GENOMICS UNBOUND: THE SCIENTIFIC AND LEGAL CASE AGAINST PATENTS BASED ON NATURALLY OCCURRING DNA SEQUENCES

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I. INTRODUCTION

In ancient Greek mythos, the gods forbade humankind from having access to the natural phenomenon of fire. Without fire, the human race was shackled to a cold and dark existence. An existence bereft of industry, arts, civilization, and, ultimately, hope. Prometheus rectified this unjust monopoly over nature by

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stealing fire from Zeus and sharing it with all of humanity.[1] On March 20, 2012, *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* (*Prometheus*) seemed to again expand the capabilities of humankind.[2] This time the eponymous savior was a unanimous Supreme Court decision that correctly reaffirmed that one cannot patent "the underlying laws of nature themselves."[3]

When Congress enacted the United States Patent Act in 1952, it specified that patentable subject matter included anything "under the sun that is made by man."[4] Three decades ago, the United States Patent and Trademark Office (USPTO) issued the first gene patent and ushered in a brave new gold rush.[5] Some genes are associated with specific diseases, so the ability to identify these sequences is an essential first step for developing genomic diagnostic tests and therapies.[6] The problem with gene patents is that they allow modern-day prospectors to cordon off access to naturally occurring DNA sequences and exclude others from conducting research or developing useful applications based on these sequences.

In 2009, a broad coalition of plaintiffs sued Myriad Genetics Laboratories, Inc. (Myriad) over its breast cancer gene patents.[7] In July 2011, the U.S. Court of Appeals for the Federal Circuit ruled two to one in favor of upholding Myriad's gene patents in *Association for Molecular Pathology v. U.S. Patent & Trademark Office* (*Myriad*).[8] Subsequently, on March 26, 2012, the Supreme Court vacated the *Myriad* decision and remanded it back to the Federal Circuit for reconsideration in light of its ruling in *Prometheus*.[9] However, in *Association for Molecular Pathology v. U.S. Patent & Trademark Office* (*Myriad II*), a two to one majority in the Federal Circuit misapplied the Supreme Court's directive and upheld Myriad's composition claims covering isolated DNA sequences of the BRCA 1/2 breast cancer genes and complementary DNA (cDNA) sequences of BRCA that nature predetermined.[10]

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[1] The gods punished Prometheus by binding him to a rock with chains and having an eagle eat out his liver every day. As an immortal Titan, his liver regenerated every night and this torture repeated in perpetuity. Eventually, mankind repays its debt when Hercules unbinds Prometheus.

[2] Mayo Collaborative Servs. v. Prometheus Laboratories, Inc., 132 S. Ct. 1289 (2012).

[3] *See id.* at 1305.

[4] Jonah D. Jackson, Note, *Something Like the Sun: Why Even "Isolated and Purified" Genes Are Still Products of Nature*, 89 TEX. L. REV. 1453, 1454 (2011) (quoting S. REP. NO. 82-1979, at 5 (1952); H.R. REP. NO. 82-1923, at 6 (1952)) (internal quotation marks omitted).

[5] *See Gene Patents and Global Competition Issues*, 26 GEN: GENETIC ENGINEERING & BIOTECHNOLOGY NEWS (Jan. 1, 2006), http://www.genengnews.com/gen-articles/gene-patents-and-global-competition-issues/1163/.

[6] *See Fact Sheet: BRCA1 and BRCA2: Cancer Risk and Genetic Testing*, NAT'L CANCER INST. (May 29, 2009), http://www.cancer.gov/cancertopics/factsheet/risk/brca [hereinafter NAT'L CANCER INST.] (explaining, for example, that humans who inherit a harmful BRCA1 or BRCA2 mutation are at a higher risk of developing breast cancer).

[7] Complaint at 1, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 669 F. Supp. 2d 365 (S.D.N.Y. May 12, 2009) (No. 09-cv-04515-RWS), 2009 WL 1343027.

[8] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 653 F.3d 1329 (Fed. Cir. 2011), *vacated*, *appeal reinstated*, 467 Fed. Appx. 890 (Fed. Cir. 2012).

[9] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012).

[10] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 689 F.3d 1303, 1337 (Fed. Cir. 2012).

Myriad is now back in the Supreme Court as oral arguments were heard on April 15, 2013.[11] While there have been mixed opinions as to whether gene patents were dead in light of *Prometheus*,[12] this Article argues that a proper understanding of patent law, genomics, and public policy concerns should lead to no other result. The primary focus of this piece is to rebut certain vested interests in the biotechnology industry and affirm the normative claim that gene patents improperly fetter genomics research and development. First, through the lens of the *Myriad* case, we will recount why there was such a strong public interest movement against recognizing such patents. Specifically, we will show how patents on naturally occurring gene sequences and complementary DNA (cDNA) derived from these sequences stifle research, impede access to affordable testing, and detrimentally affect future developments in the cancer world. Second, we will briefly examine the Supreme Court's legal reasoning in *Prometheus* and how the Federal Circuit did not address the Court's concerns on remand. Finally, we will argue that, in order to significantly advance, the field of genomics needs freedom from ill-considered monopolies over naturally occurring DNA sequences as much as the ancients needed fire.

II. WHAT IS "NATURAL" IN GENOMICS? UNDERSTANDING THE SCIENCE TO ARRIVE AT THE PROPER LEGAL STANDARD

Since 2009, the American Civil Liberties Union (ACLU) has led the fight against Myriad and its strict enforcement of the BRCA1 and BRCA2 (BRCA1/2) patents.[13] Almost twenty percent of human genes are patented, including those associated with Alzheimer's disease, asthma, colon cancer, muscular dystrophy, and breast and ovarian cancer.[14] The USPTO, also a party-defendant in *Myriad*, grants these patents and gives the holders exclusive rights to the particular genetic sequences and their usage for twenty years.[15] By controlling the sequence to BRCA1/2, "Myriad also controls exclusive rights to mutations along those genes, any methods for locating mutations (whether those methods are currently known or not), and correlations between mutations and breast cancer."[16] In other words, Myriad has the right to prevent anyone else from testing, studying, or even looking at these genes.

The ACLU and joined co-parties contend that gene patents "undermine the free exchange of information and scientific freedom, bodily integrity, and women's health."[17] Their argument is that the contested gene patents create a

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[11] Transcript of Oral Argument at 1, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012) (No. 12–398), *available at* http://www.supremecourt.gov/oral_arguments/argument_transcripts/12-398-amc7.pdf.

[12] *See, e.g.*, Andrew Pollack, *Justices Send Back Gene Case*, N.Y. TIMES, Mar. 27, 2012, at B1.

[13] *FAQ: Legal Challenge to Patenting of Human Genes*, ACLU (Sept. 10, 2010), http://www.aclu.org/files/assets/legal_faq_brca.pdf [hereinafter *ACLU FAQ*].

