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Myriad Lessons Learned

Amelia Rinehart
S.J. Quinney College of Law, University of Utah, amelia.rinehart@law.utah.edu

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Amelia Smith Rinehart*

INTRODUCTION

In June 2013, in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.* (*Myriad*), the Supreme Court answered the provocative question, "Are human genes patentable?" with an equivocal, "Probably not."[1] Since then, a lot of ink has been spilled speculating on the impact of the decision, yet many questions remain unanswered for biotechnology companies, genetic researchers, and healthcare providers who must navigate its legal aftermath—what influence will *Myriad* have over the patent subject matter eligibility doctrine,[2] how will *Myriad* impact investment decisions within the biotechnology industry,[3] will Myriad Genetics, Inc.'s (Myriad) remaining patents and proprietary data successfully keep competitors at bay,[4] and how might personalized cancer care change as a result?[5] Although these questions are important, this Article doesn't promise to answer them. Instead, it presents the *Myriad* saga as a cautionary patent tale, one that explores a more fundamental question—how can patent law, in the

* Associate Professor of Law, S. J. Quinney College of Law, University of Utah. I am grateful to Teneille Brown, Dan Burk, Jorge Contreras, Lincoln Davies, Leslie Francis, Andy Hessick, Carissa Hessick, Leslie Francis, Marc Rinehart, participants in the 2014 Rocky Mountain Junior Scholars conference, and participants in the present symposium, *The Meaning of* Myriad*,* for their helpful comments. Many thanks also to Danny Barber and Angela Silvers for their exemplary research assistance. Any errors are my own.

[1] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2111 (2013) [hereinafter *Myriad*]. The Court held that isolated gene sequences are not patent eligible, even when removed from the body, but cDNA sequences, which are ostensibly man-made, are eligible for patenting. *Id.*

[2] *See, e.g.*, Anna B. Laakmann, *The New Genomic Semicommons*, __ U.C. IRVINE L. REV. (forthcoming 2015); Timothy R. Holbrook & Mark D. Janis, *Expressive Eligibility*, __ U.C. IRVINE L. REV. (forthcoming 2015).

[3] One early account indicates minimal impact on biotechnology investment overall, in light of technological advancements. *See* Howard Wolinsky, *Gene Patents And Capital Investment*, 14 EUR. MOLECULAR BIOLOGY ORG. REP. 871 (2013).

[4] Soon after the Court's decision, Myriad filed suit against new entrants, some of which sued Myriad for declaratory relief in other jurisdictions. The Judicial Panel on Multidistrict Litigation consolidated these in the District of Utah. Order Granting Motion to Transfer and Consolidate, *In Re* BRCA1 and BRCA2-Based Hereditary Cancer Test Patent Litig., MDL Case No. 2:14-MD-2510 (D. Utah July 7, 2014). Myriad is the co-owner or exclusive licensee of the patents in both *Myriad* and the newer litigations, and Myriad commercialized the diagnostic tests at issue in *Myriad*. This Article refers to Myriad as the patent owner, and this designation indicates its ability to control the patent rights to exclude others including other joint owners. *See* Vaupel Textilmaschinen KG v. Meccancia Euro Italia SPA, 944 F.2d 870, 875–76 (Fed. Cir. 1991) (holding that an exclusive licensee possesses all of the substantial rights in a patent).

[5] Kenneth Offit et al*., Gene Patents and Personalized Cancer Care: Impact of the Myriad Case on Clinical Oncology*, 31 J. CLINICAL ONCOLOGY 2743, 2743 (2013) (suggesting that *Myriad* "will likely not have a large immediate impact of oncologic care patients . . . [but] may have a larger long-term impact on the role of intellectual property protection in modern genomic and medical science.").

words of Benjamin Cardozo, "mediate between the conflicting claims of stability and progress?"[6]

The *Myriad* story began long before the *Myriad* plaintiffs filed suit in 2009,[7] and even before Myriad and others raced to discover the genes linked to hereditary breast cancer in 1994.[8] In 1980, the Supreme Court in *Diamond v. Chakrabarty* confirmed the patent eligibility of biological organisms.[9] In doing so, the Court welcomed an exciting new field of biotechnology to play by the existing patent rules. As Myriad won the race to isolate and sequence the breast cancer genes, obtained patent protection over them, enforced its patents against others, built and monopolized a market for diagnostic tests, and, finally, defended its patents against challenges, it did so within, not outside of, the confines of patent law. The commercialization of breast cancer diagnostic testing, chronicled from *Chakrabarty* to *Myriad*, demonstrates how stability within patent law's eligibility doctrine, a limited ability to challenge gene patents despite vocal critics, and the strength of gene patents to exclude others within markets like those for diagnostic testing converged to slow progress within the law. This resulted in a commercial monopoly based upon later-invalidated patents and unintended consequences for all stakeholders.

This Article explores the *Myriad* case as an illustration of patent law's unremitting struggle to mediate between stability and progress. Part I describes the scientific and commercialization background necessary for understanding the *Myriad* litigation. Part II examines the patent eligibility doctrine through the lens of *Myriad* and the doctrine of standing as it related to the *Myriad* plaintiffs. It also discusses how its patents enabled Myriad to monopolize the market for commercial breast cancer diagnostic testing in the United States and the consequences (perceived and real) for genetic researchers, healthcare professionals, and their patients. Part III tells the *Myriad* story as one of slow progress in the law with many important and lasting effects. It offers several suggestions that might mitigate the mistake of relying too heavily on patent law stability at the cost of progress of both law and technology, especially in light of ever-changing social, scientific, and economic realities, as demonstrated in *Myriad* itself.

I. FROM MANDEL TO MYRIAD GENETICS

In a May 14, 2013, op-ed in the *New York Times*, Angelina Jolie, the actress and humanitarian, announced that she had undergone a preventive double mastectomy after testing positive for BRCA1, a gene linked to an exceedingly high risk of breast and ovarian cancer.[10] Discussing the diagnostic testing that she received, Jolie wrote:

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[6] BENJAMIN CARDOZO, THE GROWTH OF THE LAW 1 (1924). Cardozo, of course, referred to progress in the law, not progress of technology, as the patent system is meant to promote. *See* U.S. CONST. art. I, § 8, cl. 8. This Article discusses progress along both dimensions, and often refers to growth in the law to indicate legal progress, as compared to technological progress.

[7] Complaint, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09-4515).

[8] *See* Yoshio Miki et al., A Strong Candidate For The Breast And Ovarian Cancer Susceptibility Gene BRCA1, 266 SCIENCE 66 (1994); Richard Wooster et al., *Identification of the Breast Cancer Susceptibility Gene BRCA2*, 378 NATURE 789 (1995).

[9] *See* Diamond v. Chakrabarty, 447 U.S. 303 (1980).

[10] Angelina Jolie, Op-Ed., *My Medical Choice*, N.Y. TIMES, May 14, 2013, at A25.

> Breast cancer alone kills some 458,000 people each year . . . mainly in low- and middle-income countries. It has got to be a priority to ensure that more women can access gene testing and lifesaving preventive treatment, whatever their means and background, wherever they live. The cost of testing for BRCA1 and BRCA2, at more than $3,000 in the United States, remains an obstacle for many women.[11]

Jolie didn't identify the provider of her diagnostic test, nor did she weigh in on the merits of gene patenting—her message encouraged women to gather information, learn more about incidences within a patient's own family, and, when appropriate, get testing for the individual patient.[12] Nevertheless, as shown by the tremendous public interest taken in Jolie's story,[13] breast cancer is an important and all too common disease among women. As described below, the disease's significance blazed a path from early scientific breakthroughs to commercial diagnostic tests like Jolie used, which set the stage for the *Myriad* litigation.

A. A Brief History of Genes and Gene Hunting

The twentieth century featured huge advances in the science of heredity beyond the basic theory of inheritance first proposed by Gregor Mendel in 1865.[14] At the turn of the century, the word "gene" first described an abstract idea, a basic unit of heredity that passed traits from parent to child—what early scientists believed to be "an inherently stable, potentially immortal, unit that could be transferred intact through the generations."[15] This old-fashioned notion gave way to the discovery that a gene is a physical thing on a chromosome[16] ("like beads on a string"[17]), which, in turn, gave way to a series of extraordinary discoveries that unraveled the concept of a gene as a linear, contiguous thing—genes are sequences of nucleotides (more familiarly, deoxyribonucleic

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[11] *Id*.
[12] *Id.*
[13] *See, e.g.*, Emily Wax, 'I Have the Angie Gene': Fostering a Sisterhood, WASH. POST, July 12, 2013, at C1, C7; Delthia Ricks, *BRCA gene mutations more common than once thought*, NEWSDAY (July 8, 2013, 12:13 AM), http://www.newsday.com/news/health/brca-gene-mutations-more-common-than-once-though-1.5641518; Jillian Berman, *Angelina Jolie Op-Ed May Fuel 'Epidemic' of Women Asking for Double Mastectomy*, HUFFINGTON POST (May 14, 2013, 6:00 PM), http://www.huffingtonpost.com/2013/05/14/angelina-jolie-oped_n_3275208.html.
[14] GREGOR MENDEL, EXPERIMENTS IN PLANT HYBRIDIZATION (1865). TED EVERSON, THE GENE: A HISTORICAL PERSPECTIVE 44 (2007). Mendel, an Augustinian friar, labored on his hybridization experiments for years "alone, and unheeded, broken off from the rest." WILLIAM BATESON, MENDEL'S PRINCIPLES OF HEREDITY: A DEFENCE (1902). Later, in 1900, a group of scientists "rediscovered" Mendel's paper to support their own research relating to heredity. EVERSON, *supra* at 44.
[15] Andrew W. Torrance, *Gene Concepts, Gene Talk, and Gene Patents*, 11 MINN. J. L. SCI. & TECH. 157, 163 (2010). Torrance recounts the naming of the hereditary unit as a gene, and describes the complexity of the gene concept—something far beyond a simple unit of heredity, as originally proposed—and argues that gene talk, how the biology community explain genes, resulted in "acceptance by the patent system of a gene concept that is inaccurately simplified and predictable." *Id.* at 187.
[16] Ingrid Lobo & Kenna Shaw, *Thomas Hunt Morgan, Genetic Recombination, and Gene Mapping*, SCITABLE (2008), http://www.nature.com/scitable/topicpage/thomas-hunt-morgan-genetic-recombination-and-gene-496.
[17] Torrance, *supra* note 15, at 164 (quoting THOMAS HUNT MORGAN, THE THEORY OF THE GENE 24 (1926)).

acid or DNA) built into a double-helical structure,[18] DNA instructs cells to make proteins and regulates cell activity, and DNA has both exons (active portions carrying instructions) and introns (inactive portions that maybe do something else or maybe nothing).[19] Geneticists have found "overlapping genes, genes within genes and countless other weird arrangements."[20]

As scientists worked to understand the gene and its intricate work within a human cell, new technologies emerged that enabled researchers more easily to hunt for genes on human chromosomes. Genes linked to inheritable diseases especially held great promise for diagnostic testing, therapeutic products, and preventative measures.[21] In the 1960s and 1970s, researchers discovered practical ways to use genetic markers (short genetic sequences at known locations on the chromosomes) to locate specific genes of interest—as markers were identified across chromosome regions, inheritance of both a trait and its marker signaled linkage to the marked gene.[22] The resulting genetic linkage maps brought studies of inherited traits within families and molecular biology together.[23] After a gene hunter located a gene in a specific region within a chromosome using markers, she could then build physical maps of DNA sequences between the markers that revealed the specific DNA sequence of the gene in question.[24] Prominent single-gene hereditary diseases first linked to specific genes during this timeframe using these or similar techniques included sickle cell anemia, Huntington's disease, Duchenne muscular dystrophy, and cystic fibrosis.[25] Despite occasional breakthroughs, locating, isolating,

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[18] James Watson & Francis Crick, *Molecular Structure of Nucleic* Acids, 171 NATURE 737 (1953). Obviously, molecular biology and genetic sequencing are highly complex areas of study and this Article does not delve deeply into the specific science and technology involved. For a more detailed explanation related to these topics in the context of Myriad's patents, see Judge Sweet's discussion in Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 193–200 (S.D.N.Y. 2010), and the citations therein.

[19] *See Ass'n for Molecular Pathology*, 702 F. Supp. 2d at 194; *see also* Helen Pearson, *What is a Gene?*, 441 NATURE 399, 399 (2006) ("The more expert scientists become in molecular genetics, the less easy it is to be sure about what, if anything, a gene actually is."). Scientists often use the term "junk DNA" to refer to an inactive DNA sequence that does not encode a protein, or more broadly, to refer to any DNA sequence that "does not play a functional role in development, physiology, or some other organism-level capacity." Alexander F. Palazzo & T. Ryan Gregory, *The Case for Junk DNA*, 10 PLOS GENETICS 1 (May 2014) (concluding that recent research does not support a finding that all DNA is functional). *See also* Lucas D. Ward & Manolis Kellis, *Evidence of Abundant Purifying Selection in Humans for Recently Acquired Regulatory Functions*, 337 SCIENCE 1675 (2012); JONATHAN WELLS, THE MYTH OF JUNK DNA (2011).

[20] Pearson, *supra* note 19, at 399.

[21] *See* Allen C. Nunnally, Note, *Commercialized Genetic Testing: The Role of Corporate Biotechnology in the New Genetic Age*, 8 B.U. J. SCI. & TECH. L. 306, 315 (2002) (describing "prophylactic measures" as "a primary goal of genetic testing"); John Bell, *Predicting Disease Using Genomics*, 429 NATURE 453, 453 (2004) ("Prediction, prevention and counselling of individuals at risk of genetic diseases have been aimed largely at single-gene disorders that have mendelian patterns of inheritance.").

[22] U.S. CONGR. OFFICE OF TECH. ASSESSMENT, OTA-BA-373, MAPPING OUR GENES—THE GENOME PROJECTS: HOW BIG, HOW FAST? 4–6 (1988).

[23] ROBERT COOK-DEEGAN, THE GENE WARS: SCIENCE, POLITICS, AND THE HUMAN GENOME 29–47 (1994) [hereinafter COOK-DEEGAN, GENE WARS]; Robert Cook-Deegan, *Mapping the Human Genome*, 65 S. CAL. L. REV. 579 (1991) [hereinafter Cook-Deegan, *Mapping*].

[24] *See* Cook-Deegan, *Mapping*, at 581–582.; U.S. CONG, OFFICE OF TECH. ASSESSMENT, *supra* note 22, at 26–28.

