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THE DISPARATE EFFECTS OF GENE PATENTS ON DIFFERENT CATEGORIES OF SCIENTIFIC RESEARCH

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I. *ASSOCIATION FOR MOLECULAR PATHOLOGY V. USPTO*[1]

A. Facts

Myriad Genetics ("Myriad") is a molecular diagnostics company that holds patents related to two important human genes: *BRCA1* and *BRCA2* ("*BRCA1/2*").[2] Scientists have determined that a person with a mutated *BRCA1* or *BRCA2* gene has an increased likelihood of developing breast and ovarian cancer.[3] The discovery of this correlation between *BRCA1/2* and a predisposition to cancer led to the creation of a diagnostic test for patients who want to assess their risk of developing breast or ovarian cancer.[4] Myriad offers this diagnostic test to clinicians and patients at a cost of over $3000 per test.[5] In the past, researchers at the University of Pennsylvania and Yale University offered similar diagnostic tests.[6] Myriad, however, has vigorously enforced its patents claiming isolated *BRCA1/2* genes and methods of comparing mutated *BRCA1/2* with the normal forms of the genes.[7] As a result, Myriad is currently the sole provider of the *BRCA1/2* diagnostic test.[8]

Due to their inability to offer the test or to obtain it for a reasonable cost, several plaintiffs filed a declaratory judgment action against Myriad on May 12, 2009, in the Southern District of New York.[9] Specifically, plaintiffs sought a declaration that fifteen claims from seven of Myriad's patents are directed to patent-ineligible subject matter under 35 U.S.C. § 101.[10] The challenged composition of matter claims cover mutations in isolated *BRCA1/2*.[11] Most of the challenged

1. Ass'n for Molecular Pathology v. USPTO (*Myriad I*), 702 F. Supp. 2d 181 (S.D.N.Y. 2010), *aff'd in part*, *rev'd in part*, 653 F.3d 1329 (Fed. Cir. 2011).

2. *Id.* at 184.

3. Ass'n for Molecular Pathology v. USPTO (*Myriad II*), 653 F.3d 1329, 1334 (Fed. Cir. 2011). ("The average woman in the United States has around a twelve to thirteen percent risk of developing breast cancer in her lifetime. Women with BRCA mutations, in contrast, face a cumulative risk of between fifty to eighty percent of developing breast cancer and a cumulative risk of ovarian cancer of between twenty to fifty percent.")

4. *Id.*

5. *Myriad I*, 702 F. Supp. 2d at 203.

6. *Id.* at 204–05.

7. *Id.* at 205. Myriad sent cease and desist letters to several university researchers and sued the University of Pennsylvania for infringement of its patents related to isolated *BRCA1/2* DNA. *Id.*

8. *Id.* at 206.

9. *Id.* at 184, 186. Plaintiffs also named the United States Patent and Trademark Office ("USPTO") and officials of the University of Utah Research Foundation as defendants.

10. *Id.* at 184. Section 101 of Title 35 describes categories of inventions that are eligible for patent protection in the United States. The section reads: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101 (2006).

11. *Myriad I*, 702 F. Supp. 2d at 212–13. Most of the controversy surrounding what is referred to as a "gene patent" involves claims on compositions of matter, rather than method

method claims cover a process of "analyzing" or "comparing" a patient's *BRCA1/2* sequences with the normal genetic sequences to determine whether the patient's genes are mutated.[12] An additional method claim at issue describes a process of screening potential cancer therapeutics in order to identify new methods of treating cancers caused by *BRCA1/2* mutations.[13]

B. District Court

Defendants moved to dismiss the complaint, but the court denied the motion after determining that plaintiffs had the necessary standing to assert their claims.[14] On March 29, 2010, Judge Robert Sweet ruled on the parties' cross-motions for summary judgment, holding that all of the challenged composition and method claims assigned to Myriad were invalid under 35 U.S.C. § 101.[15] In so holding, the court determined that the isolated *BRCA1/2* claimed in Myriad's patents were not "markedly different" from the *BRCA1/2* found in the human body.[16] The court described DNA as "a physical embodiment of information," stating that "[t]he preservation of this defining characteristic of DNA in its native and isolated forms mandates the conclusion that the challenged composition claims are directed to unpatentable products of nature."[17]

C. Federal Circuit

On appeal, the Federal Circuit affirmed in part and reversed in part.[18] The panel affirmed the district court's decision to exercise declaratory judgment jurisdiction, holding that at least one plaintiff had standing to assert claims against the defendants.[19] Turning to the merits of the case, the Federal Circuit reversed the district court's grant of summary judgment with regard to Myriad's composition claims to

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claims covering diagnostic or therapeutic uses of a gene. *See, e.g.*, Alan R. Williamson, *Gene Patents: Socially Acceptable Monopolies or an Unnecessary Hindrance to Research?*, 17 TRENDS IN GENETICS 670 (2001). Williamson argues that "[d]iscovering genes is now a routine process that does not warrant a 'composition-of-matter' patent. By contrast, determining the function(s) of a gene might be an inventive step worthy of the allowance of a 'use' patent on the gene product covering that function." *Id.* at 673. Because they are at the center of the gene patent controversy, composition of matter claims are the focus of this analysis.

12. *Myriad I*, 702 F. Supp. 2d at 213–14.

13. *Id.* at 214.

14. *Id.*

15. *Id.* at 181, 238.

16. *Id.* at 229.