[14] *Id.*

[15] *Id.*

[16] *Id.*

[17] Ann Weilbaecher, *Can Patent Protections Trample Civil Liberties? The ACLU Challenges the Patentability of Breast Cancer Genes*, 15 LOY. PUB. INT. L. REP. 10, 10 (2009) (quoting AMERICAN CIVIL LIBERTIES UNION, LEGAL CHALLENGE TO HUMAN GENE PATENTS

dangerous monopoly that restricts health care options for women, obstructs diagnostic testing, and stifles research.[18] Myriad, and its supporters in the biotechnology industry, allege that without intellectual property protection, companies will not invest the millions of dollars necessary to validate genetic tests. Myriad supporters also argue that this would work contrary to the original intent of the patent system, which was designed as a way to incentivize research and reward companies for their inventions.[19]

The breadth of amicus briefs filed in favor of the ACLU's position by professional medical societies, researchers, and cancer-afflicted individuals is very telling and demonstrates the outmoded and counter-normative analysis of the Court of Appeals of the Federal Circuit.[20] Essentially, the Federal Circuit validated patents for isolated DNA molecules and Myriad's BRCA1/2 genes, which vested interests within the biotechnology and pharma industries considered a victory.[21]

The direct consequence of upholding Myriad's patents was to ultimately redirect the standard of care for breast cancer testing.[22] Further, this appellate decision naturally caused great concern within the diagnostic field[23] and among those who are personally vested and impacted by the case. In the words of presiding Judge Sweet of the District Court:

> The challenges to the patents-in-suit raise questions of difficult legal dimensions concerning constitutional protections over the information that serves as our genetic identities and the need to adopt policies that promote scientific innovation in biomedical research. The widespread use of gene sequence information as the foundation for biomedical research means that resolution of these issues will have far-reaching implications, not only for gene-based health care and the health of millions of women facing the specter of breast cancer, but also for the future course of biomedical research.[24]

A. Who "Owns" Breast Cancer Genes?

> I am a business owner, artist and writer and I live in Austin, Texas. I was diagnosed with breast cancer in July of 2006 at age 36 and I had a double mastectomy. . . .

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5 (May 27, 2009), http://www.aclu.org/pdfs/freespeech/brca_qanda.pdf) (internal quotation marks omitted).

[18] *Id.* at 10–11.

[19] *Id.* at 11.

[20] *See* Jennifer A. Camacho, *Myriad and the Patent-Eligibility of Genetic Inventions: What's the Matter Under 35 U.S.C. § 101?*, 23 INTELL. PROP. & TECH. L.J. 10, 10, 12–16 (2011) (discussing the Federal Circuit's analysis).

[21] *Id.* at 10.

[22] *See* Declaration of Shobita Parthasarathy at ¶ 31, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 669 F. Supp. 2d 365 (S.D.N.Y. 2009) (No. 09 Civ. 4515 (RWS)), *available at* http://www.aclu.org/files/pdfs/freespeech/brca_Parthasarathy_declaration_20090826.pdf [hereinafter Declaration of Shobita Parthasarathy].

[23] *See* Jackie Wright Bonilla, *Highly Anticipated "ACLU/Myriad" Gene Patenting Case Decided by Federal Circuit*, PERSONALIZED MED. BULL. (July 29, 2011), http://www.personalizedmedicinebulletin.com/2011/07/29/highly-anticipated-aclumyriad-gene-patenting-case-decided-by-federal-circuit-subject-matter-paten/.

[24] Order Denying Defendant's Motion to Dismiss at 2–3, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 669 F. Supp. 2d 365 (S.D.N.Y. 2009) (No. 09 Civ. 4515).

> When I was confronted with this alien invasion (cancer), I decided to be as aggressive as I could to prevent the potential spread. I also decided to be diligent about getting second opinions along the treatment path. In one important area, however, I couldn't follow my second opinion treatment protocol . . . .
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> . . . .
>
> Because of patents on the BRCA genes, only one company out there has the ability to sequence them. I can't get a second sequencing done at a different company to validate my results. I am thinking about having my ovaries removed because of my risk for ovarian cancer. It is uncomfortable making such an important decision based on only one test.[25]

For the 12% of women who develop breast cancer in their lifetime, and the 1.4% of women who develop ovarian cancer,[26] prior knowledge of an inherited mutation makes the difference between life and death. "BRCA1 and BRCA2 are two human genes . . . associated with hereditary forms of breast and ovarian cancer," and, though everyone has these genes, mutations sometimes occur.[27] When they do, these individuals have an "elevated lifetime risk" of developing cancer.[28] In fact, studies have shown that a woman who inherits a harmful mutation in BRCA1/2 "is about five times more likely to develop breast cancer than a woman who does not have such a mutation."[29] Harmful BRCA1/2 mutations are also associated with breast and prostate cancer in men.[30]

Research indicates that individuals who test positive for BRCA1/2 gene mutations face an increased risk of breast cancer ranging from 40% to 85% and an increased risk of ovarian cancer of 15% to 40%.[31] Statistics from 2007 revealed that the relative lifetime risk of breast cancer was 2.7 to 6.4 times greater for those with BRCA mutations, and for ovarian cancer it was 9.3 to 35.3 times greater compared with other women.[32]

Myriad Genetics is a private biotechnology company based in Utah.[33] The company's research helped develop the BRCA1/2 patents, supported in part by grants from the National Institutes of Health (NIH).[34] In December of 1995, Myriad Genetics filed for patents of its "BRACAnalysis," which consists of a full analysis of the BRCA1/2 genes and detects five common mutations.[35] Although NIH investigators are listed as co-inventors, they assign the administration of the BRCA1/2 patents to the University of Utah with exclusive licens-

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[25] Genae Girard, *BRCA—Plaintiff Statements*, AMERICAN CIVIL LIBERTIES UNION (May 12, 2009), http://www.aclu.org/free-speech_womens-rights/brca-plaintiff-statements#girard [hereinafter Girard, *Plaintiff Statement*].

[26] NAT'L CANCER INST., *supra* note 6, at ¶ 2.

[27] *See ACLU FAQ*, *supra* note 13.

[28] *Id.*

[29] NAT'L CANCER INST., *supra* note 6, at ¶ 2.

[30] *ACLU FAQ*, *supra* note 13.

[31] Weilbaecher, *supra* note 17, at 11.

[32] Robert Cook-Deegan et al., *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers with Colon Cancers*, 12 GENETICS MED. S15, S19–S20 (Apr. 2010 Supp.).

[33] *ACLU FAQ*, *supra* note 13.

[34] Cook-Deegan et al., *supra* note 32, at S20.

[35] Suzanne Conaboy, Note, *Mirror, Mirror on the Wall: Why cDNA Is Deserving of Patent Protection* Ass'n for Molecular Pathology v. USPTO*, 2010 U.S. Dist. LEXIS 35418 (S.D.N.Y. Apr. 2, 2010)*, 30 TEMP. J. SCI., TECH. & ENVTL. L. 111, 125 (2011).

ing to Myriad Genetics.[36] The patents are co-assigned to the University of Utah and United States Department of Health and Human Services, but Myriad Genetics effectively controls the patent rights. Myriad's patent rights extend to both the BRCA1/2 genes and the accompanying tests.[37] "If Myriad had simply patented a test, then other scientists and laboratories could offer alternative testing on these genes."[38] Instead, Myriad's power extends to all research, testing, and future developments involving the BRCA genes.[39]

B. Misreading Precedent: Why Gene Sequences Fail the Patentability Test

The founder of Myriad Genetics, Dr. Mark Skolnick, has a strong belief that his company earned the patents because of the large financial investment involved in obtaining them.[40] He further claims that Myriad Genetics obtained the "right" to administer these tests. Myriad receives approximately 350 new samples per day.[41] Each analyzed sample undergoes one or both of the two tests Myriad performs: the Comprehensive BRACAnalysis test and an additional expanded BRACAnalysis Rearrangement Test (BART), which detects large rearrangement mutations.[42] According to Dr. Skolnick, "no women would have been tested for the BRCA mutations if not for Myriad."[43] Further, patent protection incentives established the reason for Myriad Genetics' inception "because the necessary funding would not have been made available by investors."[44]

