *Id.*

185. See, e.g., Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (1998) (citing Michael A. Heller, *The Tragedy of the Anticommons: Property in the Transition from Marx to Markets*, 111 HARV. L. REV. 621 (1998)).

186. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 127 (2006) (Breyer, J., dissenting).



highly disputed with respect to intellectual property,”<sup>187</sup> in the case of gene patents, the “tragedy of the anti-commons” is supported by empirical research. One survey of laboratory directors found that 53% had decided against developing new clinical tests because of existing gene patents, and 67% believed that gene patents impeded their ability to conduct research.<sup>188</sup> In particular, some studies have noted that patents appear to be more problematic in the area of DNA diagnostics than in other fields of biomedical research,<sup>189</sup> and that diagnostic laboratories have been the most critical of the impact of patents on gene sequences and products.<sup>190</sup>

The potential chilling effect of gene patents is particularly prevalent in determining variations of unknown significance (“VUS”) within genes. By way of example, the monopoly over the BRCA1 and BRCA2 genes has hindered other laboratories and scientists from determining the meaning of VUSs tied to breast and ovarian cancer and prevented a better understanding of those genes.<sup>191</sup> One study found that Myriad Genetics’ breast cancer gene patents negatively impacted the public knowledge of those genes by as much as five to ten percent.<sup>192</sup>

For example, if genetic testing reveals a mutation in a gene that has not previously been associated with any diseases in other individuals, the person’s test result may be interpreted as ambiguous (VUS). One study found that ten percent of women who underwent BRCA1/2 testing received an ambiguous result.<sup>193</sup> Because people have genetic differences that are not associated with an increased risk of diseases, it is

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187. Richard A. Epstein & Bruce N. Kuhlik, *Is There a Biomedical Anticommons?*, 27 REG. 54 (2004).

188. *Ass’n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 702 F. Supp. 2d 181, 208 (S.D.N.Y. 2010) (citing Cho Decl. ¶ 10).

189. Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 HOUS. L. REV. 1059, 1071 (2008) (citing John P. Walsh, Ashish Arora & Wesley M. Cohen, *Effects of Research Tool Patents and Licensing on Biomedical Innovation*, in PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285, 317–19 (2003)).

190. Eisenberg, *supra* note 189, at 1069 (citing Dianne Nicol & Jane Nielsen, Patents and Medical Biotechnology: An Empirical Analysis of Issues Facing the Australian Industry 64-71 (Univ. of Tasmania Ctr. For Law and Genetics, Occasional Paper No. 6, 2003), available at <http://www.lawgenecentre.org/Publication%20PDF/OccPaper%206.pdf> (“noting that 77% of respondents from diagnostic facilities stated that patents on gene sequences have a negative impact and 69% stated that patents on gene products have a negative impact”)).

191. *Ass’n of Molecular Pathology*, 702 F. Supp. 2d at 208 (citing Cho Decl. ¶ 10).

192. *Id.* (citing Murray Decl. ¶¶ 7–15, 20).

193. Beth N. Peshkin et al., *BRCA1/2 Testing: Complex Themes in Result Interpretation*, 19 J. OF CLINICAL ONCOLOGY 2555, 2560 (2001).

often unclear whether a specific DNA mutation will affect a person's risk of developing a disease. The more research that is conducted and the more people are tested for BRCA1 or BRCA2 changes, the more scientists will learn about variations of unknown significance.

Moreover, the negative effects of gene patents are likely to escalate. Currently, the majority of diagnostic genetic testing involves direct correlations between a particular gene and the corresponding disease, i.e. Tay-Sachs, Huntingtons, BRCA1/2. In these cases, a disease (often a rare one) will map directly onto one particular gene.<sup>194</sup> However, as scientific knowledge of the human genome improves, it will become increasingly possible to correlate diseases to combinations of different genes. Gene patents threaten to impede this research by blocking the collaborative efforts of researchers. This problem has been referred to as a "patent thicket" - a "dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology."<sup>195</sup> As of yet, the potential negative effects of these "patent thickets" have not yet fully manifested, as the current state of diagnostic testing predominantly focuses on discrete genes. However, in the future, many scientific advances may depend upon the testing on multiple genes - the rights of which may be owned by numerous different companies. As the scientific community moves towards an increased use of the genome to inform diagnostic and therapeutic decisions, the existence of gene patents threaten to roadblock these advances. The owner of one gene patent would be able to effectively block an entire line of research or clinical testing. As scientific research progresses, the number of overlapping, or stacked, patents on genes will likely increase. "Since many 'stacked' patents on the same disease gene will increase the licensing costs of the diagnostic test, it is possible, if not likely, that gene-based diagnostic tests will be kept out of the market not by scientific obstacles, but rather by commercial ones."<sup>196</sup>