17. *Id.*

18. Ass'n for Molecular Pathology v. USPTO (*Myriad II*), 653 F.3d 1329, 1358 (Fed. Cir. 2011).

19. *Id.*

isolated *BRCA1/2*.[20] In so holding, the court concluded that "the challenged claims are drawn to patentable subject matter because the claims cover molecules that are markedly different — that is, have a distinctive chemical identity and nature — from molecules that exist in nature."[21] The court emphasized that while DNA in the human body is combined with other genetic materials, isolated DNA has been chemically cleaved and exists as a free-standing molecule.[22] The court explained that the process of isolating DNA requires the breaking of covalent bonds, thus creating a molecule with a different chemical structure than that of DNA found in nature.[23]

The Federal Circuit went on to affirm the district court's grant of summary judgment with regard to Myriad's method claims for "analyzing" or "comparing" mutated *BRCA1/2* sequences with normal *BRCA1/2* sequences.[24] The court held that these method claims are unpatentable because they "recite[] nothing more than the abstract mental steps necessary to compare two different nucleotide sequences."[25] At the end of its opinion, the court considered the patentability of a claim directed to a method for screening potential cancer therapeutics.[26] Reversing the district court's decision, the Federal Circuit held that this method claim was patentable, in part because it contains transformative steps that satisfy the machine-or-transformation test.[27]

Judge Moore wrote separately to emphasize the distinction between cDNA and isolated DNA.[28] She explained that while cDNA is "markedly different" from DNA found in the human body and is clearly eligible for a patent, isolated DNA presents a closer case of eligibility.[29] Ultimately, she concurred in the court's opinion to up-

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20. *Id.* at 1358.
21. *Id.* at 1351.
22. *Id.*
23. *Id.*
24. *Id.* at 1355–58.
25. *Id.* at 1357.
26. *Id.* at 1358.
27. *Id.* The "machine-or-transformation" test can be used as "a useful and important clue" to determine whether a process satisfies the patentable subject matter eligibility requirements of 35 U.S.C. § 101. Bilski v. Kappos, 130 S. Ct. 3218, 3227 (2010). Under this test, it is more likely that an invention will qualify as a patentable process "if (1) it is tied to a particular *machine* or apparatus, or (2) it *transforms* a particular article into a different state or thing." *Id.* at 3224 (emphasis added) (internal quotation marks omitted).
28. Complimentary DNA ("cDNA") is created using a mature RNA molecule as a template. As a result, the chemical structure of cDNA is different from anything found in the human body. The chemical structure of isolated DNA, in contrast, is more similar to the chemical structure of natural DNA molecules in that it is made up of an identical sequence of base pairs. *Myriad II*, 653 F.3d at 1362–63 (Moore, J., concurring in part).
29. *Id.* at 1366. The distinction Judge Moore draws between cDNA and isolated DNA echoes the position taken by the government in its amicus brief. *See* Brief for United States as Amicus Curiae Supporting Neither Party at *14–18, *Myriad II*, 653 F.3d 1329 (No. 2010-1406), 2010 WL 4853320. The Department of Justice argued that, while cDNA and other

hold Myriad's composition claims, emphasizing the deference owed to longstanding policy choices of the United States Patent and Trademark Office ("USPTO") that Congress has never challenged.[30]

Judge Bryson dissented from the court's holding that Myriad's claims to isolated *BRCA1/2* are valid under 35 U.S.C. § 101.[31] Judge Bryson argued that "there is no magic to a chemical bond that requires us to recognize a new product when a chemical bond is created or broken."[32] He described the process of isolating a gene as "akin to snapping a leaf from a tree": merely "plucking the leaf would not turn it into a human-made invention."[33] Judge Bryson disagreed with Judge Moore that any deference was owed to the longstanding policy choices of the USPTO.[34] According to Judge Bryson, the USPTO lacks substantive rulemaking authority with regard to issues such as patentability, and the role of the courts is to interpret the law passed by Congress in accordance with common law precedents.[35]

D. Significance

The *Myriad* case has intensified the focus of the scientific and legal communities on the costs and benefits of gene patenting. Proponents of gene patents argue that such patents are necessary to serve the primary goal of the patent system, namely to call forth new technologies that would not be invented without monopoly incentives.[36] Critics respond that gene patents do more to hinder innovation than to encourage it because monopoly control of genes impedes the ability of scientists to engage in subsequent research and limits patient access to innovative medical technologies.[37]

Should we continue to grant gene patents or should we ban them altogether? Legal scholars and scientists on both sides of the issue present compelling arguments, and both proponents and critics of gene patents are correct to some extent. This is because gene patents are important for the development of a wide range of scientific dis-

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forms of purified DNA should be patentable, isolated DNA is a product of nature that should not be patentable. *Id.*

30. *Myriad II*, 653 F.3d at 1372–73.

31. *Id.* at 1373 (Bryson, J., concurring in part and dissenting in part).

32. *Id.* at 1375.

33. *Id.* at 1377.

34. *Id.* at 1380–81.

35. *Id.*

36. *See, e.g.*, Robert Mullan Cook-Deegan & Stephen J. McCormack, *Patents, Secrecy, & DNA*, 293 SCIENCE 217, 217 (2001).

37. *See* Timothy Caulfield, *Human Gene Patents: Proof of Problems?*, 84 CHI.-KENT L. REV. 133, 133–34 (2010); Matthew M. Karlan, *Patent Policy, Natural Products, and the Gene Patent Debate: Seeking the Proper Judicial Mode of Analysis*, 67 N.Y.U. ANN. SURV. AM. L. 95, 102 n.38 (2011).

coveries, including therapeutic proteins,[38] diagnostic methods[39] (like the patents at issue in *Myriad*), and research tools.[40] Each of these genetic technologies is governed by different research and development ("R&D") costs, incentives to invent, and opportunities for licensing and follow-on research.

The scholarly literature lacks a comprehensive, nuanced analysis of the disparate effects of gene patents on different types of genetic technologies. Many articles consider the effect that banning gene patents would have on one type of technology and draw conclusions without analyzing the effects of such a ban on other types of technology.[41] With each side of the debate attempting to prove its point, nobody has stopped to consider whether we are even asking the right question. Rather than debating whether to ban or to allow all gene patents, perhaps we should be asking: *under what circumstances* are gene patents more beneficial than they are costly, and vice versa?