To meet eligibility requirements for a patent in the United States, the USPTO must certify that the invention meets three separate conditions: (1) novelty, (2) utility, and (3) nonobviousness.[45] When it comes to biological material, whether genetic or not, much controversy surrounds the patent eligibility of those "inventions" naturally occurring in humans. When the Patent Act was enacted in 1952, it applied to any subject matter "under the sun that is made by man."[46] Later, this assertion was modified by the "product of nature" doctrine, which prohibits patents based on the "laws of nature, physical phenomena, and abstract ideas" and mental processes.[47] These three exceptions to patent eligibility came from a 1980 United States Supreme Court case, *Diamond v. Chakrabarty*, which is the first and only decision directly addressing the patentability of living organisms.[48] The Court in *Chakrabarty* upheld a

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[36] Cook-Deegan et al., *supra* note 32, at S20.
[37] *Id.*
[38] *ACLU FAQ*, *supra* note 13.
[39] *Id.*
[40] Marisa Noelle Pins, Note, *Impeding Access to Quality Patient Care and Patient Rights: How Myriad Genetics' Gene Patents Are Unknowingly Killing Cancer Patients and How to Calm the Ripple Effect*, 17 J. INTELL. PROP. L. 377, 381–82 (2010).
[41] *Id.* at 382.
[42] Conaboy, *supra* note 35, at 125.
[43] Pins, *supra* note 40, at 382.
[44] *Id.*
[45] *Id.* at 385.
[46] Jackson, *supra* note 4, at 1454 (quoting S. REP. NO. 82-1979, at 5 (1952); H.R. REP. NO. 82-1923, at 6 (1952)).
[47] *Id.* (quoting Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980).
[48] *Chakrabarty*, 447 U.S. at 309.

"patent for a laboratory-created bacterium with properties not found in nature."[49] Two years later, the USPTO granted its first human genetic material patent.[50]

The patent system originally granted "certain rights to inventors for their inventions in order to reward and encourage human ingenuity."[51] But, as the ACLU correctly argues, genes are not inventions but, rather, natural parts of the human body. In fact, the USPTO recognizes this differentiation by maintaining the *Chakrabarty* exception: that products of nature are not patentable.[52] Reflecting a lack of familiarity with genomics, for the past three decades the USPTO has stated that genetic sequence may qualify as patentable material if it is "isolated and purified" by removing the gene from the human body and stripping away its "non-coding regions."[53] However, this isolation and purification process as applied to human genes is "simple enough for any graduate student in genetics or a related field to perform."[54] Therefore, the BRCA1/2 patenting process is properly analogized as if one mined (i.e., "isolated") gold from a mountain and then patented the gold,[55] therefore violating the novelty and non-obviousness requirements for patentable material.

Consequently, the ACLU and twenty others initiated a lawsuit against Myriad Genetics on May 12, 2009, officially challenging the BRCA1/2 gene patents. Generally, the plaintiffs attacked patents on: (1) natural human genes, (2) genes with natural mutations, (3) any method of looking for mutations in natural human genes, and (4) the concept that individual gene variants are different and have specific effects, which "correlate with an increased risk of breast and/or ovarian cancer."[56] On March 29, 2010, the district court granted the plaintiffs' motion for summary judgment, effectively declaring Myriad's patents invalid based on the theory that they contain products of nature and abstract ideas.[57] Shortly after, the defendants appealed.[58]

On July 29, 2011, the appellate court found for Myriad Genetics, reversing in part the prior decision.[59] In the majority opinion, the court first held that isolated DNA does not stem from products of nature, and therefore is patent-eligible.[60] The court held valid Myriad's "growing" and "determining" method for screening potential cancer therapeutics.[61] However, the "comparing" or "analyzing" diagnostic methods used on DNA sequences were not patent-eligi-

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[49] Jackson, *supra* note 4, at 1454.
[50] *Id.*
[51] *ACLU FAQ*, *supra* note 13.
[52] *Id.*
[53] *Id.*
[54] *Id.*
[55] *Id.*
[56] Pins, *supra* note 40, at 380–81 (quoting Complaint at 15, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, No. 09 Civ. 4515 (S.D.N.Y. May 12, 2009), 2009 WL 1343027).
[57] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181, 185–86 (S.D.N.Y. 2010).
[58] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 653 F.3d 1329, 1333 (Fed. Cir. 2011).
[59] *Id.* at 1329, 1333.
[60] *Id.* at 1350.
[61] *Id.* at 1357.

ble because they involve abstract mental processes.[62] Jim Greenwood, the President and CEO of co-defendant Biotechnology Industry Organization (BIO), released a statement directly following Myriad's "win."[63] Reiterating the patentability of gene processes, he said, "patented DNA molecules have been put to countless uses that have benefited society. . . . [T]hey are fundamentally different from anything that occurs in nature."[64] Yet the court's decision regarding the products of nature doctrine was close at two to one, with a strong dissent.[65]

C. Ruling in Prometheus Should Invalidate Patents on Isolated Gene Sequences and Complementary DNA (cDNA)

Only months after the Supreme Court granted certiorari to Myriad, the Court ruled a blood-test patent developed by Prometheus invalid, reinforcing the "law of nature" doctrine.[66] The test at issue examined the chemical reaction of a prescription drug, directing a doctor to modify the dosage and make the treatment more effective or avoid unwanted side effects based upon measured metabolite levels within the patient.[67] In a unanimous decision, Justice Breyer wrote that inventors must do more than "recite a law of nature and then add the instruction 'apply the law.' "[68] Thus, the Court highlighted that invention requires going beyond merely describing what nature has already predetermined.

> The laws of nature involved here are the "relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm." The legal question then becomes, "do the patent claims add *enough* to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws?" For all nine members of the Court, the answer was a clear no.[69]

Subsequently, the Court vacated the *Myriad* decision and remanded it back to the Federal Circuit for reconsideration in light of its ruling in *Prometheus*.[70]

On remand, in addition to ruling on several method claims, a two to one majority upheld Myriad's composition claims covering both i) isolated BRCA

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[62] *Id.* at 1355.

[63] *See* Pins, *supra* note 40, at 396.

[64] *Id.* (quoting Press Release, Biotechnology Industry Organization, BIO Statement on Initial Decision in Myriad Genetics Lawsuit (Mar. 30, 2010), *available at* http://www.bio.org/media/press-release/bio-statement-initial-decision-myriad-genetics-lawsuit).

[65] John Conley, *ACLU and Myriad Both Seek Further Federal Circuit Review*, GENOMICS L. REP. (Sept. 2, 2011), http://www.genomicslawreport.com/index.php/2011/09/02/aclu-and-myriad-both-seek-further-federal-circuit-review.

[66] Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1305 (2012).

[67] *Id.* at 1295.

[68] *Id.* at 1297.

[69] John Conley & Allison Williams Dobson, *Prometheus Patents Struck Down, 9-0:* Mayo Collaborative Services v. Prometheus Laboratories, Inc. *Analysis*, GENOMICS L. REP. (Mar. 21, 2012), http://www.genomicslawreport.com/index.php/2012/03/21/prometheus-patents-struck-down-9-0-mayo-collaborative-services-v-prometheus-laboratories-inc-analysis/#more-6594.