[25] KEVIN DAVIES & MICHAEL WHITE, BREAKTHROUGH: THE QUEST TO ISOLATE THE GENE FOR HEREDITARY BREAST CANCER 251 (1995).

and sequencing genes associated with particular proteins or diseases proved difficult.[26] Better markers, known as restriction fragment length polymorphisms (RFLPs),[27] offered improvements, but the basic process remained tedious and repetitive: locate a chromosomal region using family studies, "pull out the genes in the . . . region and screen them for mutations."[28]

The hunt for a gene linked to hereditary breast cancer proved no different, but captured the imagination of many vying to find it, as well as the popular press.[29] Breast cancer, like other cancers, derives from a large number of factors, including genetic and environmental ones.[30] However, researchers as early as the 1800s noted that some forms of breast cancer appeared to have higher incidences within families.[31] By the late 1980s, several groups in the United States, England, France, Germany, Japan, and other countries were working to find the genetic basis for hereditary breast and ovarian cancer.[32] In 1990, Mary-Claire King announced that her team at the University of California, Berkeley, had localized the first gene associated with increased risk for breast cancer, known as BRCA1, to a region of chromosome 17.[33] Researchers around the world then used every available technology to dissect and scrutinize this genomic region as they raced to isolate and sequence BRCA1.[34] Myriad won the "most impassioned and publicly visible of all genetic races" when it announced on September 15, 1994, that the company had isolated and sequenced BRCA1.[36]

Following the discovery of BRCA1, researchers at Myriad and elsewhere continued to hunt for a second gene using similar approaches.[37] In late December 1995,

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[26] *See* John M. Golden, *Biotechnology, Technology Policy, and Patentability*, 50 EMORY L. J. 101, 114–15 (2001) (explaining the historical difficulties with gene sequencing encountered by the biotechnology industry).

[27] DAVIES & WHITE, *supra* note 25, at 131–33; COOK-DEEGAN, GENE WARS, *supra* note 23, at 40–44.

[28] DAVIES & WHITE, *supra* note 25, at 266. *See* Declaration of Sir John E. Sulston, Ph.D. at 5–8, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09-4515).

[29] Natalie Angier, *Fierce Competition Marked Fervid Race for Cancer Gene,* N.Y. TIMES, Sept. 20, 1994, at C1.

[30] DAVIES & WHITE, *supra* note 25, at 50; *see* Bernadine Healy, *BRCA Genes — Bookmaking, Fortunetelling, and Medical Care*, 336 New Engl. J. Med. 1448–1449 (1997).

[31] DAVIES & WHITE, *supra* note 25, at 120 (describing French surgeon Pierre Paul Broca as the "first to notice the potential significance of the clustering of cancers, notably breast cancer, within a single family").

[32] *See* Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing*, 10 HEALTH L.J. 123, 131 (2002); *see also* Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 201 (S.D.N.Y. 2010).

[33] Williams-Jones, *supra* note 32, at 131 (citing M.-C. King, *Localization of the Early-Onset Breast Cancer Gene*, 26 HOSPITAL PRACTICE 121 (1991)); Jeff M. Hall et al., *Linkage of Early-Onset Familial Breast Cancer to Chromosome 17q21*, 250 SCIENCE 1684, 1684–89 (1990). *See also* DAVIES & WHITE, *supra* note 25, at 1–6.

[34] Ass'n for Molecular Pathology, 702 F. Supp. 2d at 201.

[36] Angier, *supra* note 29 at C1. *See also* Miki et al., *supra* note 8; Natalie Angier, *Scientists Identify a Mutant Gene Tied to Hereditary Breast Cancer*, N.Y. TIMES, Sept. 15, 1994, at A1. As is typical for many medical innovations, Myriad did not claim credit singularly. Researchers at Myriad worked with others at the University of Utah, the National Institute of Environmental Health Sciences, McGill University, and the Eli Lilly and Company to discover the gene. *See* Miki et al., *supra* note 8 for a complete listing of researchers and their affiliations.

[37] *See* Declaration of Dr. Sean Tavtigian at 2, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09-4515) [hereinafter Tavtigian Declaration].

Myriad isolated and sequenced BRCA2, a gene previously linked to chromosome 13.[38] After Myriad isolated and sequenced the genes, it sought and obtained a number of patents claiming sequences identified with the BRCA genes, in whole or in part, and methods for comparing those claimed sequences to the identified BRCA genes to determine whether predisposing mutations are present in patients.[39] The first patent was issued on December 2, 1997; eventually, Myriad would own (or exclusively license) nine patents in all covering the BRCA genes.[40]

B. Myriad Genetics and BRCA Diagnostic Testing Commercialization

Myriad's beginnings as a company were humbler than its declared diagnostic testing revenues of $748 million in 2014,[41] In the early 1970s, the University of Utah hired Mark Skolnick, a young geneticist, to collaborate on its grant proposals for a new cancer center.[42] Skolnick began developing what became the key to Myriad's later success: a database of medical, demographic, and ancestral information collected from large Utah families.[43] To look for evidence of a genetic predisposition to cancer of any kind, Skolnick and his group linked family pedigrees recorded by the Utah Genealogical Society to the Utah Cancer Registry, which included records for all cancer cases statewide.[44] At about the same time, the University of Utah established a cancer screening clinic to support Skolnick's effort.[45] This immense amount of data associated with Utah families enabled Skolnick to develop an innovative population-based analysis of cancer incidence within the family pedigrees.[46]

Although technology had advanced such that groups like Skolnick's could more easily sequence DNA, locating and isolating genes continued to be a highly laborious process.[48] Skolnick and his group found some success studying colon cancer[49] and

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[38] *See* Richard Wooster et al., *Localization of a Breast Cancer Susceptibility Gene, BRCA2, to Chromosome 13q12-13*, 265 SCIENCE 2088 (1994). For more information about Myriad's approach to isolating and sequencing the BRCA1 and BRCA2 genes, see Declaration of Donna Shattuck, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09-4515).

[39] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2113 (2013).

[40] E. Richard Gold & Julia Carbone, *Myriad Genetics: In the Eye of the Policy Storm*, 12 GENETICS IN MED. S39, at S42 (2010).

[41] Myriad Genetics, Inc., Annual Report (Form 10-K), 47 (Aug. 13, 2014).

[42] DAVIES & WHITE, *supra* note 25, at 244.

[43] The Utah Population Database, as it's now known, continues to receive "annual updates from contributors for Utah births, marriages, divorces, deaths, cancer records, and driver licenses, as well as from Idaho cancer records." *Utah Population Database*, UNIV. OF UTAH, http://healthcare.utah.edu/huntsmancancerinstitute/research/updb/data (last updated Apr. 8, 2014).

[44] *Id.*

[45] In the end, "large and genetically informative families . . . and detailed family information, such as detailed genealogical records, [were] an important component" to the search for an inherited gene implicated in breast and ovarian cancer. Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 201 (S.D.N.Y. 2010). The Utah Genealogical Society compiles the extensive genealogy done by the Church of Jesus Christ of Latter-day Saints, a valuable resource for researchers looking for this kind of familial information.

[46] Declaration of Dr. Mark Skolnick at 3–4, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09-4515) [hereinafter Skolnick Declaration].

[48] *Id.* at 4. These early advances featured the use of better markers for a more systematic search for specific genes to sequence. *Id.*

continued to work on breast cancer at a slow pace.[50] At the same time, the group also worked on easier to locate genes like the ones underlying Alport Syndrome, a kidney disorder, and neurofibromatosis, a form of cancer.[51] Skolnick succeeded in mapping the Alport gene in 1988, but lost the race to map the neurofibromatosis gene to Ray White, a well-known University of Utah colleague.[52] This loss proved to Skolnick that he could not compete with bigger groups hunting genes—Skolnick and his group had the skills and talent necessary to make important gene discoveries, but they lacked the funding required for a search of enigmatic genes like BRCA1 and BRCA2.[53]

Skolnick knew that he had something even more valuable than skills and talent—he had data from the most extensive family studies, thanks to the detailed genealogical database incorporating cancer incidences within Utah families.[54] To hit the ground running, Skolnick took a path often taken by early-stage inventors—he joined forces with a venture capital group to create a private company named Myriad Genetics, Inc.[55] Myriad, as a private company, could support Skolnick's gene hunting research by attracting capital from private investors.[56] Myriad raised $55 million in this manner in 1992 alone.[57] In August 1992, Eli Lilly and Company, a large pharmaceutical firm, contributed $4 million in corporate research funding and purchased $1 million of Myriad's stock.[58] Private placement offerings raised an additional $8.8 million in March 1993 and $59 million in 1994.[59] The infusion of cash worked wonders, allowing the Myriad team "to work at a superior pace."[60] In September 1994, as a result of intense search efforts, the team announced that they had sequenced the BRCA1 gene.[61] The sequence for BRCA2 came along in much the same way not long after Myriad became a public company in 1995.[62]

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[49] Harold M. Schmeck, *50% of Colo-Rectal Cancers Tied to Genetic Predisposition*, N.Y. TIMES, Sept. 1, 1988, A1; *see* Lisa A. Cannon-Albright et al., *Common Inheritance of Susceptibility to Colonic Adenomatous Polyps and Associated Colorectal Cancers*, 319 NEW ENGL. J. MED. 533 (1988).

[50] DAVIES & WHITE, *supra* note 25, at 195.

[51] Skolnick Declaration, *supra* note 46, at 4. *See also* DAVIES & WHITE, *supra* note 25, at 256.

[52] DAVIES & WHITE, *supra* note 25, at 256–57.

[53] Skolnick Declaration, *supra* note 46, at 5.

[54] *Id.* at 4–5; DAVIES & WHITE, *supra* note 25, at 261; Gold & Carbone, *supra* note 40, at S40. As Gold and Carbone note, control of the Utah family database remained (and remains still) with the University of Utah, but "Skolnick was best positioned to use it, giving Myriad the inside track in the race to sequence BRCA1." *Id.* at S41.

[55] Williams-Jones, *supra* note 32, at 129. One of Skolnick's partners was Walter Gilbert, the 1980 Nobel Laureate in Chemistry. *Id.*

[56] Skolnick Declaration, *supra*, note 46, at 5.

[57] *See* Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 201 (S.D.N.Y. 2010).

[58] *See* Skolnick Declaration, *supra* note 46, at 5–6. Eli Lilly obtained the rights to future therapeutics related to BRCA1, which it believed would lead to future blockbuster drugs. *See* Gold & Carbone, *supra* note 40, at S40; *see also* William-Jones, *supra* note 32, at 129. Myriad retained the rights for development of BRCA2 therapeutics. *See id.*

[59] *See* Skolnick Declaration, *supra* note 46, at 5–6; *see also Ass'n for Molecular Pathology*, 702 F. Supp. 2d at 201.

[60] *See* Skolnick Declaration, *supra* note 46, at 6–7.

[61] *See* Angier, *supra* note 29. Roger Wiseman, one Myriad collaborator, stated, "What do I attribute our success to? . . . [l]uck." *Id.*

[62] *See* Tavtigian Declaration, *supra* note 37, at 2 (explaining that U.S. Patent App. Ser. No. 08/576,559, filed on December 21, 1995, disclosed the full sequence of the BRCA2 cDNA and protein). Myriad's initial

The discovery of a gene linked to a disease, like the BRCA genes, facilitates development of predictive or pre-symptomatic diagnostic tests—tests that give a genomic diagnosis based on "deciphering the genes of a patient instead of diagnosing the patient based on signs and symptoms."[63] A genomic diagnosis, in turn, facilitates "personalized medicine"—a brave new world of drug development for individual patients.[64] The researchers on the hunt for the BRCA genes recognized the commercial opportunities for diagnostic testing and subsequent research and development of gene therapies.[65] Myriad, under the leadership of Skolnick, an "astute businessman," was "intent on being the first to exploit the commercial potential of the breakthrough when it came."[66] The first commercial product for a company like Myriad had to be a diagnostic test to detect BRCA1 and BRCA2 mutations. Myriad moved quickly to develop one after discovering the genes and securing all patent rights (through exclusive licenses from other joint owners).[67]

Myriad's flagship diagnostic test, marketed under the name BRAC*Analysis*®, came onto the market in 1996. Currently, a physician must order the test so that the patient receives the physician's interpretation of the results as well as genetic counseling and support.[68] BRAC*Analysis*® originally included only full sequencing of the patient's BRCA genes,[69] but later added detection of large rearrangements.[70] At present, BRAC*Analysis*® costs about $3,340 for the full sequence (and about $475 for testing of family members when a relative has already tested positive for one specific rearrangement or mutation).[71] *BRACAnalysis*® accounted for $400 million, or 80% of Myriad's revenues in 2011.[72] Myriad also offers cheaper tests for single mutations and a $700 test for many major rearrangements, marketed under the name *BART*®—these account for most of the remainder of Myriad's revenues.[73]

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public offering was held on October 6, 1995. *See Myriad Genetics Inc. – Offers Common for Initial Public Sale – NASDAQ Symbol*, STANDARD & POOR'S DAILY NEWS, Oct. 10, 1995, *available at* 1995 WLNR 571993.

[63] George Annas, *Genetic Prophecy and Genetic Privacy*, 32 TRIAL 18, 20 (1996).

[64] The term "personalized medicine" describes healthcare based on the individual patient's genetic risks and drug sensitivities. *See* Nancy Shute, *Personalized Medicine*, 306 SCI. AM. 44 (2012). For more information about the history of the Human Genome Project and the future of personalized medicine, see FRANCIS S. COLLINS, THE LANGUAGE OF LIFE: DNA AND THE REVOLUTION IN PERSONALIZED MEDICINE (2010).

[65] *See* Gold & Carbone, *supra* note 40, at S44.

[66] *See* DAVIES & WHITE, *supra* note 25, at 222.

[67] *See* Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 203 (S.D.N.Y. 2010).

[68] *See* Williams-Jones, *supra* note 32, at 133. Myriad initially sold BRAC*Analysis*® to the public for $900 as a direct-to-consumer product. However, concerns regarding inadequate genetic counseling support for customers and potential liability exposure forced Myriad to recall the test from the market. *Id.*

[69] *See* Declaration of Dr. Gregory Critchfield at 20–21, *Ass'n for Molecular Pathology*, 702 F. Supp. 2d 181 (No. 09-4515) [hereinafter Critchfield Declaration].

[70] *See id.* at 23–24.

[71] Advanced Beneficiary Notice of Non-Care, Myriad Genetics, Inc., available at http://www.myriad.com/lib/abn/Myriad-ABN.pdf.

[72] *See* A. Lane Baldwin & Robert Cook-Deegan, *Constructing Narratives of Heroism and Villiany: Case Study of Myriad's BRACAnalysis® Compared to Genetech's Herceptin®*, 5 GENOME MED. 8, 11 (2013) (citing Myriad Genetics, Inc., Annual Report (Form 10-K), 42 (Aug. 14, 2013).