This Comment attempts to answer this question by analyzing whether gene patents advance or impede the primary goals of the patent system when they are used to develop different kinds of genetic technology. The two goals of the patent system that will be the focus of this analysis are: (1) incentivizing the invention, development, and commercialization of new technology;[42] and (2) encouraging and fa-

38. Therapeutic proteins are large, complex molecules used to treat disease. Examples include antibodies, insulin, and coagulation factors. *See* Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, 76 UMKC L. REV. 295, 324 (2007).

39. One type of gene patent important to the development of diagnostic methods is directed to a mutation in a single gene that is associated with either a disease or a predisposition to a disease. *See* Birgit Verbeure et al., *Analysing DNA Patents in Relation with Diagnostic Genetic Testing*, 14 EUR. J. HUM. GENETICS 26, 30 (2006). Another type of gene patent claims a stretch of non-protein-coding DNA that is useful for genetic identification and has applications in forensic analysis and paternity testing. Holman, *supra* note 38, at 317, 351.

40. The term "research tool" generally refers to a resource used by scientists that has "no immediate therapeutic or diagnostic value." E. Richard Gold et al., *Genetic Research Tools, the Research Exception, and Open Science*, 3 GENEDIT 1, 1 (2005), http://www.cipp.mcgill.ca/data/publications/00000040.pdf. An "upstream" technology research tool is valuable because it furthers the development of "downstream" commercial products. Holman, *supra* note 38, at 340.

41. *See, e.g.*, Robert Cook-Deegan et al., *The Dangers of Diagnostic Monopolies*, 458 NATURE 405 (2009) (analyzing the gene patent controversy with regard to diagnostic methods); Gold, *supra* note 40 (studying the impact of patented genetic research tools on biomedical research).

42. The patent system functions by correcting market failure caused by the public goods nature of knowledge-based innovation. Because knowledge is a nonrivalrous and nonexcludable public good, innovators who bear the cost of invention may be unable to recoup such costs because others can easily free ride without investing in research and development. This situation constitutes market failure because it insufficiently incentivizes the invention of new technologies. The patent system corrects this failure by awarding limited monopolies to inventors of knowledge-based goods, giving them the right to exclude others from making, using, or selling their discoveries. Arguably, the most important function of the patent system is that it encourages inventors to create technology that they otherwise would not have created. *See generally* Michael S. Mireles, *An Examination of Patents,*

cilitating further innovation.[43] Parts II, III, and IV, respectively, consider the extent to which these goals are advanced by gene patents in the context of three kinds of genetic technology: therapeutic proteins, diagnostic methods, and research tools. When gene patents are involved in the development of different genetic technologies, they serve the goals of the patent system in varying ways according to the costs and incentives associated with each kind of technology. Accordingly, a one-size-fits-all solution — all gene patents are allowed or no gene patents are allowed — is not the best way to resolve the current debate about gene patenting. Part V concludes by discussing potential resolutions to the gene patenting debate.

II. THERAPEUTIC PROTEINS

A. Do Gene Patents Provide Crucial Incentives to Invent, Develop, and Commercialize?

It is very expensive for pharmaceutical and biotechnology companies that make and sell therapeutic proteins to find a new chemical entity and engage in the R&D needed to bring the therapy to market.[44] Some of the up-front costs are associated with the initial research that is necessary to discover proteins and other large molecules with the potential to treat human disease.[45] The rest of a company's R&D money is spent on clinical trials and other research phases that are required by the Food and Drug Administration (FDA) before the agency will approve a drug for sale.[46]

Licensing, Research Tools, and the Tragedy of the Anticommons in Biotechnology Innovation, 38 U. MICH. J.L. REFORM 141, 151–52 (2004).

43. One way the patent system accomplishes this goal is by requiring patentees to describe their inventions in sufficient detail to enable a person skilled in the relevant art to make and use the invention without undue experimentation. The patent system's incentive to disclose is thought to benefit society by encouraging innovators to publicize information that they might otherwise protect as a trade secret. Although patented information is subject to monopoly control by the patentee, inventions that are disclosed to the public may inspire follow-on innovators to license and improve the technology. Additionally, a patentee's monopoly rights expire twenty years after the inventor files for a patent, at which point the information enters the public domain and is available to everyone free of charge. *See id.* at 153–54.

44. *See* Rochelle C. Dreyfuss, *The Patentability of Genetic Diagnostics in U.S. Law and Policy* 14 (N.Y.U. Sch. of Law, Pub. Law Research Paper No. 10-68, 2010), *available at* http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1678123.

45. Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 469, 477 (2007).

46. A 2007 study that calculated the costs associated with the discovery and development of therapeutic biopharmaceuticals reported that total R&D costs per approved molecule are about $1.2 billion. The study found that about half of this money ($615 million) is spent during the preclinical phase, and the other half ($626 million) is spent on clinical trials and the FDA approval process. These totals take into account both the cost of biopharmaceuticals that fail before they receive FDA approval and time costs (without time costs, the figures decrease by about fifty percent). *Id.*

If a pharmaceutical or biotechnology company has a patent on a gene encoding a protein that shows promise as a therapy for human disease, the company can spend considerable time and money developing the therapy without threat from competitors interested in selling the same or similar product.[47] Once the therapeutic protein is on the market, the company can continue to enjoy the monopoly secured by the gene patent for the remainder of the patent term.[48] If, however, the company is not able to patent the gene encoding a particular protein of interest, other pharmaceutical and biotechnology companies would not be prohibited from using the gene and its protein to develop the same therapy. Competition would then drive down the price of the drug, and the company's return on its investment would be significantly reduced. In such a case, there is a substantial risk that the company will not be able to recoup the R&D costs of bringing the therapy to market.[49] A company considering whether to pursue R&D of a potentially promising protein will usually be averse to the risk of failing to recoup R&D costs.[50] Therefore, gene patents offer a form of market exclusivity that incentivizes firms to take on the project of developing a therapeutic protein, getting FDA approval for it, and ultimately selling it to consumers.[51]