[70] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012).

sequences and ii) cDNA sequences derived from such isolated sequences.[71] Focusing on these composition claims, it is clear that the Federal Circuit reached its conclusions based upon erroneous scientific assumptions regarding isolated DNA sequences and unfamiliarity with natural laws that predetermine how complementary DNA is formed given a naturally occurring predicate strand of mRNA. These scientific misconceptions are material as a matter of patent law because they relate to the threshold issue of patent eligibility under Section 101. As illustrated below, the Federal Circuit incorrectly applied the threshold tests of "markedly different" from *Chakrabarty* and "law of nature" from *Prometheus*.

i. Isolated DNA Sequences Are Not "Markedly Different" from What Exists in Nature

As Judge Bryson noted in his dissent, the *Chakrabarty* test "requires us to focus on two things: (1) the similarity in structure between what is claimed and what is found in nature and (2) the similarity in utility between what is claimed and what is found in nature."[72] Applying this test, Bryson correctly reasoned that isolated gene sequences should not be patent eligible as "extracting a gene is akin to snapping a leaf from a tree . . . [a] human kidney is a product of nature; it does not become a patentable invention when it is removed from the body, even if the patentee has developed an improved procedure for extracting the kidney."[73] The majority rejected this characterization based on the empirically false assumption that isolated DNA sequences are unique molecules that do not exist absent human actions:

> In this case, the claimed isolated DNA molecules do not exist in nature . . . . They have to be chemically cleaved from their native chemical combination . . . . In other words, in nature, the claimed isolated DNAs are covalently bonded to such other materials. Thus, when cleaved, an isolated DNA molecule is not a purified form of a natural material, but a distinct chemical entity that is obtained by human intervention.[74]

However, as the renowned geneticist Dr. Eric Lander explains in his Supreme Court amicus brief, it has been empirically "established for over 30 years that isolated DNA fragments of human chromosomes routinely occur in the human body."[75] These isolated DNA fragments (which typically arise after a cell dies) with their cleaved covalent bonds at the ends of the fragments, are not chemically distinct in their composition from the type of isolated DNA claimed by Myriad.[76] More specifically, "these isolated DNA fragments span the entire human genome, including the BRCA1 and BRCA2 genes."[77] This means that it is certain that isolated sequences of the BRCA gene exist in nature

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[71] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 689 F.3d 1303, 1337 (Fed. Cir. 2012).
[72] *Id.* at 1354 (Bryson, J., dissenting).
[73] *Id.* at 1352 (Bryson, J., dissenting).
[74] *Id.* at 1325, 1329.
[75] Brief for Amicus Curiae Eric S. Lander in Support of Neither Party at 12, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012) (No. 12–398).
[76] *Id.* at 17.
[77] *Id.* at 12.

and that Myriad's composition claims cover these naturally occurring sequences as it claims isolated BRCA sequences 15 nucleotide bases or longer.[78] Thus, since Myriad's composition patent claims cover molecules that already exist in nature, these claims obviously fail the "markedly different" threshold.

During oral arguments on *Myriad II* in April 2013, Myriad's attorney, Gregory Castanias, essentially conceded that Myriad's composition claims on BRCA 1/2 were justified, not because of substantive physical differences from what existed in nature, but merely because Myriad articulated a use (diagnosis of breast cancer risk) that was different from its natural function (coding for a protein).[79] Interrogating the consequence of this logic, Justice Kagan inquired whether "the first person who isolated chromosomes could have gotten a patent on that?"[80] Being logically consistent but wrong on the law, Castanias replied that under Myriad's theory an isolated chromosome would be patent eligible under Section 101: "if that chromosome had a specific substantial and credible utility, in other words, it could be used in some . . . diagnostic way in the way that we're talking about here, then yes, it would pass through the Section 101 gate."[81] As Justice Kagan alertly noted, the above statement is an admission by Myriad that the supposed differences in chemical structure between isolated DNA and chromosomal DNA are irrelevant for its patent eligibility theory, "[a]nd that's interesting . . . because then it's not a question about, you know, breaking these covalent bonds or whatever Judge Lourie thought it was about."[82] Furthermore, Myriad's argument is again wrong on the science, because it is based on the erroneous assumption that isolated chromosomes can serve no diagnostic purpose. Of course, as any doctor or older couple that is planning a pregnancy can tell you, the presence of an extra chromosome 21 in a pregnant woman's blood indicates that her fetus has trisomy 21, which is diagnostic for Down syndrome. Thus, if we accept Myriad's logic, Dr. Jerome Lejeune could have filed a patent for the third copy of chromosome 21 when he associated its presence with Down syndrome.[83]

ii. The Synthesis of cDNA Results from a "Law of Nature"

Complementary DNA (cDNA) composition claims should not be patent eligible because the laws of nature predetermine their sequence and function. First, we will explain what cDNA is and why it does not pass the "law of nature" patent eligibility test. Second, we will distinguish cDNA from DNA probes, primers, and recombinant DNA, all of which should be considered patent eligible because their sequence and functions are not predetermined by nature.

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[78] *See id.* at 17.

[79] Transcript of Oral Argument at 40, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012) (No. 12–398).

[80] *Id.* at 52.

[81] *Id.* at 53–54.

[82] *Id.* at 54.

[83] *Discovering Trisomy 21*, JEROMELEJEUNE.ORG, http://jeromelejeune.org/the-scientist/discovering-trisomy-21.html (last visited May 15, 2013).

As explained in *Myriad II*, most human genes contain both exon and intron sequences: "Exons are DNA segments that are necessary for the creation of a protein . . . . Introns are segments of DNA interspersed between the exons that, unlike exons, do not code for a protein."[84] In order to create a protein from this DNA sequence, it first has to be transcribed into RNA.[85] During transcription, "the DNA double helix is unwound and each nucleotide on the non-coding, or template, DNA strand is used to make a complementary, single-stranded RNA molecule that mirrors the coding DNA strand."[86] However, the resulting "pre-RNA" strand cannot be directly translated into a protein because it still contains the non-coding intron sequences.[87] What happens next is that "the introns are physically excised from the pre-RNA molecule, followed by "splicing" the exons to produce a messenger RNA ("mRNA")."[88] It is only after transcription and splicing that the resulting mRNA can be translated into a protein.[89] Using this naturally occurring mRNA: "cDNA is synthesized . . . using complementary base pairing in a manner analogous to RNA transcription. The process results in a double-stranded DNA molecule with a sequence corresponding to the sequence of an mRNA produced by the body."[90] Since the cDNA is synthesized from mRNA, it only contains exon sequences which differentiates it from the chromosomal gene sequence which contains both exons and introns.[91]

From the simple description above, one might conclude that cDNA should be patent eligible because it does not occur naturally within the body. However, as the majority opinion in *Myriad II* acknowledges, the cDNA claimed by Myriad is not produced by some novel process, but rather by "*complementary base pairing in a manner analogous to RNA transcription*."[92] In other words, the cDNA is produced using a law of nature that evolution, not Myriad, fashioned. Further, the exact sequence is also predetermined by evolution as the majority opinion notes that the resultant cDNA is "*a sequence corresponding to the sequence of an mRNA produced by the body*."[93]

In *Chakrabarty*, the patentable invention was an oil-degrading bacteria "genetically engineered with four naturally occurring DNA plasmids."[94] Plasmids are small DNA molecules that are "physically separate from, and can replicate independently of, chromosomal DNA within a cell."[95] From *Chakrabarty*, it is clear that the four naturally occurring DNA plasmids would not be patent eligible on their own––they are obviously products of nature.

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[84] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad II*), 689 F.3d 1303, 1311 (Fed. Cir. 2012).
[85] *Id.*
[86] *Id.*
[87] *Id.*
[88] *Id.*
[89] *Id.* at 1312.
[90] *Id.* at 1313.
[91] *Id.* at 1313–14.
[92] *Id.* at 1313 (emphasis added).
[93] *Id.* at 1313 (emphasis added).
[94] *Id.* at 1327.
[95] *Plasmids: General Principles*, BOUNDLESS, https://www.boundless.com/microbiology/microbial-genetics/plasmids/plasmids-general-principles/ (last visited May 16, 2013).