[73] *See* Myriad Genetics, Inc., *supra* note 41, at 42. Because of expenditures in research and development, including failed pharmaceutical products, Myriad was not profitable until 2008. *See* Shuwen Lu, Sustainable Development of an Innovative Enterprise in the US Biopharmaceutical Industry—A Case

Myriad is the only commercial provider of BRCA testing in the United States and all of its testing is conducted at its state-of-the-art facility in Salt Lake City, Utah.[74] In January 1996, OncorMed, Inc., the owner of a competing patent on a BRCA1 sequence, began selling a diagnostic test for BRCA1.[75] Later, other laboratories began performing diagnostic testing for BRCA genes, including Genetics & IVF Institute (GIVF), the University of Pennsylvania's Genetic Diagnostic Laboratory (GDL), and the Yale DNA Diagnostics Laboratory (YDL).[76] In 1998, after patents issued with broad claims covering the isolated BRCA sequences, Myriad sent cease-and-desist letters to GDL, GIVF, YDL, and several researchers who used the services of the GDL. These letters notified the recipients of Myriad's patents and offered a commercial testing license.[77] GIVF acquiesced to Myriad's demand, but GDL continued to provide diagnostic testing, claiming a research exemption.[78] In 1997 and 1998, Myriad sued OncorMed for patent infringement, eventually obtaining its patents in a settlement.[79] Myriad also sued the University of Pennsylvania for infringement, but the case was later dismissed without prejudice after the university agreed to discontinue its BRCA diagnostic testing.[80]

Myriad's business model leaned on its patents in the beginning, but its role as the single provider of BRCA diagnostic tests in the United States enables it to collect valuable information about the mutations found in its patients' genes. In addition to deleterious mutations (indicating the patient has an identifiable increased risk of cancer) or neutral ones (indicating the patient has roughly the same risk as someone with a normal version of the gene), BRAC*Analysis*® might detect a mutation known as a "genetic variant of uncertain significance," or a "VUS,"[82] which presents an unknown cancer risk.[83] With data collected from patients, including ethnicity and family pedigrees, Myriad built a large, proprietary database of information about the BRCA genes.[84] Myriad initially shared much of this information with public databases; it stopped doing so in 2004, and now keeps its data, including algorithms for interpreting VUS effects and specific sequences, as trade secrets.[85] As a result, one study suggests that Myriad likely

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Study of Myriad Genetics, Inc. 22 (Apr. 19, 2010) (unpublished Ph.D. dissertation, Univ. of Mass., Lowell) (on file with author).

[74] *See* Derek So & Yann Joly, *Commercial Opportunities and Ethical Pitfalls in Personalized Medicine: A Myriad of Reasons to Revisit the Myriad Genetics Saga*, 11 CURRENT PHARMACOGENOMICS PERSON. MED. 98, 100 (2013). Myriad licensed thirteen other laboratories to conduct single mutation testing in the relatives of women who had an identified mutation in Myriad's testing. *See* Gold & Carbone, *supra* note 40, at S42.

[75] See Michael J. Malinowski & Robin J.R. Blatt, *Commercialization of Genetic Testing Services: The FDA, Market Forces, and Biological Tarot Cards*, 71 TUL. L. REV. 1211, 1213–16 (1997).

[76] *See id.*; *see also* Ass'n for Molecular Pathology v. USPTO, 669 F. Supp. 2d 365, 398 (S.DN.Y. 2009) (denying Myriad's motion to dismiss the case); Gold & Carbone, *supra* note 40, at S42.

[77] *See Ass'n for Molecular Pathology*, 669 F. Supp. 2d at 378–79; *see also* So & Joly, *supra* note 72, at 99.

[78] *See Ass'n for Molecular Pathology*, 669 F. Supp. 2d at 372; *see also* Julia Carbone et al., *DNA Patents and Diagnostics: Not a Pretty Picture*, 28 NATURE BIOTECH. 784, 788 (2010); So & Joly, *supra* note 72, at 99–100.

[79] *See* So & Joly, *supra* note 72, at 99.

[80] See Ass'n for Molecular Pathology, 669 F. Supp. 2d at 379.

[82] Approximately 7% to 15% of women tested for a BRCA gene have a VUS, but most VUS do not increase these patients' risk of cancer. So & Joly, *supra* note 72, at 103.

[83] *See* Critchfield Declaration, *supra* note 67, at 25–28.

[84] *See* So & Joly, *supra* note 72, at 104.

[85] See *id.*

will dominate the BRCA diagnostic testing market long after its patents expire (or are declared invalid claim by claim).[86] Its access to extensive family data, the VUS database, an efficient laboratory, a network of health professionals and payers, and countless salespeople guarantee that Myriad remains an enduring player in the genetic testing market regardless of its patent claims remaining after *Myriad*.

II. FROM *CHAKRABARTY* TO *MYRIAD*

Myriad's domination of the BRCA diagnostic test market caused its litigation to attract unusual attention for a patent case—during the *Myriad* oral arguments in April 2013, protesters held signs outside the Supreme Court saying, "Your corporate greed is killing my friends" and, "My genes are not property."[87] The case was not unusual for a patent case in that it involved a narrow question of patent law—whether certain Myriad's claims were patent eligible subject matter under 35 U.S.C. § 101 (Section 101).[88] This narrow question of law masked a couple of underlying questions about the import of the case—how did patent claims covering genetic sequences allow one company to monopolize a market, and how did the legal mechanisms for obtaining, enforcing, and invalidating patents take so long to effect change?

The *Myriad* litigation began in 2009, when a group of plaintiffs, supported by the American Civil Liberties Union (ACLU), filed suit against Myriad, as the exclusive licensee and co-owner of BRCA patents, as well as the United States Patent & Trademark Office (USPTO), and individual directors of the University of Utah Research Foundation (UURF), another co-owner of the patents.[89] The details of the litigation have been extensively reported in the scientific and popular press, as well as in scholarly work.[90] Part II.A uses the case to highlight the tension between stability and growth in the patent eligibility doctrine (in other words, how Myriad obtained patents claiming the BRCA genes). Part II.B contends that standing, a procedural device, played a role in delaying challenges to the patents despite vocal critics from several sectors. Finally, Part II.C explains how Myriad used its patents to develop a monopoly and surveys the consequences stemming from its patent enforcement.

A. Patent Subject Matter Eligibility

It is common knowledge that patent law derives from Congress' constitutional authority "to promote the Progress of Science and the useful Arts."[91] To that end, Congress enacted its first patent laws in 1790.[92] The patent system tends to be viewed as utilitarian—patents promote technological progress by giving to an inventor the exclusive right to his discovery for a limited time.[93] This traditional view of patents assumes that

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[86] See *id.*

[87] Bill Mears, *Justices at Odds Over Gene Patents*, CNN WIRE (Apr. 17, 2013, 6:15 PM EDT), http://www.cnn.com/2013/04/15/health/court-genes/.

[88] *See* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S.Ct. 2107, 2111 (2013).

[89] *See* Ass'n for Molecular Pathology v. USPTO, 669 F. Supp. 2d 365, 370–77 (S.D.N.Y. 2009).

[90] *See, e.g.*, Jake Gipson, Note, Patentable Subject Matter: A Myriad of Problems, 65 ALA. L. REV. 815 (2014).

[91] U.S. CONST. art. I, § 8, cl. 8.

[92] *See* Patent Act of 1790, ch. 7, 1 Stat. 109, 109 (1790).

[93] U.S. CONST. art. 1, § 8, cl. 8; *see also* CRAIG ALLEN NARD & R. POLK WAGNER, PATENT LAW 7 (2008) ("Patent law is thus straightforwardly utilitarian in outlook: we grant patent rights not to reward inventors

the incentives created by the patent's exclusive rights (what others have called "the prospect of a marketplace reward"[94]) will encourage inventions and superior innovation, two public benefits meant to outweigh the costs of granting exclusive rights (administrative costs, the deadweight losses of monopolies, and so on).[95] Because this commonly accepted rationale for granting patents in the first place implicates incentives to would-be inventors—incentives to invent, disclose, commercialize, etc.[96]—participants at every level of the patenting process prefer uniformity and predictability in the law.[97] After all, uncertainty in the law makes for qualms about *ex ante* investment.[98] Yet, even patent law must grow and change to accommodate new technology and social and economic thought. *Myriad* illustrates this eternal struggle between certainty and change.

Compared to the dramatic race to locate and sequence genes related to breast and ovarian cancer, the race to patent them was anticlimactic in the wake of *Diamond v. Chakrabarty*, the seminal 1980 case declaring a genetically engineered microorganism patent eligible.[99] Before *Chakrabarty* and after, activists protested the patenting of life forms and expressed concerns about the privatization of life itself.[100] Despite generating scholarly, media, and policy discussion, these activists did not successfully change patent policy.[101] Fifteen years after Myriad filed its first patent applications, the ACLU decided to challenge Myriad's BRCA gene patents.[102] The ACLU and its named plaintiffs faced an uphill battle—as one ACLU litigator noted, "[A]lmost everyone we talked with said we would lose in court."[103]

Why was *Myriad* perceived as such a loser? The answer lies within the patent eligibility doctrine, a feature of U.S. patent law since 1790. The first patent statutes allowed for issuance of patents to inventors who "invented or discovered any useful art, manufacture, engine, machine, or device, or any improvement therein not before known or used."[104] Section 101, the present statute, reads similarly: "Whoever invents or

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for their achievements, but to stimulate others to seek the same reward—and thereby contribute new innovations for the good of society."). In an insightful book devoted to exploring the broader group of intellectual property rights, Robert Merges challenges the utilitarian view of patent rights as inadequate and develops some underlying mid-level principles based upon distributive justice. *See* ROBERT P. MERGES, JUSTIFYING INTELLECTUAL PROPERTY (2011).

[94] NARD & WAGNER, *supra* note 93, at 7, 11.

[95] *See id.* at 11; *see also* Lee Petherbridge, *On the Development of Patent Law*, 43 LOY. L.A. L. REV. 893, 899 (2010).

[96] *See* F. SCOTT KIEFF ET AL., PRINCIPLES OF PATENT LAW 63–68 (6th ed. 2013).

[97] *See* Bilski v. Kappos, 561 U.S. 593, 613 (2010) (Stevens, J., concurring) ("In the area of patents, it is especially important that the law remain stable and clear. . .").

[98] *See* Brief for Genetech, Inc. et al. as Amici Curiae Supporting Respondents at 11, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013) (No. 12-398) [hereinafter Genetech, Inc. et al. Amicus Brief]; *see also* Sung, *Medical Alert: Alarming Challenges Facing Medical Technology Innovation*, 6. J. BUS. & TECH. L. 35, 38 (2011).

[99] *See* Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980).

[100] *See* Shobita Parthasarathy, *Breaking the Expertise Barrier: Understanding Activist Strategies in Science and Technology Policy Domains*, 37 SCI. & PUB. POL'Y 355, 359 (2010).

[101] *See id.* at 364. *See also* Cardozo Law School Symposium, *Patenting People* (2006), *available at* http://www.justinhughes.net/patentingpeople/index.html.

[102] *See* Sandra Park, *Gene Patents and the Public Interest*, 15 N.C. J. L. TECH. 519, 520 (2014).

[103] *Id.* at 524.

[104] Patent Act of 1790, ch. 7, § 1, 1 Stat. 109, 109 (1790). In 1793, Congress amended the statute to grant patents for "any new and useful art, machine, manufacture or composition of matter, or any new and useful

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."[106] The same statutory language has defined patent eligible subject matter for over 220 years, reflecting an eligibility standard that courts view as broad, technologically neutral, and unchanging.[107]

Based upon case law dating to the nineteenth century,[108] the Supreme Court decides patent eligibility disputes based upon the four categories enumerated in Section 101: compositions of matter, manufactures, machines, or processes. The Court also describes three categories of inventions that do not merit patenting despite arguably falling within the statutory categories: laws or principles of nature (processes), natural or physical phenomena (compositions of matter), and abstract ideas (processes)..[109]

In patent eligibility cases, the Court appears wary of the danger of unwarranted monopolies that might arise from the patent owner's right to exclude others (commonly referred to as a preemption concern).[110] As the Court stated in *Le Roy v. Tatham*, "A patent is not good for an effect, or the result of a certain process, as that would prohibit all other persons from making the same thing by any means whatsoever. This, by creating monopolies, would discourage arts and manufactures, against the avowed policy of the patent laws."[111] The Court, in *O'Reilly v. Morse*, explained further, "[I]f he can secure the exclusive use by his present patent he may vary it with every new discovery and development of the science, and need place no description of the new manner, process or machinery, upon the records of the patent office."[112] In other words, the discovery of a novel scientific principle would not be (and should not be) patentable, even if the statute did not explicitly deny patentability to such principles.[113] The Court's ongoing concerns

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improvement on any art, machine, manufacture or composition of matter, not known or used before. . . ." Patent Act of 1793, ch 7, § 1, 1 Stat. 318, 318–23 (1793).

[106] 35 U.S.C. § 101 (2012).

[107] *See* J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124, 130 (2001) ("[T]he language of § 101 is extremely broad."); Diamond v. Chakrabarty, 447 U.S. 303, 308 (1980) ("In choosing such expansive terms as 'manufacture' and 'composition of matter,' modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope.").

[108] The contemporaneous cases of Le Roy v. Tatham, 55 U.S. 156 (1852) and O'Reilly v. Morse, 56 U.S. 62 (1853), involved mid-nineteenth century inventions called into question as not patent eligible. Le Roy's claim for a lead pipe manufactured according to a newly discovered quality of lead and Morse's claim for any method or machine using electromagnetic motive power to print at a distance were both found not patentable; their ineligibility hinged on the Court's refusal to allow patent claims solely to newly discovered principles or qualities. In both cases, the Court insisted that any newly discovered principle or quality, to be patentable, must be applied to a new composition of matter, manufacture, machine, or process adequately described in the patent specification. *See Le Roy*, 55 U.S. at 174–77; *O'Reilly*, 56 U.S. at 105. Though the cases might better be described as inadequate written disclosure cases (admonishing the inventors in each to better describe what their invention was), the Court's insistence that patent subject matter necessarily excludes natural laws and principles remains relevant in the most modern cases of subject matter eligibility.

[109] *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1293–94 (2012).

[110] See *id.*

[111] *Le Roy*, 55 U.S. at 175.

[112] *O'Reilly*, 56 U.S. at 113.

[113] *Id.* at 124–37 (Grier, J., dissenting). Justice Grier, a dissenter in both cases, suggested something subtler—that the statute allowed an inventor to claim *all* applications of the discovered principle as his reward for turning the discovery of a scientific principle into a useful art. *Id.*

for unwarranted monopolies and preemption compel its insistence upon the implicit judicial exceptions to the statutory language. [114]. Thus, the patent eligibility doctrine might best be described as an expansive but bounded set—a pragmatic model meant to incentivize the application of discoveries to new and useful purposes, rather than the scientific discoveries themselves.[116] An inventor whose invention lies out of bounds obtains no patent, regardless of any extraordinary expense or ingenuity in his endeavors.[117]

The product of nature exception plays an important role in defining patent eligible subject matter in biological inventions because such inventions inherently implicate natural products. As the Court remarked in *Mayo Collaborative Services v. Prometheus Laboratories*, "[A]ll inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas."[118] Section 101 includes new and useful compositions of matter, but "[t]he 'matter' of which patentable new and useful compositions are composed necessarily includes naturally existing elements and materials."[119] That makes it difficult to determine whether a biological composition falls within the bounds of patent eligibility, especially as advances in biological engineering might lead to blurred lines between products of nature and patent eligible inventions.[120]

Moreover, the judicial exceptions define patent eligible subject matter by defining what it is not—a pragmatic rule, but hard to pin down.[121] Justice Frankfurter presciently noted in *Funk Brothers*:

> It only confuses the issue, however, to introduce such terms as "the work of nature" and the "laws of nature." For these are vague and malleable terms infected with too much ambiguity and equivocation. Everything that happens may be deemed "the work of nature" and any patentable composite exemplifies in its properties "the laws of nature."