Of course, patents are not the only way to attain market exclusivity. The new regulatory pathway for therapeutic proteins recently established by Congress might diminish the role that gene patents play in the development and commercialization of therapeutic proteins. A provision of the Patient Protection and Affordable Care Act ("PPACA") passed in 2010 gives the FDA the power to grant twelve years of market exclusivity for an innovative therapeutic protein.[52] Critics of the new regime worry that twelve years of FDA exclusivity will not sufficiently incentivize the development and commercialization of protein drugs, but others believe it is a positive development.[53] It remains to be seen whether the pharmaceutical industry's reliance

47. *See* Frederic M. Scherer, *The Economics of Human Gene Patents*, 77 ACAD. MED. 1348, 1349–50 (2002).

48. *See id.*

49. *See id.* at 1350.

50. *See id.* at 1354.

51. *See id.* at 1350.

52. Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 7002, 124 Stat. 119, 807 (2010) (codified at 42 U.S.C.A. § 262(k)(7)(A) (West Supp. 2010)).

53. *See* Mari Edlin, *PPACA Creates Approval Pathway for Follow-On Biologics*, DRUG TOPICS (Aug. 15, 2010), http://drugtopics.modernmedicine.com/drugtopics/Chains+%26+Business/Web-extra-PPACA-creates-approval-pathway-for-follo/ArticleStandard/Article/detail/680424 ("While some industry leaders agree [that a twelve-year exclusivity period is sufficient to encourage research and development], others are concerned that an insufficient period of patent protection for brand-name manufacturers' intellectual property could be a limited incentive to invest in the costly development of biologics.").

on gene patents will decrease in the coming years as the new PPACA regime is implemented.[54]

B. To What Extent Do Gene Patents Encourage and Facilitate Follow-On Innovation?

Because patents contribute to the storehouse of public knowledge by providing an incentive to disclose new discoveries, banning gene patents might reduce the quantity of socially valuable information available to the public. This concern is especially salient with regard to therapeutic proteins since they are complex molecules that are incredibly difficult to reverse engineer.[55] If gene patents are not available and a biotechnology company decides to protect its upstream innovations as trade secrets, the public will not have access to that information and will not be able to use it for follow-on innovation. As a result, scientists who would have been interested in licensing the patented technology might not even know that the technology exists.

Even if gene patents are banned, however, it still might be possible to encourage pharmaceutical companies to disclose information about therapeutic proteins. Under the new regulatory regime for biologics, the FDA could require drug manufacturers to disclose certain information in order to receive market exclusivity for an innovative drug.[56] For example, the FDA could deny a firm market exclusivity until it discloses all manufacturing trade secrets associated with the drug product.[57] Alternatively, the FDA could publish the clinical trial data submitted by a manufacturer whose therapeutic protein drug has been approved.[58] Although these suggestions are highly controversial and would almost certainly be opposed by pharmaceutical companies, minor adjustments to the newly enacted regulatory regime for biologics could incentivize protein drug manufacturers to disclose socially valuable information without relying on gene patents.

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54. President Obama's plan for economic growth and deficit reduction, unveiled on September 8, 2011, includes a proposal to reduce the length of exclusivity awarded to brand name biologics from twelve years to seven years. *See* Donald Zuhn, *President's Deficit Reduction Plan Seeks to Reduce Exclusivity Period for Biologics and Prohibit Pay-for-Delay Deals*, PAT. DOCS (Sept. 21, 2011), http://www.patentdocs.org/2011/09/presidents-deficit-reduction-plan-seeks-to-reduce-exclusivity-period-for-biologics-and-prohibit-pay-.html.

55. Erika Jonietz, Generic Biotech, tech. rev. (2004), available at http://www.technologyreview.com/biotech/13970.

56. Maxwell R. Morgan, Regulation of Innovation Under Follow-On Biologics Legislation: FDA Exclusivity as an Efficient Incentive Mechanism, 11 Colum. Sci. & Tech. L. Rev. 93, 116 (2010).

57. *Id.*

58. *Id.*

III. DIAGNOSTIC METHODS

A. Do Gene Patents Provide Crucial Incentives to Invent, Develop, and Commercialize?

While there is strong evidence that gene patents are important, or even necessary, to promote the development and commercialization of therapeutic proteins, the evidence suggests that such patents may be more detrimental than beneficial in the diagnostic testing arena. The cost of developing diagnostics is generally low, especially as compared to the cost of developing therapeutic proteins.[59] According to a report on gene patents issued last year by the Department of Health and Human Services Advisory Committee on Genetics, Health, and Society, it typically costs between $8000 and $10,000 per sequenced gene to develop a diagnostic test.[60] One reason that the cost of developing a diagnostic method is much lower than the cost of developing a protein drug is because the FDA does not usually require expensive premarket review for genetic tests.[61] As a result, it is relatively cheap to conduct a correlation study and translate the findings into a diagnostic test that can be performed on patients.[62] Because R&D costs are low for diagnostic tests, a company interested in developing such a test is likely to pay for R&D even if it does not have a patent on the gene of interest. If the diagnostic test is a success, there is a good chance that the company will recoup its R&D costs without needing the market exclusivity conferred by a gene patent.[63] Thus, gene patents may not be necessary to incentivize companies to develop and commercialize new diagnostic methods.

Another reason why gene patents may not be needed to call forth diagnostic tests is that scientists working in academic and government-funded labs have incentives to develop such tests even when

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59. Dreyfuss, *supra* note 44, at 14.