However, the process of inserting these products of nature into a microorganism that did not previously contain them, transformed the bacteria into something that had "markedly different characteristics from any found in nature."[96] In contrast, in *Funk Brothers*, the Court ruled that a mix of naturally occurring bacteria strains that had cooperative nitrogen-fixing qualities was not patentable since the underlying process was "the work of nature."[97] As the Federal Circuit reasoned, "applying the newly discovered bacterial compatibility to create a mixed culture was not a patentable advance because no species acquired a different property or use."[98]

The cDNA claimed by Myriad is analogous to the naturally occurring DNA plasmids in *Chakrabarty* and bacteria cultures in *Funk Brothers*. On its own the cDNA codes for proteins already found in nature and the exact sequence of protein-encoding cDNA has already been pre-determined by nature, not the putative inventors. Under the logic of *Chakrabarty*, cDNA only seems to be patentable as a component of some larger composition that was "markedly different" from what existed in nature, which brings us to recombinant DNA technology.

The importance of cDNA is that it can be used as a building block sequence to create recombinant DNA ("rDNA") sequences that code for human proteins such as insulin. In other words, cDNA has no therapeutic value unless something more is added to it. Recombinant DNA technology is a process that "uses enzymes to cut and paste together DNA sequences of interest."[99] For example, one could make rDNA that consisted of the cDNA and splice it together with the appropriate DNA sequences that code for mRNA that can be used by the host organism's (e.g., bacteria) translational apparatus. Making rDNA using an isolated human gene sequence instead of the corresponding cDNA would not work in the above scenario as bacteria (and all prokaryotes) lack the splicing mechanism to remove the non-coding introns (see description of transcription and splicing above). cDNA solves this problem because it is "pre-spliced." Transcription of cDNA within bacteria thus results in mRNA that can then be translated into human protein.

Clearly rDNA should be patentable because not only do such sequences not exist in nature, but in addition their sequences are not predetermined by any law of nature.[100] rDNA creation is an art that requires cutting, pasting, and

[96] Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980).

[97] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

[98] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad II*), 689 F.3d 1303, 1327 (Fed. Cir. 2012).

[99] *Recombinant DNA (rDNA)*, GENOME.GOV, http://www.genome.gov/glossary/index.cfm?id=173 (last visited May 16, 2013).

[100] By the same logic, DNA probes and primers should be patent-eligible because their sequence and functions are not predetermined by nature. *See Probe*, GENOME.GOV, http://www.genome.gov/glossary/index.cfm?id=165 (last visited May 16, 2013) ("A probe is a single-stranded sequence of DNA or RNA used to search for its complementary sequence in a sample genome. The probe is placed into contact with the sample under conditions that allow the probe sequence to hybridize with its complementary sequence. The probe is labeled with a radioactive or chemical tag that allows its binding to be visualized. In a similar way, labeled antibodies are used to probe a sample for the presence of a specific protein."); *Primer*, GENOME.GOV, http://www.genome.gov/glossary/index.cfm?id=163 (last visited May 16, 2013) ("A primer is a short, single-stranded DNA sequence used in the polymerase chain

recombining DNA sequences in the correct order to make these sequences operational in their host organisms. Thus, starting with the same cDNA building block, multiple parties can make differing (and all patentable) rDNA sequences that code for the same human protein but that perhaps use different hosts (e.g., yeast instead of bacteria) or result in higher or more pure yields of the desired protein product. Allowing a monopoly on the underlying and naturally predetermined cDNA sequence would block innovation in the recombinant DNA marketplace.

III. The Harmful Medical and Economic Impacts of Myriad's Gene Monopoly

> I'm a 41-year-old mother of two . . . . Both my mother and maternal grandmother died from breast cancer. I'm worried about having a genetic predisposition for cancer but haven't been able to afford an additional test that would give me information about my genes. . . .
>
> . . . .
>
> Since childhood I have worried about cancer. This test would give me information I need to make life-changing medical decisions. There are so many unknowns. Why did my mother and her mother die from breast cancer? . . .
>
> I keep thinking about the legacy of motherless children in my family. From breast cancer, my mother died when she was only 28; my grandmother, at 52. My great grandmother (maternal grandmother's mother) died from the influenza at 33. I really want to be here for my kids. It is important for me to make informed decisions about my health. . . .
>
> If I learned that I definitely inherited a genetic link to cancer, it would significantly change how I would protect my health.[101]

The *Myriad* case attracted a large amount of media attention and the lawsuit evoked a variety of challenges. From genetic counselors to cancer patients, and researchers to corporate directors, multiple arguments developed for and against patenting BRCA1/2. It would be impossible to encompass the breadth and depth of perspectives that take issue with human gene patenting, but it is necessary to delve into a few in order to understand the impact of the *Myriad* case. Some entities focus on the damaging consequences resulting from Myriad's monopoly and patent exclusivity. Others, like the ACLU, see gene patenting as a constitutional issue that infringes upon First Amendment rights.[102] Ultimately, many agree that the patients are the ones who are eventually harmed, as BRCA1/2 tests are expensive and insurance does not always cover the costs.

A. Gene Patents Lock Down Innovation

Myriad Genetics' strict enforcement of its license creates a monopoly in the field. Using its patent power, Myriad has sent several cease-and-desist let-

reaction (PCR) technique. In the PCR method, a pair of primers is used to hybridize with the sample DNA and define the region of the DNA that will be amplified. Primers are also referred to as oligonucleotides.").

[101] Kathleen Raker, *BRCA—Plaintiff Statements*, American Civil Liberties Union (May 12, 2009), http://www.aclu.org/free-speech_womens-rights/brca-plaintiff-statements#raker.

[102] *ACLU FAQ*, *supra* note 13.

ters to laboratories and researchers throughout the United States, ordering them to stop testing on BRCA1/2 genes.[103] Out of fear of patent infringement penalties, this resulted in a chilling effect among the various parties who deal with diagnostic testing. Dr. Harry Ostrer, a professor of pediatrics, pathology, and medicine, and a plaintiff in the case,[104] is a working example of this fear that many are experiencing. Dr. Ostrer was unable to provide patients with results of BRCA1/2 tests due to Myriad's patents, something he desired to do, and testified that he would do if the patents were invalidated.[105] Dr. Ostrer displayed frustration with the BRCA1/2 patents as they currently stand:

> Currently, I am recruiting hundreds of women into a new study to identify other genes associated with a risk of breast cancer. . . . Unfortunately, once such new genes are identified, the use of this information in clinical practice could be limited because it might be viewed by Myriad Genetics as infringing on its BRCA patents.
>
> . . . .
>
> Every day I think about how the findings of the research laboratory can be translated into new genetic tests that might benefit, not harm, people.[106]

In 2010, Myriad Genetics brought in $353 million (eighty-eight percent of their total revenue) from the breast cancer tests.[107] However, the industry has not seen any innovations from Myriad in the past five years, when it last introduced the most recent BRCA1/2 test.[108] Executives at Myriad say they plan to prepare for technological improvements in response to claims of newer DNA-sequencing techniques being faster and less expensive compared to the technology Myriad uses, which is reportedly from the 1990s.[109] Former Myriad employee Sean Tavtigian admitted that the company "is trying to catch up, but 'it's kind of slow going.' "[110]

In fact, Life Technologies has developed a new Proton Sequencer that can read a person's entire genome for $1,000,[111] much less than Myriad charges for its two-gene test. A British company, Oxford Nanopore, recently introduced the world's first miniature DNA sequencer that will be available commercially this year for $900.[112] But, because of strict patent protection on BRCA1/2, lawyers

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[103] *Id.*

[104] Declaration of Harry Ostrer at ¶ 1, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 669 F. Supp. 2d 365 (S.D.N.Y. 2009) (No. 09-4515), *available at* http://www.aclu.org/files/pdfs/freespeech/brca_Ostrer_declaration_20090826.pdf.

[105] *Id.* at ¶¶ 4, 8.