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[114] Alice Corp. v. CLS Bank Int'l, 134 S. Ct. 2347, 2354 (2014) ("[The Court has] interpreted § 101 and its predecessors in light of this exception for more than 150 years") (quoting Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2116 (2013)). *Le Roy* and *O'Reilly* denied patents to claims directed toward a newly discovered scientific principle or what might be called a natural law. *See Le Roy*, 55 U.S. at 173; *O'Reilly*, 56 U.S. at 113. Later cases denied patents to inventors claiming abstract ideas and natural or physical phenomena. *See*, *e.g.*, Diamond v. Diehr, 450 U.S. 175, 185 (1981) (abstract ideas); Gottschalk v. Benson, 409 U.S. 63, 67 (1972) (same); Parker v. Flook, 437 U.S. 584, 594 (1978) (same); Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) (products of nature); *Myriad*, 133 S. Ct. at 2116 (same).

[116] *Alice Corp*., 134 S. Ct. at 2354 ("[A]pplication[s] of such concepts to a new and useful end, we have said, remain eligible for patent protection.") (quoting *Gottschalk*, 409 U.S. at 67) (internal quotation marks omitted).

[117] *See Myriad*, 133 S. Ct. at 2117.

[118] Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1293 (2012). Everything "with which man deals and for which patent protection is granted are products of nature in the sense that nature provides the basic source materials." Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156, 162 (4th Cir. 1958).

[119] *Merck*, 253 F.2d at 162.

[120] *See*, *e.g.*, Jacob S. Sherkow, *The Natural Complexity of Patent Eligibility*, 99 IOWA. L. REV. 1137 (2014) (developing a test for eligibility based on the scientific philosophy of complexity).

[121] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948) (holding claims ineligible by characterizing the final product as merely repackaging products of nature).

> Arguments drawn from such terms for ascertaining patentability would fairly be employed to challenge almost every patent.[122]

The Court recently explained in *Alice Corp. v. CLS Bank* that the exceptions exist (and must exist) because otherwise "'[m]onopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it,' thereby thwarting the primary object of the patent laws."[123] This worry—inhibiting the future use of "the basic tools of scientific and technological work"[124] and "building blocks of human ingenuity"[125]—ties squarely into the commonly accepted rationale for patents as incentives to aspiring inventors. Justice Breyer once described the patent system as "not only encourag[ing] research by providing monetary incentives for invention" but also as potentially "discourag[ing] research by impeding the free exchange of information."[126] In other words, the patent system should be concerned as much with avoiding the dangers of overprotection as it is with avoiding the diminished incentives of too little protection.[127] Because stability in the law is paramount to encourage invention and investment, the "vague and malleable terms" used to define what is not patent eligible have caused mischief, especially in cases where the technology at issue is difficult to characterize.[128]

In 1980, the Court stepped into this fray in *Diamond v. Chakrabarty*.[129] No case has had more of a lasting impact in the biotechnology field.[130] The inventor claimed a bacterium modified by the insertion of two or more plasmids into the bacteria cells.[131] The resulting genetically modified organism could break down multiple components of crude oil, a property no naturally occurring bacteria possessed—was it patent eligible?[132] The Court first repeated the incentive account of patent law.[133] It then moved to Section

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[122] *Id.* at 134–35.
[123] Alice Corp. v. CLS Bank Int'l, 134 S. Ct. 2347, 2354 (2014) (quoting *Mayo*, 132 S. Ct. at 1923).
[124] *Id.* (quoting Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2116 (2013)).
[125] *Id.* (citing *Mayo*, 132 S. Ct. at 1301 (2012)).
[126] Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 127 (2006) (Breyer, J., dissenting).
[127] *Id.*
[128] See *id.* at 134.
[129] Diamond v. Chakrabarty, 447 U.S. 303 (1980). *See* Daniel J. Kevles, *Ananda Chakrabarty Wins a Patent: Biotechnology, Law, & Society*, 25 HIST. STUD. PHYS. & BIOL. SCI. 111, 131 (1994); [Cite other articles.]
[130] Kevles, *supra* note 125, at 135. *See*, *e.g.*, Anna Lumelsky, *Diamond v. Chakrabarty: Gauging Congress's Response to Dynamic Statutory Interpretation by the Supreme Court*, 39 U.S.F. L. REV. 641, 691 (2005) ("[T]he impact of the *Chakrabarty* holding continues to be extraordinarily broad twenty-five years after the decision.); Eileen M. Kane, *Splitting the Gene: DNA Patents and the Genetic Code*, 71 TENN. L. REV. 707, 736 (2004) ("The [*Chakrabarty*] decision is frequently characterized and cited for its effect on opening the gates of the patent system to biotechnology…").
[131] *Chakrabarty*, 447 U.S. at 305.
[132] *Id.* At first, the USPTO rejected Chakrabarty's product claims as not eligible for patenting under Section 101 on two grounds: 1) microorganisms are products of nature; and 2) living things are not eligible for patenting under § 101. The Board of Patent Appeals affirmed this rejection on the latter ground, but the Court of Customs and Patent Appeals reversed the rejection to allow the claims as eligible subject matter. Following the Court's order vacating and remanding the case for further consideration in light of *Parker v. Flook* (a case involving the abstract ideas exception), the case made its way back to the Supreme Court for a final decision on the patent eligibility question. *Id.* at 306–07.
[133] *Id.* at 307. The Court noted that "[t]he authority of Congress is exercised in the hope that '[t]he productive effort thereby fostered will have a positive effect on society through the introduction of new products and processes of manufacture into the economy, and the emanations by way of increased

101 and its enumerated categories, concluding that the statute intended to cover expansive ground by "includ[ing] anything under the sun that is made by man."[134] But it does not embrace every discovery, excluding "[t]he laws of nature, physical phenomena, and abstract ideas."[135] Based on this restatement of by-then almost 130 years of doctrine, the Court held the microorganism patent eligible; it was a "nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use.'"[136]

The Court did not alter its classic model of Section 101 in light of the "gruesome parade of horribles" offered by the USPTO and amici.[137] The Court firmly stated that a determination of patent eligibility "[would] not deter the scientific mind from probing into the unknown any more than Canute could command the tides."[138] The Court invited gene patent critics to bring their complaints to the executive or legislative branches, and insisted that the language of Section 101 "fairly embraces [Chakrabarty's] invention."[139]

The *Chakrabarty* case was contentious, but the Court avoided some of the ethical and moral questions raised by kicking them over to Congress or the executive branch. It embraced a clear vision of patent eligibility for all things made by man and distinctive from naturally occurring things.[140] That vision signaled to biotechnology companies that their research endeavors—including genetically modified products and maybe products isolated or purified from naturally occurring states—would not be categorically excluded from patenting.[141] As one newspaper reported, "The decision opened a floodgate."[142] Biotechnology companies filed patent applications at a record pace.[143]

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employment and better lives for our citizens.'" *Id.* (quoting Kewanee Oil Co. v. Bicron Corp., 416 U.S. 470, 480 (1974)).

[134] *Id.* at 309 (quoting S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952); H.R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952)).

[135] *Id.*

[136] *Id.* at 309–10 (quoting Hartranft v. Wiegmann, 121 U.S. 609, 615 (1887)). The Court also rejected the USPTO's argument that microorganisms cannot be patentable until Congress declares them so. In doing so, the Court noted, "[t]he subject-matter provisions of the patent law have been cast in broad terms to fulfill the constitutional and statutory goal of promoting 'the Progress of Science and the useful Arts' with all that means for the social and economic benefits envisioned by Jefferson. Broad general language is not necessarily ambiguous when congressional objectives require broad terms." *Id.* at 315.

[137] *Id.* at 316.

[138] *Id.* at 317 ("Whether respondent's claims are patentable may determine whether research efforts are accelerated by the hope of reward or slowed by want of incentives, but that is all.").

[139] *Id.* at 318.

[140] *Id.* at 317–318. The decision was decided by a 5-4 vote, and Justice Brennan wrote a dissent arguing that the Patent Plant Act precluded patenting. *Id.* at 318–19 (Brennan, J., dissenting).

[141] *See* Thomas A. Hemphill, *The Biotechnology Sector and US Gene Patents: Legal Challenges to Intellectual Property Rights and the Impact on Basic Research and Development*, 39 SCI. & PUB. POLICY 815, 816 (2012). This signal to investors came along at exactly the right time and in exactly the right place, following the emergence of the biotechnology industry in the United States in the late 1970s with recombinant human insulin, developed by Genentech, Inc. and Eli Lilly & Co. *See id.*

[142] Julia Fortier, *Biotechnology Faces a Fight Over Patents*, BOSTON GLOBE, Aug. 13, 1985, at 25.

[143] *Id.*

The *Chakrabarty* vision embraced by biotechnology companies underscored the role of human intervention in patent eligibility,[144] but it did not say anything about the eligibility of isolated genomic sequences.[145] Companies isolating them filed patent applications, and the USPTO had to make its own post-*Chakrabarty* determination. Based upon its own finding that these gene sequences were compositions of matter isolated by man and markedly different from what is found in nature, it granted the first patent claiming a new and useful isolated gene sequence in 1982 and thousands followed.[146] In 1995 and again in 2001, the USPTO reconsidered its policy granting claims to isolated genomic sequences but affirmed eligibility (although it did provide guidelines for other patentability requirements, like utility). [147]

By this time, the Federal Circuit had come into existence, charged with injecting patent law with consistency and uniformity across the country.[148] The Federal Circuit agreed with the USPTO's policy, recognized isolated gene sequences as patent eligible compositions of matter, but grappled with how other patentability requirements applied to nucleotide sequences. For example, the court considered whether an applicant met 35 U.S.C. § 112's enablement requirement in *Amgen, Inc. v. Chumai Pharmaceutical Co.*, where the patent claimed, "[A]ll possible DNA sequences that . . . encode any polypeptide having an amino acid sequence 'sufficiently duplicative' of [erythropoietin] to possess the property of increasing the production of red blood cells."[149] Without questioning eligibility, the Federal Circuit held that the patent's disclosure failed to enable such a broad array of sequences without undue experimentation.[150] Likewise, Section 101's utility requirement presented another problem for some gene patents. As sequencing grew easier and easier, researchers located more and more sequences they hoped to correlate to diseases, but that were not yet connected with any use other than as research intermediaries.[151] As researchers filed patent applications on these gene

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[144] Christopher M. Holman, *Gene Patents under Fire: Weighing the Costs and Benefits*, *in* BIOTECHNOLOGY AND SOFTWARE PATENT LAW: A COMPARATIVE REVIEW ON NEW DEVELOPMENTS 260 (Emanuela Arezzo & Gustavo Ghidini eds., 2011).

[145] Rebecca S. Eisenberg, *Proprietary Rights and Norms of Science in Biotechnology Research*, 97 YALE L. J. 177, 189 (1987).

[146] U.S. Patent No. 4,363,877 (filed Apr. 19, 1978) "was the first 'gene' patent, claiming genes per se." Andrew W. Torrance, *Gene Concepts, Gene Talk, and Gene Patents*, 11 MINN. J.L. SCI. & TECH. 157, 177 (2010).

[147] Notice of Hearings and Request for Comments on Issues Relating to Patent Protection for Nucleic Acid Sequences, 60 Fed. Reg. 57,223 (Nov. 14, 1995).

[148] Lighting Ballast Control L.L.C. v. Philips Elec. N. Am. Corp., 744 F.3d 1272, 1282 (Fed. Cir. 2014).

[149] Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1212 (Fed. Cir. 1991).

[150] *Id.* at 1214; *see also In re* Kubin, 561 F.3d 1351 (Fed. Cir. 2009) (holding claims to certain DNA molecules obvious).

[151] Rebecca S. Eisenberg, *Why the Gene Patenting Controversy Persists*, 77 ACADEMIC MED. 1381, 1383 (2002) [hereinafter Eisenberg, *Gene Patenting Controversy*]. Eisenberg describes the NIH's filing of patent applications on the first express sequence tags (ESTs) as "sett[ing] off alarm bells in the scientific community, although research scientists had previously expressed little concern about the patenting of genes encoding therapeutic proteins," like the BRCA genes. *Id.* As Eisenberg notes, the applications filed on ESTs "coincided with a broader trend in the biomedical research community to claim intellectual property rights in research tools, and to assert these rights against academic researchers." *Id.; see also* Rebecca S. Eisenberg, *Intellectual Property at the Public-Private Divide: The Case of Large Scale cDNA Sequencing*, 3 U. CHI. L. SCH. ROUNDTABLE 557 (1996) (examining ESTs as representative of the

fragments, the USPTO clarified its position that such sequences were patent eligible only if they demonstrated "specific, substantial, and credible" utility, such as diagnosing or treating a particular disease.[152]

Litigants in these cases did not seem to doubt the eligibility of gene sequences under Section 101—no case arrived at the Federal Circuit to consider the eligibility of isolated gene sequences. In fact, most commentators took as a given that gene patents like the ones at issue in *Myriad* were eligible for patenting. An op-ed in *Nature*, the prestigious scientific journal, declared with respect to gene patenting, "Under present law, there is no reason why that should not be done. The question that arises is whether the law is sound."[153] One article declared, "It is undisputed that DNA (including genes, gene fragments, and their corresponding products) can be patented."[154] Yet another sounded regretful, stating, "It is too late to prevent patents on individual genes."[155]

Given law, custom, and history, it makes sense that the ACLU would have been pessimistic about its case against Myriad's BRCA patents. Nevertheless, the ACLU's plaintiffs moved the court for a judgment of invalidity on eligibility grounds.[156] The plaintiffs argued that Section 101 implicitly excluded isolated gene sequences and cDNA because they function identically to the genes found in the body (i.e., they encode the same instructions for making the same proteins).[157] Of course, Myriad argued the opposite, focusing on the expansive nature of Section 101, stating, "[I]t is well-settled that isolated or purified products, even if they originated in nature prior to being isolated or purified, are patent eligible under Section 101."[158] The isolation or purification of the claimed molecules, Myriad argued, created a physically different molecule compared to its native counterpart, and could function as "physical probes [and] primers to identify mutations and diagnose cancer susceptibility in a patient."[159]

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increasing difficulty drawing a line between public research typically given to the public domain and private research typically appropriated as intellectual property).

[152] Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001). The USPTO addressed public comments about gene patent eligibility: "If a patent application discloses only nucleic acid molecular structure for a newly discovered gene, and no utility for the claimed isolated gene, the claimed invention is not patentable. But when the inventor also discloses how to use the purified gene isolated from its natural state, the application satisfies the 'utility' requirement. That is, where the application discloses a specific, substantial, and credible utility for the claimed isolated and purified gene, the isolated and purified gene composition may be patentable." *Id.* In *In Re* Fisher, the Federal Circuit invalidated claims to ESTs because there was no evidence that the claimed genomic sequences were tied to any specific function. *In re* Fisher, 421 F.3d 1365, 1372–74 (Fed. Cir. 2005).

[153] Opinion, *Genes and Patent Laws*, 371 NATURE 270 (1994).

[154] Melissa A. Horn, Note, *DNA Patenting and Access to Healthcare: Achieving the Balance Among Competing Interests*, 50 CLEV. ST. L. REV. 253, 255 (2002).

[155] Jack Wilson, *No Patents for Semantic Information*, 2 AM. J. BIOETHICS 15, 15 (2002).

[156] Plaintiffs' Memorandum of Law in Support of Motion for Summary Judgment at 34, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09-4515).