60. SECRETARY'S ADVISORY COMM. ON GENETICS, HEALTH, & SOC'Y, DEP'T OF HEALTH & HUMAN SERVS., GENE PATENTS & LICENSING PRACTICES & THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 34 (2010) [hereinafter SACGHS], *available at* http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_patents_report_2010.pdf. A recent study found that "[t]he development of human genome research has been accompanied by a shift of attention from the classical model of discovering loci involved in single-gene disorders (Mendelian traits) to elucidation of multiple genetic factors of small effect involved in common complex diseases." Quanhe Yang et al., *How Many Genes Underlie the Occurrence of Common Complex Diseases in the Population?*, 34 INT'L J. EPIDEMIOLOGY 1129, 1129 (2005). As a result, as scientists continue to investigate diseases that are caused by multiple genes, it will grow increasingly difficult to correlate specific genes with specific diseases. It is therefore possible that the cost of developing a genetic test will increase in the future.

61. SACGHS, *supra* note 60, at 94. The FDA does require premarket approval for the small minority of genetic tests that are manufactured and sold as kits to clinical labs. *Id.* at 61.

62. Dreyfuss, *supra* note 44, at 15.

63. *See id.*

their work is not protected by a patent.[64] Researchers in academia and the public sector are motivated by many factors that have nothing to do with patents, including general scientific curiosity or a commitment to helping patients.[65] Encouraged by these incentives, academic and public sector scientists conduct important basic research related to the development of diagnostic methods, including identifying mutations and making associations between genetic traits and disease.[66] Additionally, because the cost of developing a diagnostic test is low, academic and government-funded labs can obtain funding for diagnostic research without getting a gene patent.[67] Support for diagnostic research often comes in the form of government grants, charitable donations from patient advocacy groups, or payment for services (such as the administration of a previously-developed genetic test to patients).[68]

Not only is it common for scientists to develop diagnostic methods independently of the patent system's monopoly incentives, but there is also evidence that gene patents actually impede progress in this arena. A 2003 study by Mildred Cho and her colleagues at the Center for Biomedical Ethics at Stanford University concluded that patents and licenses have had a significant negative effect on the ability of clinical laboratories to develop and provide genetic tests.[69] Many of the surveyed labs reported that their inclination to develop a new diagnostic test had been adversely affected by the threat of a patent infringement lawsuit,[70] since "holders of gene-based diagnostic patents are active in asserting their intellectual property rights."[71]

Despite the disheartening results of Cho's study, there is evidence that gene patents do not *inevitably* hinder the development and commercialization of diagnostic methods. For example, Johns Hopkins University is committed to a non-exclusive licensing regime for its gene patents related to cystic fibrosis, and diagnostic testing for cystic

64. *Id.*
65. *Id.*
66. *Id.*
67. *Id.*
68. *Id.*
69. Mildred K. Cho et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3 (2003). Out of 122 labs that were surveyed, seventy-nine had been contacted by a patent or license holder regarding the lab's potential infringement of a patent due to its administration of a diagnostic test. *Id.* at 4–5. Thirty of the labs that had received infringement warnings reported that these warnings had deterred the lab from continuing to offer the test. *Id.* at 5.
70. *See id.* at 8.
71. NAT'L RESEARCH COUNCIL, REAPING THE BENEFITS OF GENOMIC AND PROTEOMIC RESEARCH: INTELLECTUAL PROPERTY RIGHTS, INNOVATION, AND PUBLIC HEALTH 131 (Stephen A. Merrill & Anne-Marie Mazza eds., 2006).

fibrosis is currently available in sixty-three labs across America.[72] The commercialization of diagnostic testing for Huntington's disease has been a similar success story; although the disease is rare, non-exclusive licensing of gene patents has led to the widespread availability of testing by over fifty private and nonprofit labs.[73] These examples demonstrate that gene patents do not interfere with the goals of the patent system when gene patent holders are committed to responsible licensing schemes. However, it is not the province of the patent system to determine what patent holders do with the intellectual property rights they have been granted by the USPTO.

B. To What Extent Do Gene Patents Encourage and Facilitate Follow-On Innovation?

One of the most serious concerns about gene patents in the diagnostic testing arena is that such patents exacerbate the tragedy of the anticommons and therefore impede advances in disease prevention and treatment.[74] The tragedy of the anticommons describes a situation in which the existence of numerous rights holders frustrates the achievement of a socially desirable outcome.[75] The large number of patents on human genes and the diverse array of patent owners make the tragedy of the anticommons a legitimate concern. With regard to diagnostics, the tragedy of the anticommons can interfere with scientific and technological advances in the detection of genetic disease.[76] Many diseases can be caused by mutations in different genes, so a complete analysis of a person's susceptibility to a particular disease often requires a diagnostic test that examines all potential sources of the disease.[77] In order to develop a suitably comprehensive diagnostic test, a scientist must obtain permission to experiment with each genetic marker for the disease.[78] If each gene has been patented by a different institution or company, the scientist may be prohibited from conducting his research due to the high transaction costs he would incur in negotiating licenses with multiple patent owners.[79] In such

72. Subhashini Chandrasekharan et al., *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Cystic Fibrosis*, 12 GENETICS MED. S194, S205 (SUPP. 2010); Dreyfuss, *supra* note 44, at 14.

73. Dreyfuss, *supra* note 44, at 14.

74. *Id.* at 1–2.

75. *See* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (1998).

76. Dreyfuss, *supra* note 44, at 1–2.

77. *Id.* at 8.

78. *See id.* at 13.