[106] Harry Ostrer, M.D., *BRCA—Plaintiff Statements*, American Civil Liberties Union (May 12, 2009), http://www.aclu.org/free-speech_womens-rights/brca-plaintiff-statements#ostrer [hereinafter Ostrer, *Plaintiff Statement*].

[107] Andrew Pollack, *Despite Gene Patent Victory, Myriad Genetics Faces Challenges*, N.Y. Times (Aug. 24, 2011), http://www.nytimes.com/2011/08/25/business/despite-gene-patent-victory-myriad-genetics-faces-challenges.html?pagewanted=all.

[108] Ostrer, *Plaintiff Statement*, *supra* note 106.

[109] *See* Pollack, *supra* note 107.

[110] *Id.*

[111] Clive Cookson, *Machine to Read Individual's DNA for $1,000*, Fin. Times (Jan. 10, 2012, 5:06 AM), http://www.ft.com/intl/cms/s/2/e3c6b7bc-3ac3-11e1-a75600144feabdc0.html%23axzz1maUoc31U.

[112] Clive Cookson, *Oxford Nanopore Unveils Mini-DNA Reader*, Fin. Times (Feb. 17, 2012, 5:09 PM), http://www.ft.com/intl/cms/s/2/318a378a-5900-11e1-b118-00144feabdc0.html#axzz1oixikxkx.

remain unsure whether other methods, like full-gene sequencing, would violate Myriad's patents on the isolated genes. Some predict that when Myriad's gene patents expire, the price of full-genome sequencing will trend as low as $100, and single-gene test methods will be moot.[113]

B. Gene Patents Limit Access to Diagnostic Tests

> Based on my personal medical history, and my family history of cancer, two genetic counselors and my oncologist all agreed that I should have Myriad's . . . test [from a clinical stand point]. . . .
>
> . . . .
>
> . . . Myriad is the only provider in the country because it has patents on the BRCA genes, but it will not enter into a contract with my insurance. Myriad holds my fate and future in its administrative hands, unless of course I am able to pay $3,225 out-of-pocket. Unfortunately, as a result of my illness and treatment, I do not have an extra three grand right now.[114]

Another compelling reason to invalidate Myriad's patents relates to patients' inability to gain access to the BRACAnalysis or BART. This occurs when patients cannot afford the price of the test, or it is not covered by insurance.[115] Both of these administrative complexities create barriers that prevent access to the latest cancer care options. Consequently, Myriad is able to charge high rates for its testing, while picking and choosing insurance companies with which to contract.[116] As Myriad remains the United States' sole provider for the full BRCA1/2 DNA sequence tests,[117] it has complete discretion regarding these important access decisions.

Myriad Genetics charges approximately $3,000 for their BRCA1/2 diagnostic test[118] and $700 for their BART test.[119] Myriad developed the BART test separately to test for genetic alterations in the BRCA1/2 genes. Instead of incorporating BART into BRACAnalysis it is offered separately. Mark Capone, president of the Myriad laboratory division, said that the company keeps BART separate because insurers would not pay for it,[120] but the company indicates that it plans to incorporate the BART test into its main product at an unspecified date.[121]

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[113] *E.g.*, Science and Technology, *Genes and Patents: More Harm Than Good? Patenting Genes Is Bad for Diagnosis*, ECONOMIST, Apr. 17, 2010, at 90–91.

[114] Lisbeth Ceriani, *BRCA—Plaintiff Statements*, AMERICAN CIVIL LIBERTIES UNION (May 12, 2009), http://www.aclu.org/free-speech_womens-rights/brca-plaintiff-statements#ceriani.

[115] Weilbaecher, *supra* note 17, at 12.

[116] *See id.*

[117] *See* Cook-Deegan et al., *supra* note 32, at S20.

[118] Weilbaecher, *supra* note 17, at 12.

[119] Pollack, *supra* note 107.

[120] *Id.*

[121] *See* Barbara Puffer, *Is Myriad's Patent on Breast Cancer Genes Valid?*, CONNECTICUT HEALTH I-TEAM (Feb. 16, 2012), http://c-hit.org/2012/02/16/is_myriads_patent_on_breast_cancer_genes_valid/; *see also* Turna Ray, *Healthcare Providers Petition Myriad to Add Large Rearrangement Analysis to Standard BRACAnalysis*, YALE CANCER GENETIC COUNSELING (Aug. 3, 2011), http://yalecancergeneticcounseling.blogspot.com/2011/08/healthcare-providers-petition-myriad-to_4368.html.

The ACLU insists that the close relationship between price and utilization is to blame for those individuals who forgo potentially beneficial tests,[122] which can be detrimental to their health. Genetic counselor Ellen Matloff is similarly concerned; she contends that ninety-five percent of patients she refers for supplementary testing do not get the test because of its high cost.[123] Without the ability to pay for another test, Matloff worries about the potential impact it will have on patients and their relatives since many of these issues are hereditary. "[F]rom a clinician's standpoint it is horrifying," she says.[124] Myriad counters this by providing free testing to first-degree relatives when results are ambiguous.[125] However, as Matloff suggests, those affected by hereditary disease can extend from siblings and children to grandchildren, nieces, and nephews.[126]

C. Lacking Competition Diminishes Quality and Efficacy of Tests

> Because of patents on the BRCA genes, only one company out there has the ability to sequence them. I can't get a second sequencing done at a different company to validate my results. I am thinking about having my ovaries removed because of my risk for ovarian cancer. It is uncomfortable making such an important decision based on only one test.[127]

One of the derivative problems stemming from Myriad's monopoly is the inability for patients to obtain a second opinion or verify their condition if they receive ambiguous results.[128] "There are thousands of mutations along the BRCA genes and the significance of many of them is unknown. But the government allows Myriad alone to determine which mutations to test for, and to limit the study of other mutations."[129] Myriad retains complete control over the data and is under no obligation to share it with other researchers in order to fully investigate these findings. "Myriad used to share such information with a public database maintained by the National Institutes of Health, and it cooperated with academic scientists trying to analyze the mutations. But a few years ago, the company quietly stopped contributing and cooperating, in favor of building its own database."[130] This raises ethical concerns regarding Myriad's behavior in withholding the mutation information. Not only would this information be vital for public health initiatives, but some question whether this extends the monopoly beyond the life of the patent itself.[131]

Because Myriad does not allow anyone else to review their diagnostic procedures, women have no way of knowing whether the test was conducted properly. Similarly, there is no entity that could verify the accuracy of results or

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122 *See* Cook-Deegan et al., *supra* note 32, at S33.
123 Amanda Wilson, *U.S.: ACLU Will Take Gene Patent Case to Supreme Court*, INTER PRESS SERV. (Oct. 14, 2011), http://ipsnews.net/news.asp?idnews=105472.
124 *Id.* (internal quotation marks omitted).
125 Cook-Deegan et al., *supra* note 32, at S17.
126 Wilson, *supra* note 123.
127 Girard, *Plaintiff Statement*, *supra* note 25.
128 *ACLU FAQ*, *supra* note 13.
129 *Id.*
130 Pollack, *supra* note 107.
131 *E.g.*, *id.*

perform alternative testing without fear of patent infringement.[132] This uncertainty becomes amplified for some minority populations because Myriad's tests are more likely to return results for them indicating that they have a "variant of uncertain significance."[133] Therefore, African-Americans, Hispanics, and Asian-Americans are at a great disadvantage for cancer treatment options, as they have no other way to determine if they are at a heightened risk for this disease.[134] This can also lead to psychological confusion for patients, who already face a great deal of stress given the nature of these diagnostic tests. Elsa Reich, M.S., is a genetic counselor in New York who provides insight on resulting difficulties when this situation arises:

> Because there is a great burden to patients when there is no answer to the question "Why?" we as genetics professionals, go to great lengths to find those answers. . . .
>
> When we have only one laboratory that we can use, we have no way of saying to our patients, "let's do this a different way", or "let's ask someone else.". . .
>
> . . . I feel that patients deserve the opportunity to benefit from competition; the competition that brings new methods to the testing procedure; the competition that allows all comers to participate in the research and provide answers to more patients; the competition that allows for the provision of a second opinion.[135]

The common perception that Myriad's exclusivity limits research is a large concern for many. Specifically, the plaintiffs worry that a lack of competition does not reassure that Myriad will continue updating its test to reflect the most current scientific standards, ultimately redirecting the standard of care for breast cancer testing.[136] Dr. Skolnick disagrees, saying the patents' profitability actually acts as an incentive to encourage the company to solve any problems that arise.[137] He argues that the limited exclusivity offered by the patent encourages research and allowed the University of Utah and Myriad Genetics to develop these tools in the first place.[138] BIO agrees, adding that a restriction on gene patents would actually harm patients because the current system promotes "physician and patient education, broader insurance coverage, and improved compliance" in the diagnostic field.[139]

D. Insurance Coverage Challenges

Health insurance providers' relationships with Myriad Genetics negatively affect patients' ability to obtain testing. Women without insurance ("[n]ationally, 18.8% of women aged 19–64 years are uninsured"[140]), or with insurance that does not cover the testing (one study found that 42% of insured women would not be covered for BRCA1/2 tests[141]), might not be able to take

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132 *ACLU FAQ*, *supra* note 13.
133 *See id.*
134 *See id.*
135 Elsa Reich, M.S., *BRCA—Plaintiff Statements*, AMERICAN CIVIL LIBERTIES UNION (May 12, 2009), http://www.aclu.org/free-speech_womens-rights/brca-plaintiff-statements#reich.
136 Declaration of Shobita Parthasarathy, *supra* note 22, at ¶ 31.
137 Pins, *supra* note 40, at 382.
138 Weilbaecher, *supra* note 17, at 11.
139 *Id.* at 13–14.
140 Cook-Deegan et al., *supra* note 32, at S33.
141 *Id.*

advantage of this "potentially life-saving diagnostic tool."[142] Insurance problems can arise when Medicaid is involved, when a policy excludes genetic testing, or if the beneficiary lives in a geographic area where the insurance plan has strong incentives to minimize utilization.[143]

Insurance coverage of BRCA1/2 tests has certainly improved since 1995, when "only 4% of insurance providers . . . had granted coverage of BRCA testing,"[144] but a long road lies ahead as problems within the industry are still creating obstacles for patients and their families. One study found that only six percent of decision makers for private health insurance plans would opt to cover Myriad's tests if they were made available to all women in the general population.[145] Additionally, only forty-eight percent would offer the tests if they "were restricted only to women with a positive family history who were enrolled in an approved research trial."[146] In 2002, another study reported that only thirty-eight percent of beneficiaries were able to get genetic testing coverage from their insurance plan.[147]

Myriad's BRACAnalysis website claims that most insurance policies today cover ninety percent of the costs and reimbursement rates associated with the test and more than 2,500 payers and health plans have reimbursed testing with Myriad.[148] However, a number of insurers still do not cover BART, and Myriad has yet to secure Medicare "participating provider" status in twenty-five states, excluding this entire population from its services.[149] In response, Myriad does offer free testing via financial assistance programs, and they provide some independent, non-profit institutions with free testing.[150] However, some consequences Myriad cannot fix, like the forty-one percent of women in 2002 who chose not to file an insurance claim despite the fact that ninety-nine percent of those women had insurance.[151] Additionally, fifteen percent of women in another study chose to self-pay their BRCA1/2 testing fees. Each of these startling statistics stems from fear of insurance and employment discrimination, another reality surrounding the BRCA1/2 debate. Myriad says that only five percent of patients now self-pay, an improvement after the Genetic Information Nondiscrimination Act of 2008 (GINA) passed, which helped to reduce these fears.[152]

Myriad's final plea in the insurance challenge is that administration of BRCA1/2 testing is actually simplified from private insurance contracting because it relieves patients of the hassle and associated paperwork. The company also claims that providers benefit too, as Myriad retains all legal liability for test inaccuracies.[153] Additionally, because Myriad is a sole-source provider,

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142 Weilbaecher, *supra* note 17, at 12.
143 Cook-Deegan et al., *supra* note 32, at S34.
144 *Id.* at S33.
145 *Id.*
146 *Id.*
147 *Id.*
148 *Id.*; Conaboy, *supra* note 35, at 125.
149 Conaboy, *supra* note 35, at 125–26.
150 *Id.* at 126.
151 Cook-Deegan et al., *supra* note 32, at S33.
152 *Id.*
153 *Id.*

it assumes the responsibilities of sample collection, paperwork, and billing that insurance companies "might otherwise handle at their own institution through internal billing and administrative procedures."[154] However, these perceived "advantages" only become available to those insurance companies and beneficiaries that have secured a contract with Myriad in the first place. This creates an additional burden on patients who learn their condition is not covered by insurance—a result that comes from Myriad's exclusivity and choice of insurance contracts.

E. Discord with International Patent Law

Recognition of Myriad's patents raises disputes of how United States patents are subsequently treated abroad. Currently there are varying regulations throughout countries, which in turn create international discrepancies in patent law, further complicating enforcement strategy in the United States. For example, our neighbors in Canada have different public policy that permits labs to continue testing.[155] After receiving various cease-and-desist letters from Myriad Genetics, the Canadian government issued the following statement, " 'it is the government's position that predictive breast and ovarian cancer tests should be available to women who require them.' "[156] In response, Myriad expressed its surprise that Canada would "continue to provide funding to laboratories that are directly infringing," which resulted in a firestorm of media criticism over Myriad's bullying tactics.[157] Only years later did Myriad give up and redirect its efforts to building its market in the United States.[158] Today, multiple entities in Canada are able to perform the BRCA1/2 tests because "Canada has not altered its original position of ignoring not only Myriad's patents but also the general issue of the interaction between the human gene patents and the public health care system."[159] This has ultimately enabled Canadians to access a valuable diagnostic tool without restriction and with more competitive pricing.[160]

Even stricter, China has laws that explicitly oppose one type of human gene patents for embryonic stem cells, which the United States currently allows.[161] Policy in China takes the same approach in challenging the validity of stem cell patents as many plaintiffs assume for Myriad's human gene patent.[162] Chinese law takes into account morality considerations that U.S. patent law ignores. Rather, in the United States, challengers of stem cell patents argue that these patents are invalid because they are neither novel nor nonobvious.[163]

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154 *Id.*

155 E. Richard Gold & Julia Carbone, *Myriad Genetics: In the Eye of the Policy Storm*, 12 GENETICS MED. S39, S54 (Apr. 2010 Supp.).

156 *Id.* at S51.

157 *Id.* at S52.

158 *Id.* at S54.

159 *Id.*

160 Weilbaecher, *supra* note 17, at 12.

161 Huan Zhu, *Comparative Study on Patenting of Human Embryonic Stem Cells*, PATENT DOCS (Nov. 16, 2011), http://www.patentdocs.org/2011/11/comparative-study-on-patenting-of-human-embryonic-stem-cells.html?utm_source=feedburner&utm_medium=email&utm_campaign=Feed%3A+PatentDocs+%28Patent+Docs%29.