[157] *Id.*

[158] Myriad Defendants' Memorandum of Law (1) in Support of Their Motion for Summary Judgment and (2) in Opposition to Plaintiffs' Motion for Summary Judgment at 22, *Ass'n for Molecular Pathology*, 702 F. Supp. 2d 181 (No. 09-4515). Indeed, Myriad argued that the exception itself was directed to physical and natural phenomenon, not natural products. *Id.*

[159] *Id.* at 32.

In a nutshell, the *Myriad* dispute centered on whether isolated gene sequences, including cDNA sequences, fell inside or outside the closed set of patent eligible subject matter. Both sides cited *Chakrabarty* and older cases to support their positions. Was an isolated gene sequence a new chemical composition "markedly different" from its naturally occurring counterpart or was it a product of nature? To underscore its position, Myriad emphasized the long-standing USPTO policy to grant patents with these claims as significant to the patent eligibility question.[160] Neither party advocated for a change in the doctrine, but that the isolated gene sequences should be characterized in a specific way to support or deny eligibility.

The Southern District of New Yorks's Judge Sweet framed the *Myriad* inquiry as whether "claims directed to isolated DNA containing naturally-occurring sequences fall within the products of nature exception to [Section] 101."[161] To answer this question, he used the "markedly different" doctrine from earlier cases, including *Chakrabarty*, and held that all of the claims were patent ineligible because genetic sequences of all stripes are not "markedly different" from their native DNA sequences.[162] In other words, the sequences described in the claims could (and did) occur in nature—even if the molecules were structurally different, they were informationally similar enough to be considered naturally occurring.[163]

The breadth of the district court's opinion surprised even patent law experts.[164] (Even the *New York Times* reported, "The decision invalidating the gene patents stunned many lawyers who follow such issues."[165]) Of course, Myriad appealed to the Federal Circuit, which reversed the trial court's decision as to the composition of matter claims.[166] The majority opinion, written by Judge Lourie, held that both isolated and cDNA gene sequences were patent eligible under Section 101, a more predictable outcome in light of *Chakrabarty*.[167] Tellingly, however, the panel members were divided as to both outcome and reasoning.[168] The central dispute among them was whether the act of isolating a gene sequence (separating a specific sequence of nucleotides from the rest of the chromosome) rendered it sufficiently different from the naturally occurring gene that the inventor deserved a patent on the gene sequence itself? Judge Lourie believed

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[160] *See id.* at 26–30. Myriad also stressed the importance of not retrospectively invalidating almost 3,000 patents with a judicial ruling when Congress could enact prospective legislation prohibiting these types of patent claims. *Id.* at 29, n.11. Myriad suggested that Congress could enact legislation to prohibit patenting of isolated gene sequences if it wanted to do. *See id.* at 28–29.

[161] Ass'n for Molecular Pathology, 702 F. Supp. 2d at 220.

[162] *Id.* at 229–32.

[163] *Id.* The court invalidated the method claims because a comparison step—comparing a patient's DNA sequence to a known database of mutations—without any other inventive step or transformation, is simply an abstract idea, not patentable. *Id.* at 236; *see* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1298 (2012).

[164] *See* Andrew Pollack, *After Patent on Genes is Rejected, Taking Stock*, N.Y. TIMES, March 31, 2010, at B1; *see also* Timothy Caulfield, *Reflections on the Gene Patent War: The Myriad Battle, Sputnik and Beyond*, 57 CLINICAL CHEM. 977 (2011). One scholar remarked, "'there isn't a whole lot of doctrinal support' for considering DNA as information rather than as a chemical." Pollack, supra, at B2.

[165] Pollack, *supra* note 160, at B2.

[166] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 1333 (Fed. Cir. 2012).

[167] *See id.* at 1333–35.

[168] *See id.* at 1337–48 (Moore, J., concurring in part); *id.* at 1348–58 (Bryson, J., concurring in part and dissenting in part).

that isolation created new molecules that are non-naturally occurring and patent eligible under *Chakrabarty*'s "anything under the sun made by man" precedent.[169] Judge Moore, concurring in part, agreed about eligibility, but couldn't agree that isolation, alone, sufficed to find the claims patent eligible.[170] Instead, she deferred to the USPTO's decades-old practice of granting gene patents because the reliance interests of gene patent holders advised maintaining eligibility over these claims.[171] Judge Bryson, dissenting, concluded that isolated gene sequences are not patent eligible.[172] Like Judge Sweet in the lower court, Bryson would have held that the breaking of chemical bonds to create a different structure was not dispositive given that the information—the real value of the genes—did not change.[173] All three judges held the patent claims relating to cDNA sequences patent eligible because, in their view, they fit the *Chakrabarty* model awarding patents to man-made inventions. When making cDNA, a person creates a sequence of nucleotides by identifying the native mRNA and reverse transcribing it back into a cDNA sequence lacking the introns originally present in the gene in question.[174]

Unlike the startling district court opinion, the Federal Circuit's opinion drew more tempered reactions.[175] Despite disagreement among the panel members, their quarrel remained rooted in the traditional version of the patent eligibility model used by the district court, by the USPTO, and by courts in cases like *Chakrabarty* and *Funk Brothers*. The only difference between the invalidation of all of the claims (Judge Sweet in the district court), invalidation of only the isolated gene sequence claims (Judge Bryson in dissent in the Federal Circuit), and eligibility of all of the composition of matter claims (Judges Lourie and Moore in the Federal Circuit) was how each decision-maker characterized the nature of the sequences. Gene sequences represent information—instructions for building proteins within the cell—but at the same time they are chemical compositions—molecules featuring specific structures and functions. If the gene is characterized as a chemical composition, the *Chakrabarty* doctrine predicts eligibility because the act of isolation creates a new molecule. If the gene sequence is characterized as mere information, the *Chakrabarty* doctrine predicts ineligibility because the information is identical to that found in the *in vivo* gene sequence. In the *Myriad* district court and appellate decisions, the judges took care to parse *Chakrabarty* and its predecessors to come to a decision after making a characterization, without amending or fine-tuning the doctrine at all.

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[169] All also agreed that the diagnostic methods were invalid under Prometheus, and that the therapeutic screening methods were valid despite Prometheus. *Id.* at 1337 (Moore, J., concurring in part).

[170] *Id.* at 1339 ("I see no reason to deviate from this long-standing flexible approach in this case.").

[171] *Id.* at 1347 ("This long-term policy of protecting isolated DNA molecules has resulted in an explosion of innovation in the biotechnology industry, an industry, which unlike the financial services industry or even the software industry, depends on patents to survive. Holding isolated DNA not patentable would destroy long settled industry expectations for no reason other than a gut feeling that DNA is too close to nature to be patentable, an arbitrary decision based on a judge-made exception."). Judge Moore also said that she might conclude differently if she were deciding the case on a blank slate. *Id.* at 1343.

[172] *Id.* at 1349 (Bryson, J., dissenting).

[173] *Id.* at 1353.

[174] *Id.* at 1356. Judge Bryson explained, "The cDNA cannot be isolated from nature, but instead must be created in the laboratory. The end product is a human-made invention with distinct structure because the introns that are found in the native gene are removed from the cDNA segment." *Id.*

[175] *See* Gipson, *supra* note 87, at 826 (describing the Federal Circuit opinion as "nothing new in the realm of patentable subject matter").

Given the high stakes, Myriad appealed the case to the Supreme Court, and the public renewed its interest in the gene patenting debate.[176] During oral arguments, the Justices actively asked questions and created humorous hypotheticals to help sort out its characterization of isolated gene sequences.[177] The incentive arguments made on behalf of Myriad and other patent owners were not lost amid the moral arguments. This Court, in particular, seemed sensitive to the need for exclusive rights in burgeoning technologies, like biotech, in order to invent and commercialize where otherwise cost would be prohibitive.[178]

The Court's 9–0 opinion held that separating the gene from its surrounding genetic material did not constitute an act of invention and that isolated gene sequences were products of nature not eligible for patenting.[179] The act of isolation might sever some covalent bonds to produce a different molecule, but a different structure proved irrelevant because the claims themselves were not drawn to a specific molecular structure, but to the genetic information itself.[180] As understood by Judges Sweet and Bryson, characterizing the gene sequences as information rather than molecules predicted invalidation under *Chakrabarty*. The Court further explained that cDNA doesn't necessarily suffer from the same patent eligibility problems as the isolated DNA sequences.[181] In fact, according to the Court, a lab technician who creates cDNA in a laboratory using reverse transcription unquestionably creates something new through her handiwork.[182]

The opinion from the Court spends a lot of time explaining the science (or attempting to), but the legal part is short and to the point. Isolated DNA is out of Section 101's bounds, but cDNA is in-bounds.[183] Justice Thofamas cites *Chakrabarty* and *Funk Brothers* and understates the ineligibility of isolated gene sequences to the public as a foregone conclusion. Even its treatment of cDNA, which turned on the lab technician's role, looks too tidy, as if to say: a human alters this thing, so it is patent eligible. Looking more closely at cDNA, it is hard to identify a guiding principle that reconciles patent eligibility for cDNA with ineligibility for isolated gene sequences apart from restatements of the doctrine found in cases like *Chakrabarty* and *Funk Brothers*. In a surprising twist unique to patent law, the doctrine's own stability undermines its predictive value when it comes to new technologies that challenge the old boundaries of what is a product of nature.

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[176] *See* Mears, *supra* note 84.

[177] Transcript of Oral Argument, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013) (No. 12-398). Justice Sotomayor asked whether patenting isolated gene sequences was like patenting the eggs, flour, and other naturally-occurring ingredients of chocolate chip cookies. *Id.* at 35. Justice Roberts, who loves a baseball reference, asked explored whether isolating sequences was akin to carving a baseball bat out of a tree. *Id.* at 41. Justice Alito asked about medicinal plants found in the jungle where simply chewing on leaves had a therapeutic effect. *Id.* at 7–8.

[178] *Id.* at 11.

[179] *Myriad*, 133 S. Ct. at 2111.

[180] *Id.* at 2118.

[181] *Id.* at 2119.

[182] *Id.*

[183] The Court noted in a footnote that some cDNA may be ineligible for patenting when a short fragment or some other psuedogene. *Id.* at 2119, n.8.

B. Standing to Sue

Patent eligible subject matter provided the substantive patent question in *Myriad*, but procedurally the case was a pioneer in a burgeoning field of public interest patent litigation.[184] As with many cases brought to further the public interest rather than private ones, the standing doctrine presented a sizable hurdle for the *Myriad* plaintiffs to overcome to continue to challenge the entrenched law of subject matter eligibility..

Despite a belief that "the odds were long" on a successful challenge to the BRCA patents on patent eligibility grounds,[185] the ACLU's mission to "[ensure] people's rights to bodily integrity, human dignity, and scientific freedom" pushed it to bring the litigation anyway.[186] It didn't have much to lose if it was unsuccessful (after all, the doctrine appeared entrenched), but it had much to gain—it hoped to revive a serious debate about gene patenting and broaden the use of patent law litigation to further the public interest.[187] Recognizing that Section 101 could be "an important lever to help advance the public interest,"[188] the ACLU seized upon the breast cancer movement to start an important conversation about social justice, innovation, scientific advancement, and the public interest in patent law.[189] Of course, patent litigation doesn't lend itself obviously to advancing the public interest because it typically involves two competitors, one typically accused of patent infringement. The Article III standing doctrine and the lack of a statutory right to invalidate patents prevented members of the public from bringing challenges.[190] It was not surprising when Myriad challenged the plaintiffs' standing to bring the suit in the first place.

When a declaratory plaintiff files a patent suit before being sued for infringement, as in *Myriad*, that plaintiff must demonstrate Article III standing to sue the patent owner.[191] The *Myriad* plaintiffs included "an assortment of medical organizations, researchers, genetic counselors, and patients,"[192] all claiming harm from Myriad's use of the patents "to prevent [the] [p]laintiffs from engaging in clinical analysis of the *BRCA1* [and *BRCA2* genes], from informing women about testing options other than by Myriad,

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[184] *See* Megan M. La Belle, *Patent Law as Public Law*, 20 GEO. MASON L. REV. 41, 70 (2012); Amelia Smith Rinehart, *Patent Cases and Public Controversies*, 89 NOTRE DAME L. REV. 361 (2013); Consumer Watchdog v. Wis. Alumni Research Found., 753 F.3d 1258, 1261 (Fed. Cir. 2014).

[185] Park, *supra* note 99, at 524.

[186] *Id.* at 520.

[187] *Id.* at 524–25.

[188] Id. at 527.

[189] *Id*. Maybe this is the most tangible result of *Myriad*: the number of posts about patent law on mainstream public websites like Slate and the Huffington Post. *See*, *e.g.*, Danny Townsend, *Myriad Genetics Can't Patent a Human Gene*, SLATE (Apr. 7, 2010, 11:34 AM), http://www.slate.com/articles/news_and_politics/jurisprudence/2010/04/myriad_genetics_cant_patent_a_human_gene.html; Emily Bazelon, *Are Your Genes Patented?*, SLATE (Apr. 12, 2013, 11:00 AM), http://www.slate.com/articles/news_and_politics/jurisprudence/2013/04/are_your_genes_patented_the_supreme_court_will_decide_if_they_can_be.html; Nancy Stordahl, *BRCA1 and BRCA2 Gene Patent Debate Reaches the Supreme Court: Why Everyone Should Care*, HUFFINGTON POST (Apr. 8, 2013, 1:29 PM), http://www.huffingtonpost.com/nancy-stordahl/brca1-and-brca2-gene-patents_b_3015595.html.

[190] *See* Megan M. La Belle, *Patent Law as Public Law*, 20 GEO. MASON L. REV. 41, 70 (2012); Amelia Smith Rinehart, *Patent Cases and Public Controversies*, 89 NOTRE DAME L. REV. 361 (2013); Consumer Watchdog v. Wis. Alumni Research Found., 753 F.3d 1258, 1261 (Fed. Cir. 2014).

[191] U.S. CONST. art. III; La Belle, *supra* note 190, at 70–71.

[192] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 1309 (Fed. Cir. 2012).

and from obtaining genetic testing or second opinions," so the district court had to consider whether any one of those plaintiffs alleged an adverse interest to Myriad with sufficient immediacy and reality.[193]

To answer the question, Judge Sweet focused on the Federal Circuit's more recent jurisprudence governing whether any party has standing to seek declaratory judgments of patent invalidity—an "all the circumstances" test requiring "some affirmative act by the defendant relating to enforcement of its patent rights," and that the plaintiff has taken some "meaningful preparation to conduct potentially infringing activity."[194] Courts often refused standing to plaintiffs who failed to specify any affirmative acts directed toward them, but Judge Sweet noted that these cases did not "establish a requirement that only acts directed towards the plaintiff could be considered for purposes of the standing analysis . . . ."[195] Myriad's enforcement activity comprised sending cease-and-desist letters and other communications, including licensing offers, to GDL and others shortly after the patent issued.[196] Myriad also filed two suits, which either settled or were dismissed without prejudice.[197] The eleven-year-old letters, standing alone, might not support standing in a declaratory patent case.[198] However, Judge Sweet found that Myriad's conduct led to a general belief that anyone engaging in BRCA diagnostic testing risked being sued by Myriad, which supported standing.[199]

The second part of the Federal Circuit's inquiry focuses on the plaintiffs' conduct and asks whether a court's decision would serve as something more than an advisory opinion.[200] Judge Sweet distinguished the *Myriad* researcher plaintiffs' outfitted laboratories from more speculative plaintiffs—they were "poised to begin BRCA1/2 testing and that the patents-in-suit present the only obstruction to doing so."[201] The non-researcher plaintiffs (patients and members of medical organizations) alleged a risk of

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[193] Ass'n for Molecular Pathology, 669 F. Supp. 2d 365, 386 (S.D.N.Y. 2009).