79. The tragedy of the anticommons also causes problems for the nascent field of personalized medicine. The idea behind personalized medicine is that it will one day be possible to specifically tailor disease treatment to an individual patient depending on his unique genetic characteristics. This process will require doctors to screen a patient's entire genome for a wide variety of genetic markers, including specific alleles and mutations that indicate the

situations, gene patents obstruct the goal of the patent system to facilitate transactions and encourage follow-on innovation.

Despite theoretically legitimate concerns about the effects of gene patents on access to technology and follow-on innovation, a 2006 analysis of human gene patenting controversies concluded that the problems predicted by the tragedy of the anticommons theory are not borne out in the available data.[80] Although it is true that numerous institutions have patented tens of thousands of human genes, studies have found a relatively low incidence of the problems that would be expected if anticommons mechanisms were in fact operating in the genetic research industry.[81] Specifically, it does not appear as if access problems are as severe as the anticommons theory would predict.[82] In addition to the wide availability of opportunities to license patented genes, researchers have found ways to get around gene patents if a patent owner withholds access. For example, scientists often take their research offshore or challenge questionable patents in court.[83] Some academic scientists even decide to risk using patented technology without a license; there is evidence that academic researchers face little or no real threat of a patent infringement lawsuit.[84]

IV. RESEARCH TOOLS

A. Do Gene Patents Provide Crucial Incentives to Invent, Develop, and Commercialize?

Rebecca Eisenberg has argued that patents on research tools are not needed to incentivize the development and commercialization of downstream technologies.[85] Because patented research tools — including gene patents — cannot prevent competing firms from manufacturing identical end products, patents on the final product provide stronger commercial protection than patents on a gene or other upstream technology.[86] Accordingly, "firms that are interested in devel-

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presence of or susceptibility to a disease. Without a streamlined or cost-effective way for scientists to get licenses from gene patent holders, the incredible potential of personalized medicine might never be realized. *See* Louis M. Solomon & Gregory J. Sieczkiewicz, *Impact of the US Patent System on the Promise of Personalized Medicine*, 4 GENDER MED. 187, 188 (2007).

80. Timothy Caulfield et al., *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 NATURE BIOTECHNOLOGY 1091, 1092 (2006).

81. *Id.*

82. *Id.*

83. *Id.* at 1093.

84. Holman, *supra* note 38, at 359.

85. Rebecca S. Eisenberg, *Technology Transfer and the Genome Project: Problems with Patenting Research Tools*, 5 RISK: HEALTH SAFETY & ENV'T 163 (1994).

86. *Id.* at 169.

oping end products for sale to consumers are unlikely to see patents on research tools as a very effective means of promoting their market exclusivity."[87] Therefore, the banning of gene patents might have little effect on the behavior of firms that already strive to develop and patent innovative downstream technologies. Eisenberg suggests that biotechnology companies might even increase their rates of development and commercialization if gene patents did not act as barriers to the development of targeted end products.[88]

Despite Eisenberg's prediction that end product development will increase in the absence of patents on research tools, some scholars have expressed concern that limiting patent protection to end products will deprive basic science research of the financial support that it requires.[89] Aaron Kesselheim and Jerry Avorn have argued that limiting basic science patenting — by banning gene patents, for example — would shift corporate investment towards ventures that can be quickly and easily developed into profitable products.[90] In such a situation, a drug company might focus its efforts on developing a "me-too" drug[91] rather than a truly innovative product that improves upon drugs already on the market.[92] Additionally, firms would have little incentive to fund basic academic research because any discoveries would immediately enter the public domain.[93] If basic research were to suffer from a lack of adequate funding, fewer upstream discoveries would be made, which in turn would narrow the scope of downstream innovation.[94]

B. To What Extent Do Gene Patents Encourage and Facilitate Follow-On Innovation?

One reason why the patent system does not efficiently facilitate transactions between users of genetic research tools is because it is usually very difficult to determine the value of a gene at the time of patenting and licensing.[95] As is the case with other research tools, it is often unclear in the early stages of investigation whether a gene or its encoded protein will lead to the development of a valuable commer-

87. *Id.* at 170.

88. *See id.*

89. Aaron S. Kesselheim & Jerry Avorn, *University-Based Science and Biotechnology Products: Defining the Boundaries of Intellectual Property*, 293 J. AM. MED. ASS'N 850, 853 (2005).

90. *Id.* at 852–53.

91. "Me-too" drugs are "minor variations of highly profitable pharmaceuticals already on the market." Marcia Angell, *Excess in the Pharmaceutical Industry*, 171 CANADIAN MED. ASS'N J. 1451, 1451 (2004).

92. Kesselheim & Avorn, *supra* note 89, at 853.

93. *Id.*

94. *See id.* at 852–53.

95. Mireles, *supra* note 42, at 165.

cial product or service.[96] As a result of this uncertainty about the ultimate value of a patented gene, the patent holder will usually include a reach-through royalty provision in any license agreement it offers to third parties.[97] If a license agreement has a reach-through royalty provision, the cost of the license includes the value of the right to use the patented technology in case the research tool leads to the development of a blockbuster commercial product.[98] Thus, the licensor can capture "a percentage of the sales of the commercial application developed from the research tool, even though the commercial application does not per se include the licensed patented gene."[99]

A scientist interested in conducting a particular study may be frustrated if the project he is working on requires him to license multiple genes. Each gene might be governed by a different license with a separate reach-through royalty provision, drastically increasing the cost of the study and eroding the profit potential of any resulting commercial product.[100] Additionally, the high transaction costs associated with negotiating licensing agreements has led to "rising frustration" among academic and industry scientists.[101] Much of this frustration stems from the difficulty of accurately gauging the value of a particular gene,[102] which makes it difficult for institutions to agree on a license that adequately protects the interests of both parties.