162 *See id.*

163 *Id.*

Although there are no plans to create a universal patent system, the European Patent Office, Japan Patent Office, and USPTO recently discussed patent harmonization strategies at a November 2011 conference.[164]

In turn, Europe responded strongly to the Myriad litigation as numerous research institutes and genetics societies filed notices of opposition to Myriad's patents.[165] There is also substantial speculation surrounding Myriad's methods of conducting the full-sequence BRACAnalysis test. A study questioned whether this was the most cost-effective method. A Lewin Group study suggests that the monopoly is to blame after it found the BRCA1/2 patents to "affect development and provision of potentially more cost-effective testing strategies."[166]

France echoed this notion, promoting three alternative techniques for BRCA1/2 diagnosis. One technique, called DDGE (denaturing gradient gel electrophoresis), "would minimize the cost of diagnosis while also ensuring a comparable level of effectiveness."[167] Also, when Myriad's method is compared to a commonly used French testing method, the average cost per detected mutation was five times higher (this does not even include pricing strategy; it only focuses on the actual costs entailed to perform the test–supplies, equipment, personnel).[168]

Further, the Australian government recently made developments in reviewing its own patent laws.[169] Specifically, Australia decided to maintain genetic material and technology within the scope of its 1990 Patents Act, and is now reexamining the diagnostic, therapeutic, and surgical treatment method. Overall, Australia hopes that this technology-neutral approach gives confidence to biotechnology research and development investments, and "ensure[s] that patients will not be denied reasonable access to affordable treatments and essential diagnostic tests" that stem from inappropriate use of patent laws in Australia.[170] The fact that such patents are present in the Australian community reflects upon the strength of the debate internationally and raises the same issues being discussed here. Awaiting decision, however, is a 2010 bill, which would eliminate biological and genetic material patents, but Australians do not anticipate it will pass: "With the Government response . . . that the Patents Act should not be amended to explicitly exclude genetic materials from patentability, it is difficult to see how the Government could now support that Bill."[171]

Perhaps lawmakers in the United States should take a closer look at other countries for guidance in the *Myriad* case, both as a matter of public policy and to examine the realities concerning patent enforcement. Additionally, with

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[164] Donald Zuhn, *USPTO News Briefs: EPO, JPO, and USPTO Meet at Annual Trilateral Conference*, PATENT DOCS (Nov. 17, 2011), http://www.patentdocs.org/2011/11/uspto-news-briefs-1.html.

[165] Weilbaecher, *supra* note 17, at 12.

[166] *See* Cook-Deegan et al., *supra* note 32, at S28 (internal quotation marks omitted).

[167] *Id.*

[168] *Id.*

[169] Martin O'Brien, *News from Abroad: The Gene Patents Debate in Australia—An Update*, PATENT DOCS (Dec. 1, 2011), http://www.patentdocs.org/2011/12/news-from-abroad-the-gene-patents-debate-in-australia-an-update.html.

[170] *Id.*

[171] *Id.*

Myriad planning to open a laboratory in Europe sometime next year,[172] these considerations are even more timely.

IV. CONCLUSION

> When I was diagnosed with breast cancer, I was only 28. Because I am younger than most breast cancer patients and because the case was so aggressive, my doctor recommended that I take the BRCA genetic test to see if I was at higher risk for a second breast cancer or ovarian cancer.
>
> I took the test but my results were ambiguous. They showed that my BRCA genes had a "variant of uncertain significance," indicating that I have a mutation that may or may not mean a higher risk of cancer. . . .
>
> I will have to make a decision about whether or not to have an oophorectomy (removal of the ovaries). I'm only 32 and don't have children. I want to be able to make an educated decision before I undergo such a serious and life changing surgery.[173]

Before *Prometheus*, gene patent opponents faced an uphill battle. With a struggling economy and almost thirty years of patent law affirming the patentability of genes,[174] companies like Myriad Genetics have found a lucrative source of revenue they will fight to protect. Although some legal pundits previously predicted that the USPTO was not ready to change its standards,[175] *Prometheus* has changed the analytical framework regarding human gene patents.

Myriad Genetics warned of the negative repercussions that would result if the Court found for the plaintiffs, claiming that the entire foundation of the biotechnology industry would unravel if human gene patents were invalidated.[176] This facile argument overlooks the advantages that could result if other companies were allowed to compete. Most importantly, the cancer patients who need access to the BRCA1/2 tests would have more affordable insurance options because more laboratories would offer the test. For individuals, like Vicky Thomason, who are unable to pay for the BRCA1/2 tests, and "get up every day not knowing if [they] have a mutation,"[177] this can make an incredible difference. But, instead of focusing on these objectives, Dr. Skolnick defends his company against the ACLU and the plaintiffs by saying:

> [T]he reason for the bilious attacks against us is that in the past various academic groups competed with each other on the one hand and various commercial groups competed with each other on the other hand. There had never previously been competition between a company and more than a dozen academic groups. If research stays in academia, the same groups which make the discoveries control the funding.

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[172] Pollack, *supra* note 107.

[173] Runi Limary, *BRCA—Plaintiff Statements*, AMERICAN CIVIL LIBERTIES UNION (May 12, 2009), http://www.aclu.org/free-speech_womens-rights/brca-plaintiff-statements#limary.

[174] Jackson, *supra* note 4, at 1487.

[175] *E.g.*, *id.* at 1488.

[176] *See* Miri Yoon, Note, *Gene Patenting Debate: The Meaning of* Myriad, 9 J. MARSHALL REV. INTELL. PROP. L. 953, 973 (2010).

[177] *See* Vicky Thomason, *BRCA—Plaintiff Statements*, AMERICAN CIVIL LIBERTIES UNION (May 12, 2009), http://www.aclu.org/free-speech_womens-rights/brca-plaintiff-statements#thomason.

> When important research migrates to biotechnology and genomics companies in particular, the funding is generated outside of academia, and they lose control.[178]

The possibilities are endless if Myriad's gene exclusivity ends: researchers would gain access to valuable data, more efficient testing methods could be developed, and future developments on the BRCA1/2 genes would not be seen as patent infringement. For the first time in patent history, the ACLU is questioning a human gene patent on constitutional grounds:[179]

> The patenting of human genes undermines the free exchange of information and scientific freedom, bodily integrity, and women's health. In granting exclusive rights to gene patent holders, the U.S. government in essence gives patent holders complete control over those genes and the information contained within them. This interferes with a person's right to know about his or her own genetic makeup and scientists' rights to study the human genome and develop new genetic tests. Granting a monopoly on fundamental pieces of knowledge infringes on First Amendment rights, which protect the freedom of scientific inquiry and the free exchange of knowledge and ideas.[180]

The Supreme Court granted certiorari in *Myriad* for the limited purpose of vacating and remanding the case for reconsideration in light of *Prometheus*.[181] In *Prometheus*, the Court reinforced the notion that "laws of nature, natural phenomena, and abstract ideas" are not patentable, thus fueling the fire against Myriad. On remand, the Federal Circuit again came out on the wrong side of the law and science. With a better understanding of the underlying science and the unrefined patent eligibility standard it set forth in *Prometheus*, hopefully the Supreme Court will not let gene patents impede the progress of researchers and medical professionals seeking to help patients through a better understanding and application of nature's laws.

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[178] Declaration of Dr. Mark Skolnick at ¶ 22, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09 Civ. 4515 (RWS)).

[179] Weilbaecher, *supra* note 17, at 16.

[180] *ACLU FAQ*, *supra* note 13.

[181] John Conley & Dan Vorhaus, Myriad *Finally Reaches the Supreme Court (But Only For a Moment)*, GENOMICS L. REP. (Mar. 27, 2012), http://www.genomicslawreport.com/index.php/2012/03/27/myriad-finally-reaches-the-supreme-court-but-only-for-a-moment/.