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194. See NATIONAL TAY-SACHS & ALLIED DISEASE ASSOCIATION, INC., <http://www.ntsad.org/> (last visited Aug. 1, 2011) (stating that genetic diseases often have higher incidence rates in genetically isolated populations). For example, Ashkenazi Jews have a heightened risk of suffering from Tay-Sachs, Canavan's disease, among other disorders.

195. Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting*, 1 INNOVATION POL'Y & ECON. 119, 120-50 (2001).

196. Gregory P. Lekovic, *Genetic Diagnosis and Intellectual Property Rights: A Proposal to Amend "The Physician Immunity Statute"*, 4 YALE J. HEALTH POL'Y, L. & ETHICS 275, 300 (2004) ("This is what Michael Heller and Rebecca Eisenberg have referred to as the 'tragedy of the anticommons' . . . in biomedical research." (citing Michael Heller &

The aforementioned concerns suggest that “data sharing is the key to the future of genetic discoveries and bioinformatics, and [that] gene patents impede[] research aimed at identifying the role of genes in medical conditions.”<sup>197</sup> From the beginning of the Human Genome project, many scientists and private companies have recognized the importance of keeping the genome freely available. In 1994, the pharmaceutical company Merck funded a massive drive to generate gene sequences and place them into public databases, thereby making them difficult to patent.<sup>198</sup> Shortly thereafter, a group of fifty prominent geneticists adopted the Bermuda principles in 1996 which advocated that all “human genome sequence information should be freely available in the public domain in order to encourage research and development and to maximize its benefit to society.”<sup>199</sup>

In fact, in the case of genetic diagnostics, patent protection may “raise the cost of healthcare while inhibiting its effective delivery.”<sup>200</sup> The cost-benefit analysis indicates that enforcing the patents carries with it significant costs and minimal benefits. “In other words, enforcing the patent would increase transaction costs and allow for the extraction of excess rents, the concerns raised by those critical of broad upstream patenting.”<sup>201</sup>

### *C. A Lower Standard of Care*

Patents on genetic diagnostics also potentially threaten to lower the quality of medical care by presenting physicians with a Hobson’s choice between violating either patent laws or their ethical duties. In 1995, controversy erupted over the case of *Pallin v. Singer*,<sup>202</sup> which involved a method patent for performing cataract surgery that did not require stitches. Pallin, the ophthalmologist who held the patent, sued another ophthalmologist for patent infringement for using his technique without obtaining a license. The case sparked a great deal of controversy and was heavily criticized by the AMA as a violation of physicians’ ethical obligations to share their discoveries.

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Rebecca Eisenberg, *Can Patents Deter Innovation?*, 280 SCIENCE 698, 701 (1996)).

197. *Ass’n of Molecular Pathology*, 702 F. Supp. 2d at 208.

198. *Id.*

199. *Id.* (citing Sulston Decl. ¶ 33).

200. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 138 (2006) (Breyer, J., dissenting).

201. Harry First, *Controlling the Intellectual Property Grab: Protect Innovation, Not Innovators*, 38 RUTGERS L.J. 365, 385 (2007).

202. *Pallin v. Singer*, 1996 WL 274407 (D. Vt. Mar. 28, 1996).

Congress ultimately amended the Patent Act in 1996 in response to these concerns. Under § 287(c), health care practitioners can be found liable for infringement, but cannot be subjected to monetary damages or injunctions for using patented medical or surgical techniques in medical practice.<sup>203</sup> However, the amendment was limited to medical practitioners who infringe a patent in the course of medical activity and did not cover clinical laboratory testing. 35 U.S.C. § 287(c) is limited to the protection of “medical practitioners who infringe a patent in the course of medical activity.”<sup>204</sup> It was not extended to cover “the practice of a patented use of a composition of matter in violation of such patent, or . . . the practice of a process in violation of a biotechnology patent,” or “the provision of pharmacy or clinical laboratory services (other than clinical laboratory services provided in a physician’s office).”<sup>205</sup> Thus, clinicians are not exempt from liability for infringing biotechnology patents and can be held liable for “contributing to infringement by others” by providing physicians with information or guidelines related to performing patented processes.<sup>206</sup>