[194] *Id.* at 384–85, 387. The USPTO, a named defendant, argued that the plaintiffs were third parties without a legal interest of their own in USPTO policies and procedures, that the plaintiffs' injuries weren't traceable to the USPTO because the harms were caused by Myriad's refusal to license the patents freely, and that the plaintiffs' injuries were not redressible by a suit declaring the USPTO policies unconstitutional. *Id.* at 384–85. The court dismissed these arguments because the statutory remedial scheme did not divest the plaintiffs of their ability to assert constitutional claims alleging constitutional harms. *Id.* at 385. The Supreme Court did not take up the question of standing, so the lower court's decision with respect to its subject matter jurisdiction over the claims against the USPTO and the plaintiffs' standing to bring them remains in effect.

[195] *Id.* at 387. In fact, such a requirement, Judge Sweet continued, would be inconsistent with the Supreme Court's *MedImmune* opinion, requiring that "all the circumstances" be considered in these cases. *Id.* at 388.

[196] *Id.* at 378–79.

[197] *Id.* at 379.

[198] *See* Avante Int'l Tech., Inc. v. Hart Intercivic, Inc., No. 08-832, 2009 WL 2431993, at *3 (S.D. Ill. July 31, 2009).

[199] Ass'n for Molecular Pathology, 669 F. Supp. 2d at 390.

[200] *Id.* at 391.

[201] *Id. But cf.* Benitec Austl., Ltd. v. Nucleonics, Inc., 495 F.3d 1340 (Fed. Cir. 2007) (denying jurisdiction to a declaratory plaintiff who practiced the invention within a statutory safe harbor free from infringement but intended to expand its operations to infringing activity in the future); Mega Lift Sys., L.L.C. v. MGM Well Serv., Inc., No. 6:08 CV 420, 2009 WL 1851919 (E.D. Tex. June 29, 2009) (denying jurisdiction to a declaratory plaintiff who intended to produce and offer for sale infringing products because the "complaint [was] silent as to any 'meaningful preparation.'").

committing contributory infringement if the researcher plaintiffs offered infringing diagnostic testing services. Therefore, Judge Sweet found standing on behalf of all of the plaintiffs.[202]

The Federal Circuit agreed in part and affirmed just one plaintiff's standing to sue.[203] Only Dr. Harry Ostrer alleged sufficient affirmative enforcement acts by Myriad (an offer for a collaborative license, plus Myriad's other assertions about which Ostrer was aware) and, of three researchers who could do so, only he alleged an intention to actually and immediately engage in allegedly infringing BRCA-related activities.[204] The others, found to have standing in the district court, did not qualify under a more rigorous examination of the Federal Circuit's test requiring affirmative acts from the patent owner and meaningful preparation by the potential infringer.[205]

Until 2007, the Federal Circuit had an exacting test for standing in declaratory patent cases: a declaratory plaintiff had standing to sue only if she had a reasonable apprehension of an infringement suit from the patent owner.[206] Plaintiffs like the ones in *Myriad* probably could not have brought a declaratory suit with stale cease-and-desist letters and a vague desire to practice the invention but for the patent-in-suit.[207] *MedImmune* abrogated the Federal Circuit's rule in favor of an all-the-circumstances approach, emphasizing the importance of patent challenges as a matter of public policy.[208] Although *MedImmune* embraced a more liberal view of standing in declaratory patent case,[209] typical declaratory plaintiffs include scorned licensing partners, disgruntled licensees, present infringers, or others with more definitive plans for infringement. A member of the public seeking to invalidate a patent does not have standing to sue for invalidity.[210] Up until the *Myriad* suit was filed, anyone without a

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[202] Ass'n for Molecular Pathology, 669 F. Supp. 2d at 392.

[203] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 1308–09 (Fed. Cir. 2012).

[204] *Id.* at 1319.

[205] *Id.* The question of standing was not granted certiorari by the Supreme Court.

[206] *See*, *e.g.*, Gen-Probe Inc. v. Vysis, Inc., 359 F.3d 1376, 1381 (Fed. Cir. 2004). As was the case in *Gen-Probe*, the Federal Circuit's reasonable apprehension of suit test was particularly onerous on a licensee in good standing who could not bring declaratory suits until he terminated or repudiated the license, even if he believed the patent was invalid. This gave rise to the Supreme Court's decision in *MedImmune*. *See* MedImmune, Inc. v. Genentech, Inc., 549 U.S. 118 (2007).

[207] *Compare* Benitec Austl., Ltd. v. Nucleonics, Inc., 495 F.3d 1340, 1346–50 (Fed. Cir. 2007) (declining jurisdiction because the declaratory plaintiff only professed plans to engage in the infringing activity), *with* Cat Tech L.L.C. v. Tubemaster, Inc., 528 F.3d 871, 881 (Fed. Cir. 2008) (affirming jurisdiction because the declaratory plaintiff had taken significant concrete steps to infringe).

[208] *MedImmune*, 549 U.S. at 127; *see* Lear v. Adkins, Inc., 395 U.S. 653, 674 (1969) (stating that "enforcing this contractual provision would undermine the strong federal policy favoring the full and free use of ideas in the public domain"); Bresnick v. U.S. Vitamin Corp., 139 F.2d 239, 242 (2d Cir. 1943) ("We have disposed of the patent as a whole because it has seemed to us proper that it should not remain in the art as a scarecrow."); Rinehart, *supra* note 185, at 363; Megan M. La Belle, *Standing to Sue in the* Myriad Genetics *Case*, 2 CAL. L. REV. CIRCUIT 68, 71 (2011) (arguing that the Federal Circuit's *Myriad* standing decision makes it more difficult for plaintiffs to challenge patents, rather than easier; the goal of the Court in *MedImmune*).

[209] *See Ass'n for Molecular Pathology*, 689 F.3d at 1318 (applying *MedImmune*'s all-the-circumstances test by using the *Lujan* test for constitutional standing).

[210] *Cf.* Consumer Watchdog v. Wis. Alumni Research Found., 753 F.3d 1258 (Fed. Cir. 2014) (denying standing for a taxpayers' group appeal to the Federal Circuit from a USPTO board decision); Organic Seed

reasonable apprehension of suit from Myriad—like most of the researchers, doctors, patients, and genetic counselors who brought suit—did not have standing to invalidate the patent. Myriad had not spent any appreciable time enforcing its patents in over a decade—any potential infringement was too remote and too speculative. Even after *MedImmune*, Judge Sweet's decision to keep the *Myriad* case moving by reframing the lack of recent enforcement by *Myriad* as an ongoing threat hanging over the heads of the plaintiffs (even non-researchers because they risked contributing to others' infringement) arguably went beyond the Federal Circuit's post-*MedImmune* jurisprudence.[211] The Federal Circuit narrowed this holding quite a bit, but both courts found standing in a way that would not have existed prior to 2006. The Federal Circuit's decision that Dr. Ostrer could sue based on his intention to infringe opens the doctrine to more plaintiffs seeking to invalidate patents, but the door is not wide open, as recent Federal Circuit cases suggest.[212]

In addition to pre-*MedImmune* standing doctrine, the inner-workings of the USPTO also served as a procedural roadblock to refinement of the law. When gene patents first began issuing, the USPTO offered only one administrative way to seek cancellation of patent claims: a reexamination.[213] This proceeding allowed for invalidation of claims "on the basis of prior art patents or printed publications," not on patent eligibility grounds.[214] Therefore, for the life of the patents at issue in *Myriad*, litigation was the only way in which a Section 101 eligibility challenge could be made.

Since then, the Leahy-Smith America Invents Act (AIA) added one procedure (post-grant review) and amended an older version of reexamination for third parties (*inter partes* review) to enable patent challenges at the USPTO instead of in federal litigation.[215] Like a reexamination, an *inter partes* review allows a third party to seek cancellation of "[one] or more claims of a patent only on a ground that could be raised under [35 U.S.C. §] 102 (novelty) and [§] 103 (non-obviousness) and only on the basis of prior art consisting of patents or printed publications."[216] A patent eligibility challenge is still impossible using this type of proceeding. In contrast, a post-grant review allows for a wider range of grounds for challenges, including eligibility, but must be brought within the first nine months after the patent issues.[217] Both proceedings subject the filer to estoppel of any claim that was raised or could have been raised in a future civil litigation involving the patent.[218] Importantly, in either proceeding, the USPTO uses its own rules and procedures for assessing the validity of the claims at issue based upon the allegations

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Growers & Trade Ass'n v. Monsanto Co., 718 F.3d 1350 (Fed. Cir. 2013) (denying standing to a group of organic seed growers who desired to not infringe the patent).

[211] In fact, Professor Megan La Belle argues that the Federal Circuit's post-*MedImmune* cases, including *Myriad*, take a formalistic approach in direct contradistinction to the Court's guidance provided by *MedImmune*. *See* La Belle, *supra* note 203, at 71.

[212] *Id*.

[213] 35 U.S.C. § 301 (2012).

[214] 37 C.F.R. § 1.510 (2012).

[215] 35 U.S.C. § 311 (2012) (inter partes review); 35 U.S.C. § 321 (2012) (post-grant review).

[216] 35 U.S.C. § 311(b) (2012). The *inter partes* review replaced *inter partes* reexamination, a similarly limited proceeding with respect to grounds and prior art.

[217] 35 U.S.C. § 321(c) (2012).

[218] *See* 35 U.S.C. § 315(e) (2012) (*inter partes* review); 35 U.S.C. § 325(e) (2012) (post-grant review).

of the third party.[219] A party seeking to challenge the USPTO's policies may appeal an adverse final decision from the Patent Trials and Appeals Board to the Federal Circuit.[220] However, the Federal Circuit recently held that a consumer interest group, like several of the plaintiffs in *Myriad*, did not have the requisite standing to appeal an adverse decision in a reexamination.[221]

Thus, USPTO alternatives may present a compounding problem for folks like the *Myriad* plaintiffs who seek to declare a category of inventions ineligible for patenting despite the USPTO's approval. First, not very many parties will be in a position to appeal the USPTO's improvident *grant* of a patent from an agency proceeding as a matter of bad policy—only those third parties who challenge a patent in a review, lose, then appeal. Then, individual members of public interest groups may have trouble establishing standing to appeal that loss to the Federal Circuit without more than a generalized harm. Even after *Myriad*, standing remains a substantial barrier to bringing challenges to patent policies like the USPTO's interpretation of Section 101.

C. Evidence of Patent Impact

The long delay between the USPTO's initial decision to grant patents claiming isolated genes and their subsequent invalidation in *Myriad*, along with the procedural impediments to challenges, produced both positive and negative consequences among many stakeholders. Myriad successfully utilized a traditional patent and license strategy to develop its diagnostic testing business model within the field of biotechnology, which drew two main criticisms: that gene patents slowed innovation related to hereditary diseases like breast cancer and limited access to diagnostic testing and other healthcare products.[222]

With respect innovation impact, Myriad's opponents alleged that research and development, in particular, academic research, slowed down due to the patent rights granted to a variety of players "upstream within the R&D pipeline."[223] Stakeholders at different levels (clinicians, researchers, patients) worried that gene patents would slow research progress, especially work that might "[identify] weaknesses in Myriad's test or [distinguish] the effects of different mutations in the genes on disease severity or progression." [224] Myriad's initially aggressive enforcement strategy encouraged a heightened rhetoric regarding research. After 1998, Myriad did not pursue researchers using the patented sequences for non-commercial purposes,[225] but its early enforcement likely affected day-to-day practices in clinics and laboratories nationwide.[226] Research,

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[219] 35 U.S.C. § 311 (2012).
[220] 35 U.S.C. § 141(c) (2012).
[221] Consumer Watchdog v. Wis. Alumni Research Found., 753 F.3d 1258, 1263 (Fed. Cir. 2014).
[222] *See* Andrew S. Robertson, *The Role of DNA Patents in Genetic Test Innovation and Access*, 9 NW. J. TECH. & INTELL. PROP. 377, 383 (2011).
[223] *Id.* at 383.
[224] Carbone et al., *supra* note 76, at 785.
[225] So & Joly, *supra* note 72, at 100 ("Myriad . . . claims not to have pursued any researchers other than those from the University of Pennsylvania's Genetic Diagnostic Laboratory, which it believed to be using the test for commercial purposes.")
[226] Carbone et al., *supra* note 76, at 785. To explain its 1998 enforcement strategy against GDL, "Myriad . . . defined the University of Pennsylvania's testing as 'commercial,' as later defined under the terms of a 1999 Memorandum of Understanding with the US National Cancer Institute." *Id.*

university, and private laboratories using the BRCA genes for research did not offer diagnostic testing to patients in the United States and, importantly, refused to reveal relevant results to people participating in BRCA research studies.[227] Myriad also allowed basic research on its patented genes, entered into over 100 scientific collaborations, and contributed data to public databases until at least 2004.[228] Myriad even offered its testing to researchers at a discounted rate.[229]

The impact of gene patents on innovation remains unclear.[230] Researchers studying the impact of gene patents in general reported, "neither anticommons nor restrictions on access . . . seriously [limited] academic research—despite the fact that these researchers operate in a patent-dense environment, without the benefit of a clear research exemption."[231] Patent scholars also conclude there is no evidence to support patent problems as a result of human gene patents.[232] In the area of diagnostic testing, however, Myriad's exclusivity resulted in some empirical evidence supporting concerns about research impact.[233] Another study investigating the disease hemochromatosis and its linked gene HFE, where one patent owner also controlled the diagnostic testing, "demonstrate[d] how a gene patent, when enforced, can serve to stifle or hinder human genetics research."[234] Others reported that, especially within the diagnostic testing markets, "university researchers [became] more secretive and less willing to share research results or materials."[235]

When it comes the impact of gene patents on clinical availability, evidence is more conclusive.[236] Myriad, by enforcing its patents, could prevent second opinion testing and obstruct access to other types of testing that might be utilized by patients or their care providers.[237] For example, Genae Girard, one of the *Myriad* plaintiffs, did not receive a desired second opinion after testing positive for a deleterious mutation within her BRCA2 gene because Myriad was the only laboratory in the country that could provide full sequencing of BRCA2.[238] Myriad explains that second opinion testing does

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[227] The Federal Circuit certainly perceived a chilling effect even from the decade-old letters sent to GDL and others. Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 1321–22 (Fed. Cir. 2012). *See also* Carbone et al., *supra* note 76, at 785–86. "[A]s a result of Myriad's enforcement actions coupled with broad patent claims, its fairly narrow conception of what constituted acceptable research and its failure to clearly state that it would not pursue those conducting such research, university and private laboratories ceased to offer the test publicly in the United States." *Id.*

[228] So & Joly, *supra* note 74, at 100, 104. Myriad's president, Greg Critchfield, identified 7,000 scientific papers that mention the BRCA genes. Critchfield Declaration, *supra* note 67, at 30.