Although in some instances it appears that patented genes and associated reach-through royalty licenses impede access to new technology, there is evidence suggesting that reach-through royalty provisions are not as detrimental to scientific progress as they seem at first glance. Some reach-through royalty provisions place a ceiling on the total amount of royalties a licensor may collect from sales of a given commercial product.[103] In addition, reach-through royalty licenses have the advantage of making research tools available at a minimal up-front cost for use in noncommercial research.[104] An academic or public sector scientist, therefore, has every incentive to use patented genes to conduct basic research,[105] and the patent owner is

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96. *Id.*

97. *Id.*

98. *Id.*; *see* Stephen G. Kunin et al., *Reach-Through Claims in the Age of Biotechnology*, 51 AM. U. L. REV. 609, 618 (2002) ("For example, an agreement might specify that the supplier of a new receptor will provide the receptor to a researcher for use in seeking new hormones so long as the supplier receives reach-through royalties on any new hormone discovered or invented by the researcher.").

99. Mireles, *supra* note 42, at 165.

100. *Id.* at 165–66.

101. *See* NAT'L INSTS. OF HEALTH, REPORT OF THE NIH WORKING GROUP ON RESEARCH TOOLS (1998).

102. Mireles, *supra* note 42, at 165.

103. *Id.* at 166.

104. NAT'L RESEARCH COUNCIL, *supra* note 71, at 90.

105. There is evidence that research tools are widely available to scientists engaged in basic research. One study found that only one percent of academic biomedical researchers in

entitled to share the wealth if the research yields a commercial product.[106]

In addition, there are two other reasons why many scholars are not concerned about the effects of gene patents on public access to research tools. First, many genes are actually patented by public sector institutions rather than private companies.[107] Because publication is "the currency of success and professional advancement" in the public sector,[108] any gene patents owned by public institutions are less likely to interfere with the patent system's goal of encouraging follow-on innovation. Second, there is evidence that academic researchers face little or no real threat of being sued for patent infringement by private firms.[109] There are several reasons for this, including "the difficulty of enforcing patents, owing to the secrecy of research programs, costs of lost goodwill among researchers, costs of litigation, [and] the relatively small damages to be collected from blocking research use."[110]

V. CONCLUSIONS AND POTENTIAL SOLUTIONS

A. Conclusions

The preceding analysis demonstrates that there are many complex factors that should be considered before legislators or judges make a decision about the patentability of genes. The disparate effects of gene patents on different types of scientific research suggest that an all-or-nothing solution — either permitting or prohibiting all gene patents — might not be the best way to resolve the current debate. Instead, legislators and policymakers should consider a narrower tailoring of the law that recognizes that a cost-benefit analysis can favor or disfavor gene patents, depending on the category of scientific research in question. The *Myriad II* panel should have considered how its decision regarding the patentability of genes would affect scientific development outside the context of isolated *BRCA1/2*.

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the U.S. reported having to delay a project as a result of another's patent; none reported having to abandon a project. Caulfield, *supra* note 80, at 1093. Another study discovered that scientists only infrequently cite "technology access issues" as reasons behind a decision to abandon a research project. NAT'L RESEARCH COUNCIL, *supra* note 71, at 123. Such access issues include "unreasonable" license terms or the existence of too many patents covering research tools. *Id.* Some commentators have concluded that limitations restricting access to patented research tools may have to do with a public institution's willingness to accept the market price and access terms rather than with a private firm's refusal to license a gene to the public sector. Caulfield, *supra* note 80.

106. NAT'L RESEARCH COUNCIL, *supra* note 71, at 90–91.

107. Andrew W. Torrance, *Gene Concepts, Gene Talk, and Gene Patents*, 11 MINN. J.L. SCI. & TECH. 157, 161 (2010).

108. NAT'L RESEARCH COUNCIL, *supra* note 71, at 25.

109. Holman, *supra* note 38, at 359.

110. Caulfield, *supra* note 80, at 1093.

With respect to therapeutic proteins, it is apparent that gene patents are important for incentivizing the development of new drugs, and it is likely that the benefits of gene patents outweigh the costs. Because R&D for protein drugs is expensive, pharmaceutical and biotechnology companies are unlikely to invest in the development and commercialization of such drugs without assurance that their products will enjoy at least some market exclusivity.[111] This market exclusivity, however, does not necessarily have to be offered by the patent system. Under the new regulatory regime for biologics established by the PPACA, market exclusivity for a therapeutic protein drug is awarded by the FDA rather than by the patent system.[112] It remains to be seen whether the new regime will reduce the importance of gene patents to pharmaceutical companies developing protein drugs.

Compared to the significant role they play with regard to therapeutic drugs, gene patents appear to be less important for incentivizing development, commercialization, and follow-on research in the diagnostic testing arena. Because diagnostic tests are relatively cheap to develop,[113] the monopoly incentives provided by the patent system are less important to call forth new and improved diagnostic methods. In addition, public sector researchers have many incentives other than patents to develop and commercialize diagnostic tests, such as general scientific curiosity or a commitment to helping patients.[114] There is also a serious concern that the tragedy of the anticommons will hinder important new developments in the diagnostic arena.[115] Although the problems anticipated by the tragedy of the anticommons have not yet reached the magnitude predicted by the theory, such problems will likely be exacerbated by advances in personalized medicine and other technological developments on the horizon.[116]

With respect to research tools, it is more difficult to determine whether the costs of gene patents outweigh the benefits, or vice versa. On balance, patents on genetic research tools are probably more beneficial than they are costly to society. Although reach-through royalties sometimes interfere with incentives to develop and commercialize research tools, such royalties have the significant advantage of making research tools available at a minimal up-front cost for use in noncommercial research.[117] Encouragingly, studies have shown that

111. *See* Scherer, *supra* note 47, at 1354.

112. Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 7002, 124 Stat. 119, 807 (2010) (codified at 42 U.S.C.A. § 262(k)(7)(A) (West Supp. 2010)).