Patents on genetic diagnostics also potentially threaten to lower the quality of medical care. These patents

[M]ay inhibit doctors from using their best medical judgment; they may force doctors to spend unnecessary time and energy to enter into license agreements; they may divert resources from the medical task of health care to the legal task of searching patent files for similar simple correlations; they may raise the cost of health care while inhibiting its effective delivery.”<sup>207</sup>

In some instances, patients may be forced into the difficult position of having to make life-changing decisions without the ability to obtain a second opinion due to the existence of a gene patent. This was

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203. 35 U.S.C. § 287(c) (2006). This is sometimes referred to as the Frist-Ganske medical procedures exemption statute.

204. *Id.*

205. *Id.*

206. See H.R. 3967, 107th Cong. (2002) (In 2002, Rep. Lynn Rivers introduced the Genomic Research and Diagnostic Accessibility Act, which included a provision which would have allowed researchers and medical practitioners to use patented gene sequences for noncommercial research purposes and exempted clinicians performing genetic tests from patent infringement liability. The bill did not become law. (<http://www.govtrack.us/congress/bill?bill=h107-3967>)).

207. Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 138 (2006) (Breyer, J., dissenting).

evidenced by Myriad Genetics' use of its gene patents, in which, in many cases, women facing potentially life-threatening decisions as to the proper course of care were prevented from obtaining a second set of test results.

Genetic diagnostic patents also may place medical practitioners in the untenable position of having to choose between violating their ethical duties as physicians or violating patent laws.<sup>208</sup> An accurate diagnosis is crucial in deciding on an effective treatment in the medical profession, where the Hippocratic Oath admonishes doctors to "First, do no harm." However, diagnostic gene patents can prevent doctors from providing their patients with an accurate diagnosis. For example, Myriad Genetics did not permit researchers to inform patients involved in research of the results of their genetic testing, which often left physicians unable to meet their ethical obligations to provide test results to research subjects, upon request.<sup>209</sup> The AMA has stated that the "use of patents . . . or other means to limit the availability of medical procedures places significant limitation on the dissemination of medical knowledge, and is therefore unethical."<sup>210</sup>

The decision in *LabCorp* highlights some of the absurdities of diagnostic patents. In upholding the diagnostic patents, the Federal Circuit was forced to find the doctors guilty of direct patent infringement based on testimony that "it would be malpractice for a doctor to receive a total homocysteine assay without determining cobalamin/folate deficiency."<sup>211</sup> Because a competent doctor reviewing the results would correlate those results with the presence or absence of a vitamin deficiency, virtually every doctor who ordered and read the tests was a direct infringer. Likewise, defendants were found guilty of inducing infringement based on publications in medical journals noting the diagnostic correlation. The Federal Circuit held that "a reasonable jury could find intent to induce infringement because *LabCorp*'s articles stated that elevated total homocysteine correlates to cobalamin/folate

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208. See, e.g., *Metabolite Labs. Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1365 (Fed. Cir. 2004) (finding the fact that doctors who did not find a correlation would be liable of medical malpractice was circumstantial evidence that doctors violated patent).

209. *Ass'n of Molecular Pathology v. U.S. Pat. & Trademark Office*, 702 F. Supp. 2d 181, 209 (S.D.N.Y. 2010).

210. American Medical Association, Op. 9.095, *The use of Patents and Other Means to Limit Availability of Medical Procedures*, (adopted June 1995), available at <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion9095.shtml> (last visited February 28, 2011).

211. *Lab. Corp. of Am. Holdings*, 370 F.3d at 1364.

deficiency.”<sup>212</sup> Thus, all that was necessary for the doctor’s application of the correlation was knowledge of it.

#### V. CONCLUSION

The diagnostic gene patents at issue in *Molecular Pathology*, and other diagnostic patents which attempt to usurp all practical applications of an abstract idea, constitute non-patentable subject matter. Diagnostic patents that give exclusive private ownership, “not of a new drug, or of a new diagnostic test, or even of a new method of diagnosing a particular disease - but rather of a scientific observation”<sup>213</sup> are not deserving of patent protection.

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212. *Id.* at 1365.

213. Brief for American Medical Ass’n, et al. as Amici Curiae Supporting Defendant-Appellees, Ass’n for Molecular Pathology v. U.S. Pat. & Trademark Office, 2009 WL 1307167 (Apr. 6, 2009).