[229] Tom Reynolds, *NCI-Myriad Agreement Offers BRCA Testing at Reduced Cost*, 92 J. NAT'L CANCER INST. 596, 596 (2000).

[230] Caulfield, *supra* note 160, at 978 (describing innovation impact as "a complex and rather muddled picture.")

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

[232] Christopher Holman, The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation, 76 UMKC L. REV. 295, 305–06 (2007).

[233] *Id.* at 299–300.

[234] Robertson, *supra* note 217, at 384.

[235] Caulfield et al., *supra* note 226, at 1092.

[236] Robertson, *supra* note 231, at 385–86.

[237] *Id.* at 386.

[238] Complaint, *supra* note 7, at 11.

and can occur at its facilities and as verification from other facilities.[239] Yet there is still limited access to alternative testing techniques. The technology that Myriad uses may not detect some mutations, possibly up to twelve percent of large genomic deletions or duplications due to a flaw in the testing strategy, yet one more extensive alternative, known multiplex ligation-dependent probe amplification, is not routinely offered to patients.[240]

Price is another sensitive issue with gene patent critics and patients. Less evidence exists to demonstrate that gene patents inflate the cost of testing. One extensive study comparing Myriad's diagnostic testing for BRCA genes with colon cancer genes, where it faces some competition, reported that BRCA testing by Myriad, despite the lack of competition in the United States, was cheaper than its colon cancer testing.[241] By directing all of the BRCA diagnostic testing into its own laboratory, Myriad may have reduced the deadweight loss of its own monopoly by pricing effectively to match demand as well as third party payers.[243]

Myriad's role as the single BRCA diagnostic testing provider created another unique consequence—its tests became the de facto clinical standard of care for patient care providers.[244] Myriad describes its own BRAC*Analysis*® test as "the standard of care in identification of individuals with hereditary breast and ovarian cancer."[245] This test utilizes full sequencing, which as noted earlier, may miss some large rearrangements or deletions, an observation confirmed in several studies.[246] In response, Myriad developed BART® to identify some of these missed rearrangements or deletions when a patient tests negative using BRACAnalysis®.[247] However, Myriad limits the availability of the BART® test to a small fraction of the patients seeking BRCA testing as a concurrent test at no additional cost.[248] Others may buy BART® for an additional fee of $650.[249] By controlling the market for genetic testing services, Myriad controls the types of tests ordered by doctors for their patients, dictates the specific method of testing for all BRCA testing, and limits the extent to which a patient can develop a comprehensive genetic profile.[250] Professor Eileen Kane describes this as a public health issue, with which patent law is "not formally burdened."[251] Notably, patent law allows for third party policing of

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[239] Myriad Genetics, Inc., Written Comments on Genetic Diagnostic Testing Study 8–9 (2012).

[240] 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–S16, S29 (2010).

[241] *See id.* at S23–24. "[C]ompetition does little to affect price overall." Robertson, *supra* note 222, at 387.

[243] *Id.* at 388.

[244] Eileen M. Kane, *Patent-Mediated Standards in Genetic Testing*, 2008 UTAH L. REV. 835, 852 (2008). "[Myriad used its patent rights] to set a de facto clinical standard by controlling the repertoire of available testing options and limiting compensating alternatives to the dominant models." *Id.* (citing Jon F. Merz, *Disease Gene Patents: Overcoming Unethical Constraints on Clinical Laboratory Medicine*, 45 CLINICAL CHEMISTRY 324, 326 (1999)).

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[246] Declaration of Elizabeth Swisher, M.D., at 9, n.2, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2009) (No. 09-4515) (describing several noteworthy studies).

[247] *Id.* at 9.

[248] *Id.* at 10.

[249] *Id.*

[250] *See id.* at 10–12.

[251] Kane, *supra* note 239, at 852.

patent invalidity.[252] Patent law does not effectively police patent owner conduct except in the extreme cases of antitrust liability.[253]

The related claims of reduced innovation due to patent enforcement, lack of access for patients to genetic testing, increased prices for tests using patented genes like BRCA, and de facto standard setting that limits the types of tests that may be ordered for patients make for a compelling story against patenting especially in the case of Myriad. However, once the USPTO grants a patent, patent law is indifferent to the effect of any reduction on competition. Indeed, patent law presumes that any negative externalities resulting from reduced competition are outweighed in all cases by the positive consequences resulting from the incentives to innovate provided by the patent to inventors. *Myriad* is a relic from an older time, when a successful diagnostic company could revolve around one or a few genes.[254] Multiplex tests, which look for many genes and proteins, and whole genome sequencing, which is becoming cheaper and cheaper, are the new realities for diagnostic companies.[255] Post-*Myriad*, gene patents on isolated sequences are invalid. New diagnostic companies escape the heavy royalty burden that existed and should be able to offer tests that provide a wide range of sequencing for patients.[256] Yet, Myriad and other companies continue to enforce their remaining patent claims against competitors, so the picture is not as rosy as initially believed until these claims are sorted out.[257]

The *Myriad* story is not yet finished. Follow-on patent infringement litigation—suits filed by Myriad Genetics immediately after the decision from the Supreme Court and suits filed by hopeful competitors against them seeking declaratory relief—has been consolidated into a multi-district litigation based in the District of Utah.[258] In a recent decision denying Myriad preliminary injunctive relief, Judge Shelby stated, "the public's

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[252] Invalidation can occur through the courts or with an *inter partes* or post-grant review procedure at the USPTO. *See supra* pp. 23–24.

[253] The plaintiffs in *Myriad* did not raise any antitrust claims. However, Ambry Genetics did make additional antitrust claims in its current litigation (now consolidated into *In Re BRCA*). Ambry claimed that Myriad brought its July 2013 lawsuit against Ambry in bad faith because Myriad believed that its remaining patent claims were invalid after *Myriad*. Judge Robert Shelby dismissed Ambry's counterclaims in June 2014, agreeing with Myriad that its litigation was not a sham one because Myriad's patent claims were obtained without inequitable conduct and because *Myriad* left open the possibility that Myriad's remaining claims were valid as directed to more inventive concepts than isolated DNA sequences or diagnostic methods invalid after *Mayo*. *See* Order Granting Plaintiffs' Motion to Dismiss Ambry's Antitrust Counterclaims, Univ. of Utah Research Found. v. Ambry Genetics, Inc., No. 2:13-00640 (D. Utah June 6, 2014), ECF No. 194; Transcript of Motion Hearing June 6, 2014 at 21–46, 59–60, *Univ. of Utah Research Found.*, No 2:13-00640, ECF No. 197.

[254] *See* Sam Kean, *The Human Genome (Patent) Project*, 331 SCI. 530, 530 (2011). *See also* CITE.

[255] *Id.*

[256] *Id.*

[257] *See, e.g.*, *In Re* BRCA1 and BRCA2-Based Hereditary Cancer Test Patent Litig., MDL Case No. 2:14-MD-2510 (D. Utah July 7, 2014). Of course, pushing up against Myriad's enforcement strategy with respect to its remaining claims is Mayo Collaborative Serv. v. Prometheus Lab., Inc., 132 S. Ct. 1289 (2012), which effectively eliminates many of the method claims being used by Myriad and other diagnostic companies to keep competitors at bay.

[258] *In Re* BRCA1 and BRCA2-Based Breast Cancer Test Patent Litig., MDL No. 2:14-2510 (D. Utah July 7, 2014). For a discussion of Myriad's current litigation in a bigger context of its post-patent-expiration legal and business strategies, see John M. Conley et al., *Myriad after Myriad: The Proprietary Data Dilemma*, 15 N.C. J. L. & TECH. 597 (2014).

interest in preserving patent rights will not always trump other considerations, especially when public health issues are at stake."[259]

As with the gene code itself, the impact of gene patents in the marketplace and the public may be too complex to understand without more rigorous empirical work. In the *Myriad* case, despite equivocality of evidence, the potential harms stemming from patent owner conduct (such as exclusive licensing and excess prices) remained salient to researchers, clinicians, and patient groups from patenting onward. Yet, due to the USPTO's early choice to patent isolated sequence claims and subsequent *sub silentio* acceptance by courts, these potential harms were relegated to a sideshow where scientists pushed for policy without capturing the attention of lawmakers in any meaningful way.[261]

Even after *Myriad*, important issues remain for companies that own patents on other biotechnology inventions now in a state of flux. For example, patents claiming human stem cells have been challenged at the USPTO through a reexamination, but the group asserting invalidity could not establish standing to appeal the final decision,[262] nor presumably to bring a declaratory judgment action the way that the ACLU did in *Myriad*. As these new cases arise, it would be wise to consider that patent law need not remain stagnant as the technological frontier moves forward. Part III addresses the meaning of *Myriad* through this lens.

III. FROM *MYRIAD* ONWARD

The *Myriad* case continues to draw attention because it is not just about simply parsing the patent eligibility doctrine within a lawsuit. Rather, the case demonstrates how patent law principles in operation create tangible and long-lasting impacts when the stability of the law pushes against the progress of technology. From the very beginning, Myriad was a lightning rod amidst the growing controversy over patenting genes and biotechnology in general.[264] As research progressed in this area, the safety concerns highlighted in *Chakrabarty* gave way to abstract concerns about the commercialization of genes in general.[267] Myriad was a single patent owner among thousands who received patents claiming significant gene sequences, yet its monopoly over breast cancer diagnostic testing placed the company within the sights of two public interest groups—

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[259] *In Re* BRCA1 and BRCA2-Based Breast Cancer Test Patent Litig., 3 F. Supp. 3d 1213, 1257 (D. Utah 2014). *See* Karuna Jaggar, *Breast Cancer Genes and Patient Protection in an Era of Personalized Medicine*, HUFFINGTON POST (Mar. 20, 2014, 11:56 AM EDT), http://www.huffingtonpost.com/karuna-jaggar/breast-cancer-genetic-testing_b_4995183.html.

[261] *See* Kane, *supra* note 244, at 853 (describing efforts to establish a research exemption for the use of diagnostic gene patents).

[262] *See* Consumer Watchdog v. Wis. Alumni Research Found., 753 F.3d 1258 (2014).

[264] See, e.g., Tamar Lewin, *Move To Patent Cancer Gene Is Called Obstacle to Research*, N.Y. TIMES, May 21, 1996, at A14.

[267] The Court in *Chakrabarty* referenced "a gruesome parade of horribles" presented by the amicus briefs—the concerns "that genetic research may pose a serious threat to the human race, . . . [that it] may spread pollution and disease, that it may result in a loss of genetic diversity, and that its practice may tend to depreciate the value of human life." Diamond v. Chakrabarty, 447 U.S. 303, 316 (1980). The Court goes on to quote Hamlet, "It is sometimes better 'to bear those ills we have than fly to others that we know not of.'" *Id.* The Court brushed aside these fears as non-patent, "high policy" matters best left to Congress, but activists continued to push for a ban on gene patents altogether. *See, e.g.*, Malcolm Gladwell, *Rights to Life: Are Scientists Wrong to Patent Genes?*, THE NEW YORKER, Nov. 13, 1995, at 120 (reviewing two books on gene patenting and approving generally of *Chakrabarty* and the patenting of BRCA genes).

those who advocated against gene patenting and those who advocated on behalf of women's health.[269] This convergence of two impassioned causes arguably provided the impetus for the *Myriad* litigation to resolve important legal questions about whether and to what extent genomic sequences (and perhaps other biotechnologies) are patent eligible. Part III explores the meaning of *Myriad* with this backdrop and offers some suggestions for mitigating the mistake of promoting stability over legal growth.

Myriad went to a great deal of expense to discover a product that straddled the boundary of Section 101 by being both created by man and found in nature. Before this discovery, the USPTO declared that it would treat products like this as patent eligible based upon analogies to related technologies. Myriad applied for and obtained patents over its discovery, presumably incentivized to make this and other discoveries by the ability to obtain them. Once they issued, Myriad prevented competitors from using the genes commercially, which created a profitable (and completely legal) monopoly for Myriad.[270] Although the patents are now mostly invalidated, Myriad should lead the market in question for some time to come because of the long time between obtaining patent protection and the litigation (which enabled Myriad to assume a dominant market position) and because diagnostic testing necessarily involves information transfer from patients (which enabled Myriad to assemble a large amount of proprietary information).

As a patent law story alone, *Myriad* is not remarkable. In addition to providing private value to Myriad, the patenting of the BRCA1 and BRCA2 sequences generated both positive and negative externalities on third parties, as often happens with patenting in general. And as often happens with patenting in general, these externalities compounded over the patent term. The Supreme Court later invalidated the patent claims that were most valuable to Myriad, but not for almost twenty years from the earliest filing dates (a length of time roughly equal to the patent term itself).[271] The patent eligibility model of *Chakrabarty* initially predicted an outcome of patent eligibility for isolated sequences, and the USPTO utilized that prediction to develop examination guidelines and policies within the agency.[272] That initial prediction, it turned out, was incorrect—upon close scrutiny by the *Myriad* Court, the isolated sequences are not patent eligible after all.[273] The same rules are in place (the 150 year old model of *O'Reilly* and *Le Roy*, carried forward in *Chakrabarty* and *Myriad*), except isolated gene sequences are better characterized as naturally-occurring information instead of man-made molecules—a change that reflects the dynamic nature of knowledge, science, and technology,[274] not a

[269] For a study of how activists over come barriers to break into technology policymaking that features both gene patent critics and breast cancer advocates, see Parthasarathy, *supra* note 97.

[270] *See* Conley, *supra* note 258, at 612 (describing how Myriad derived an extensive proprietary database of patient information from its long-term monopoly involving over one million patients).

[271] 35 U.S.C. § 154(a)(2) (2012).

[272] *See* Utility Examination Guidelines, *supra* note 148. The USPTO issued new examination guidelines to reflect recent caselaw, including *Myriad*. U.S. PATENT & TRADEMARK OFFICE, Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature, Natural Phenomena, & Natural Products (2014), *available at* http://www.uspto.gov/patents/law/exam/myriad-mayo-guidance.pdf.

[273] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2120 (2013).

[274] Professors Helen Berman and Rochelle Dreyfuss persuasively suggest that *Chakrabarty*'s eligibility doctrine must make a more realistic appraisal of underlying science to support patents further downstream and at the same time preserve incentives to drug developers. *See* Helen M. Berman & Rochelle C.

more enlightened or robust version of patent law eligibility. In this simple version of *Myriad*, patent law works for its intended purpose—it incentivized Myriad (and many others) to invest significantly in research and development in reliance on the potential for obtaining patent rights over the discoveries.[276]

But *Myriad* is not just a simple patent law story A growing cadre of detractors kept Myriad and other diagnostic testing companies under fire after the patents issued.[277] Gene patent critics maintained the ethical controversy surrounding privatization of genes.[278] Physicians worried that Myriad's monopoly interfered with healthcare decisions made by and on behalf of patients.[279] Concerns applicable to any patented good or service—restrictions on access, supracompetitive prices, and reduced innovation—looked more problematic when applied to Myriad. Opponents claimed that gene patents allowed Myriad to restrict patient access to necessary medical care and to maintain a supracompetitive price for its diagnostic tests,[280] that consumers were limited to only the tests provided by Myriad even though alternative tests and providers might be available, and that consolidating testing to one or a few laboratories could slow progress being made to understand the disease itself.[281] Myriad countered these concerns by arguing that gene patents did not slow innovation, that start-up companies like Myriad relied on patent incentives to disclose their inventions and to commercialize them based upon the ability to exclude others from practicing their claimed inventions, and that its "single-source model" had "faster turnaround times for results . . . a significantly lower rate of uncertain test results in the U.S.,"[282] and pricing consistent with a competitive market.[283]

A polarized debate is nothing new when it comes to patent law—factions have long argued over whether broad rights are required to provide enough incentive to innovate or whether narrower rights are preferred to encourage follow-on improvements.[284] Patents carry exclusive rights that can be very valuable to their owners. However, despite a presumption of validity, patents can be (and often are) challenged

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Dreyfuss, *Reflections on the Science and Law of Structural Biology, Genomics, and Drug Development*, 53 UCLA L. REV. 871 (2006).