113. Dreyfuss, *supra* note 44, at 15.

114. *Id.*

115. *Id.* at 1–2.

116. *See supra* text accompanying note 79.

117. *See* Mireles, *supra* note 42, at 164–65.

patented genetic research tools are widely available to scientists interested in conducting basic research.[118]

B. Potential Solutions

Gene patents impose significant costs on society and the progress of science, but removing genes from the scope of patentable subject matter might not be the best solution to the problem. Using the patentable subject matter doctrine of patent law to ban gene patents, as the district court did in *Myriad I*, does not necessarily serve the patent system's goals of incentivizing the development and commercialization of new technologies and encouraging follow-on innovation. There are several options for continuing to allow gene patents while still facilitating technological and scientific advancement. Unfortunately, there is no perfect solution that serves both goals of the patent system with regard to all three scientific arenas (i.e., therapeutic proteins, diagnostic methods, and research tools).

One possible solution is to adopt some form of experimental use exemption,[119] perhaps as a "fair use" doctrine that exempts scientists from patent infringement if they use patented genes for basic research or diagnostic test development. The biggest strength of this solution is that it would facilitate follow-on innovation by generally increasing the quantity of legal, non-commercial, scientific research. One of the biggest weaknesses of an experimental use exemption is that it would be incredibly hard to implement in this Bayh-Dole era, in which almost all basic research is undertaken with some commercial purpose.[120] Additionally, creating a research exemption doctrine in patent law would significantly weaken the market exclusivity associated with gene patents: manufacturers of commercial products such as drugs or diagnostics would be threatened by the possibility that "fair use" research might lead to a better drug or diagnostic for a particular genetic disease. Thus, an experimental use exemption might erode the incentives that the patent system currently provides to encourage the development and commercialization of therapeutic proteins and diagnostic methods.

Another possible solution is for the government to institute a compulsory licensing scheme that would require gene patent holders

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118. *See supra* text accompanying note 105.

119. The Federal Circuit effectively eliminated patent law's experimental use defense in *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002).

120. *See generally* Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289 (2003). The Bayh-Dole Act codified a U.S. policy allowing scientists to seek patent rights in the results of government-sponsored research. The Act prompted universities and public institutions to a file an increased number of patents on basic research discoveries with the expectation that those patents would prove commercially valuable. *Id.* at 290–91.

to offer reasonable licenses to public sector scientists engaged in non-commercial research. In the United Kingdom, for example, the government is permitted to compel a company to license a patent if the invention has not been commercialized "to the fullest extent that is reasonably practical" after three years.[121] The U.S. has taken the position that there should be no general provision for compulsory patent licensing,[122] but the government could design a compulsory licensing scheme that limits licensees to specifically-defined uses of gene patents. As with the previous solution, compulsory licensing would undoubtedly serve the patent system's goal of facilitating follow-on innovation by increasing access to patented genes. Unfortunately, like a "fair use" exemption, compulsory licensing would probably weaken gene patent rights so that such rights would no longer offer a robust incentive for firms to invest in developing and commercializing certain technologies. The slight advantage this solution has over the experimental use exemption is that gene patent holders would at least be rewarded with licensing fees for discovering and patenting important genes.

A final solution is to use institutional mechanisms to increase communication between patent holders and scientists interested in conducting genetic research. Historically, innovators engaged in mutually dependent relationships have created institutions to reduce the transaction costs of licensing patented technology.[123] A good example of this behavior is the establishment of cooperative cross-licensing agreements between members of the computer industry.[124] There are three institutional mechanisms that might alleviate some of the problems associated with gene patents: guidelines or best practices issued by industry leaders, patent pools, and clearinghouses.[125] All of these mechanisms attempt to reconcile the interests of patent holders, researchers, and patients.[126] Encouraging widespread and reasonable licensing would generally facilitate follow-on innovation with regard to therapeutic proteins, diagnostic methods, and research tools. The advantage of institutional mechanisms over an experimental use exemption or a compulsory licensing scheme is that such mechanisms have a less severe impact on incentives to develop and commercialize new technologies. More opportunities for licensing revenue may in fact increase incentives for scientists to discover and patent genes with important implications for human development or health. Pharmaceutical and diagnostic companies, however, may be leery of li-

121. NAT'L RESEARCH COUNCIL, *supra* note 71, at 96.

122. *Id.*

123. James Bradshaw, *Gene Patent Policy: Does Issuing Gene Patents Accord with the Purposes of the U.S. Patent System?*, 37 WILLAMETTE L. REV. 637, 659 (2001).

124. *Id.*

125. Dreyfuss, *supra* note 44, at 22–27.

126. *Id.*

censing their patented genes to others who could use them to invent a new and better commercial product.[127] One of the biggest challenges to establishing meaningful best practices, patent pools, or clearinghouses, therefore, is gene patent holders' resistance to participate.[128]

Finding a solution to the gene patent problem requires balancing two important goals of the patent system: encouraging meaningful follow-on research while maintaining patent rights that offer a robust incentive to develop and commercialize new technology. Of the three proposed solutions, implementing institutional mechanisms seems to be the most promising, but there are significant hurdles to establishing patent pools and clearinghouses and encouraging gene patent holders to participate.[129] Whatever solution is ultimately chosen by legislators and judges, it should not be to apply the patentable subject matter doctrine to ban all gene patents or to allow all gene patents, as the courts did in *Myriad I* and *Myriad II*, respectively. The ultimate goal should be to narrowly tailor the law in order to counteract the disparate effects that gene patents have on different types of scientific research.

127. *See* Kourtney Baltzer, Note, *A Clearinghouse: The Solution to Clearing Up Confusion in Gene Patent Licensing*, 24 HARV. J.L. & TECH. 519, 537–38 (2011); *see also* Mireles, *supra* note 42, at 177–78.

128. *See id.*

129. *See id.*