[276] Eisenberg, *Gene Patenting Controversy*, *supra* note 147, at 1383.

[277] Two other diagnostic companies have been singled out as contributing to the reduced innovation and access concerns raised by gene patents. Athena Diagnostics, Inc., by virtue of large numbers of exclusively licensed patents, became "the sole provider of genetic testing for many neurological and endocrine conditions (including muscular dystrophies, Alzheimer's disease, hereditary deafness, spinocerebellar ataxia, and other conditions)." Robert Cook-Deegan & Christopher Heaney, *Patents in Genomics and Human Genetics*, 11 ANN. REV. OF GENOMICS & HUM. GENETICS 383, 412 (2010). PGxHealth, Inc. likewise, used gene patents to become the sole provider of diagnostic testing associated with Long-QT Syndrome. *Id.* Another entrant subsequently broke PGxHealth's monopoly with patents over variant sequences. *Id.* [CITE]

[278] Eisenberg, Gene Patenting Controversy, supra note 147, at 1381. See Lori B. Andrews, The Gene Patent Dilemma: Balancing Commercial Incentives with Health Needs, 2 HOUS. J. HEALTH. L. & POL'Y 65 (2002).

[279] Eisenberg, *Gene Patenting Controversy*, *supra* note 147, at 1382–83; [CITE]

[280] Cook-Deegan et al., *supra* note 240, at S18.

[281] Eisenberg, *Gene Patenting Controversy*, *supra* note 147, at 1383.

[282] MYRIAD GENETICS, INC., *supra* note 234, at 23.

[283] *Id*. at 23–24.

[284] For example, *O'Reilly v. Morse* can be considered an early example of that basic debate when comparing Justice Taney's majority opinion (favoring narrower rights) to Justice Grier's dissenting opinion (favoring broader rights for pioneering inventions). [Adam Mossoff's new paper.]

regularly in courts by private litigants and in USPTO reviews filed by third parties or the patent owners themselves. What makes *Myriad* a case for reflection is not that the Supreme Court corrected an earlier interpretation of Section 101—courts contour patent doctrines all of the time in ways that leave winners and losers.[285] Rather, *Myriad* reminds us that patent law's inherent affinity for stability can and will be challenged by outside pressures to grow and adapt. The question becomes how best to manage smart adaptation without unraveling the important incentives connected to patents—in other words, how to manage the tension between stability and progress. The remainder of this Part presents three general insights to improve the dialogue within patent law about this important (and eternal) tension: 1) patent law is not certain; 2) procedural rules can, and do, have substantive impact; and 3) promoting progress in technology may mean more than simply incentivizing actors to invent. Each is addressed in turn.

A. Patent Law is Not Certain

Myriad introduces an important lesson: patent law is not certain. As Cardozo reminded his early twentieth century audience, the law is not a quest for absolute certainty, but a way to predict an outcome in the next case to come along.[286] It's easy to read *Myriad* and come to the conclusion that isolated genomic sequences are not patent eligible subject matter and never have been—that the USPTO was simply wrong in its characterization for so many years, as was the Federal Circuit in *Myriad*.[287] In reality, the USPTO and courts make decisions on the patentability of individual claims in individual patents based on all of the information that they have at that time, but scientists are constantly working to learn more.

In the early 1980s, the USPTO allowed claims drawn to new and useful isolated genomic sequences by fitting them to its older chemical composition case law. Using this analogy, the post-*Chakrabarty* patent eligibility model predicted patent eligibility because isolated sequences are different chemical compounds from the sequences found inside human cells.[288] Few doubted this policy as sound legal reasoning from *Chakrabarty*, even though some believed that unmodified genetic sequences should not be patentable at all, that such sequences were better characterized as information, or that *Chakrabarty* should be adapted to a more realistic understanding of the underlying science.[289] Years later, explaining that unaltered isolated sequences (as compared to cDNA sequences) are more informational than chemical, the *Myriad* Court emphasized

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[285] KSR Int'l Co. v. Teleflex, Inc., 550 U.S. 398 (2007) (invalidating patent claims on obviousness grounds); eBay, Inc. v. MercExchange, L.L.C., 547 U.S. 388 (2006) (eliminating automatic injunctions for patent owners who succeed on an infringement claim); Alice Corp. v. CLS Bank Int'l, 134 S.Ct. 2347 (2014) (invalidating patent claims on eligibility grounds).

[286] CARDOZO, *supra* note 6.

[287] Debra J. H. Mathews, et al., *Patents and Misplaced Angst: Lessons for Translational Stem Cell Research from Genomics*, 12 CELL STEM CELL 508, 509 (May 2, 2013) ("It will indeed be a deep irony for genomics . . . if, just as key patents near expiration, the Supreme Court rules that the broadest patent claims enforced for over a decade should never have been granted.").

[288] Utility Examination Guidelines, *supra* note 148, at 1093.

[289] Berman & Dreyfuss, *supra* note 274, at 871, 882.

its adherence to the old eligibility model to find these same inventions patent ineligible.[290]

Myriad highlights the Court's attempts over the years to preserve a stable doctrine—a wide and expansive in scope despite limited, implicit exceptions to preclude products of nature, abstract ideas, and natural laws. This model forces courts to draw a line between man-made inventions and naturally occurring discoveries, which should involve a carefully considered weighing of the benefits and harms of granting exclusive rights. Indeed, as the Court stated in *Myriad*, "[P]atent [law] strikes a delicate balance between creating 'incentives that lead to creation, invention, and discovery' and 'impeding the flow of information that might permit, indeed, spur invention.'"[291] Despite recognizing the "uneasy compromises"[292] that should be made in drawing such fine lines, the Court chose to focus its short inquiry on whether the claims at issue were created by man. For example, denying patent eligibility to the isolated gene sequences, the Court stated that "Myriad did not create or alter either the genetic information encoded in the BRCA1 and BRCA2 genes or the genetic structure of the DNA," and that Myriad's patents did not "depend[] upon the creation of a unique molecule."[293] In contrast, the Court describes cDNA sequences as "not naturally occurring" because "the lab technician unquestionably creates something new when cDNA is made."[294] This narrow distinction may be less useful in future cases because courts addressing new and complex technologies will still use the same standard for products, asking whether the claimed invention is a composition of matter, manufacture, or machine, and if so, whether the product is naturally occurring. Whether a product is not naturally occurring carries the same meaning that it did in 1980 and long before that—is it made by man?

The *Myriad* story reminds us that developing a stable rule to predict the patent eligibility of future technologies is difficult. The *Myriad* Court, like other courts before it, approaches this difficulty by examining the new technology under the old rule. The advantage to this approach is that it maintains stability in the rule itself to comfort stakeholders at all levels of investment in inventing and commercialization. The disadvantage is the worst case scenario illustrated by *Myriad*—an initial judgment call to grant exclusive rights granted for some time and in great numbers followed by a decision that reverses this course and renders the issued patents (and others in the same category) invalid. Patent stakeholders must accept the costs of overprotection in the interim as part and parcel of patent law. Despite vocal critics, Myriad's business model enforcing its patents to the full extent of the law apparently did not influence the underlying eligibility questions. Myriad enforced its valid patent claims to protect its own business, until they were not valid anymore.

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[290] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2118, 2119 (2013). This is true, at least, for the inventions as claimed by Myriad in its patents.
[291] *Id.* at 2116.
[292] Transcript of Oral Argument, *supra* note 173, at 49.
[293] *Myriad*, 133 S. Ct. at 2118.
[294] *Id.* at 2119.

A different approach to shoehorning new technology into old law might be to embrace a paradigm shift within the doctrine of patent eligibility.[295] Thomas Kuhn famously introduced the concept of paradigm shifts in the science world in his seminal 1962 work, *The Structure of Scientific Revolutions*.[296] In the legal world, Cardozo hinted at the same concept when he talked about growth in the law.[297] Building upon these concepts, individual rules of law might best be described as hypotheses that predict future interests. These hypotheses can be reworked as courts and scientists learn more, not just with respect to deductively reasoning forward from cases (as shown in the patent eligibility cases, including *Myriad*), but also with respect to history, custom, and social science.[298] Prediction plays a large role in our modern legal system.[300] The legal system in general, and patent law in particular, craves rules with black and white answers.[302] Yet, as principles or precedent grow, the goal should not be to establish certainty but to establish probabilities. At some point, the probabilities might suggest the old principle should give way to a new one. In this manner, the rule of law develops as a scientific theory might, and thus could experience similar major shifts in doctrine.[303]

Patent law encourages doctrinal uniformity and predictability because the quid pro quo developed for granting patents in the first place relies on *ex ante* investment in research, invention, and commercialization. In that light, stability in patent law is a great thing (as it is in other areas of the law). Yet, paradigm shifts can be warranted. The *Myriad* opinion is narrowly confined to its reading of *Chakrabarty* and *Funk Brothers*. The Court says quite a bit about genetic sequences, but it does not say that much about patent eligibility that has not been said time and time again in cases that force courts to consider new technology in light of old laws.[304] Under that rubric, cDNA survives Justice Thomas' opinion as patent eligible. Perhaps patent owners and others should not be so quick to take these determinations as unchanging. New information will come to light. That the law is wide open yet bounded does not mean that the boundaries need to be fixed absolutely, they just need to be fixed relative to this day and age. As Cardozo

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[295] This is not a novel idea. *See* Bermand & Dreyfuss, *supra* note 274, at 873 (suggesting that the default rule of *Chakrabarty* should be replaced with a more organic version to reflect advancing scientific discoveries).

[296] THOMAS S. KUHN, THE STRUCTURE OF SCIENTIFIC REVOLUTIONS 23 (3d. ed. 1996).

[297] CARDOZO, *supra* note 6, at 62.

[298] *Id.*

[300] *Id.* at 37–38. "When the uniformities of antecedents and consequents are sufficiently constant to be the subject of prediction with reasonable certainty, we say that law exists." Cardozo refers to Dr. John C. H. Wu's article on Justice Holmes, *Juristic Philosophy of Mr. Justice Holmes*, as closely related to his own thoughts on this topic. *Id.* at 44–46. In Wu's article, Holmes is quoted as saying, "The prophecies of what the courts will do in fact, and nothing more pretentious, are what I mean by the law." John C. H. Wu, *The Juristic Philosophy of Mr. Justice Holmes*, 21 MICH. L. R. 523, 530 (1923). Cardozo summarizes Wu's argument as one regarding the law as "concern[ing] primarily our future interest." CARDOZO, *supra* note 6, at 45.

[302] CARDOZO, *supra* note 6, at 67–68. Continuing a theme from earlier in this work, Cardozo refers to "the pain of marking off such zones from others" as the pain of choosing a method for making decisions even within such formal systems, necessary for the law to grow. *Id.* at 68.

[303] *See* KUHN, *supra* note 287 (introducing a descriptive account of how paradigm shifts occur in scientific theories).

[304] *See e.g.*, Le Roy v. Tatham, 55 U.S. 156 (1852); Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948).

wrote, "The good of one generation is not always the good of its successor."[305] Courts will continue to consider whether Section 101 should be confined meaningfully by the implicit exceptions or whether it should be a low threshold that courts should not bother to gatekeep.[306] While they do so, technology will continue to move forward. Patent law, like other areas of the law, has the capacity to grow and reverse course. What makes *Myriad* both important and inevitable is that the issues raised in the litigation about patent eligibility (and the resulting consequences of overprotection in the meantime) expose patent law as particularly susceptible to doctrinal entrenchment. The long delay from the patents issuing to their invalidation had important consequences, including the potential for reduced innovation, limited access to important inventions, and a protected market share for Myriad. Additionally, the *Myriad* Court introduced no major legal innovations to the patent eligibility doctrine suggesting that this will not happen again. *Myriad*, above all, cautions that no law should be a dead letter.

B. Procedural Rules Can Have Substantive Impact

As described above, the plaintiffs in *Myriad* faced an uphill battle to establish standing to bring suit, despite many allegations of harm from Myriad's business practices and from gene patents themselves. Under the Federal Circuit's pre-*MedImmune* case law, a declaratory plaintiff seeking to challenge a patent had to establish a reasonable apprehension of suit,[307] something none of the plaintiffs realistically could have proven.[308] Researchers and others who believed that gene patents in general, and patents claiming isolated BRCA sequences in particular, harmed patients and the public had to be content to criticize the policies in journal articles, popular press, and USPTO hearings on related topics. The post-*MedImmune* liberalized approach to determining whether a case is sufficiently real and immediate to warrant federal adjudication enabled one plaintiff to establish the required interest in the case to keep it alive in federal court. One plaintiff is all it takes to challenge a patent. Arguably, the ACLU or another interest group could have brought suit ten years prior or in the interim, if enough facts existed to establish a reasonable apprehension of suit from Myriad, but it is equally likely that the rigorous standing requirement prior to 2007 prevented any meaningful challenge by plaintiffs similarly situated to the ones in *Myriad*.

The same could be said for challenges brought through agency proceedings, where any USPTO policy will be difficult to challenge within the agency itself (although not impossible). These procedures, even after recent revisions, are limited in scope and

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[305] CARDOZO, *supra* note 6, at 84.

[306] Former Federal Circuit Chief Judge Randall Rader described subject matter eligibility as "merely a threshold check," and stated, "[T]he categories of patent eligible subject matter are no more than a 'coarse eligibility filter.'" Ultramercial, Inc. v. Hulu, LLC, 722 F.3d 1335, 1341 (2013) (quoting Research Corp. Tech. v. Microsoft Corp., 627 F.3d 859, 869 (2010)). *See* Classen Immunotherapies, Inc. v. Biogen IDEC, 659 F.3d 1057 (describing Section 101 as governing the threshold of entry into the patent system for further consideration,). In a concurrence in *Classen*, joined by Judge Newman, Judge Rader boldly states, "This court should decline to accept invitations to restrict subject matter eligibility." *Classen*, 659 F.3d at 1074 (Rader, J., concurring). .

[307] *See* Gen-Probe, 359 F.3d 1376.

[308] Myriad's cease-and-desist letters were over ten years old by the time they filed suit. *See* Sierra Applied Sciences, Inc. v. Advanced Energy Indus., Inc., 363 F.3d 1361, 1374 (Fed. Cir. 2004) (finding no jurisdiction when the parties didn't communicate for four years).

time, and carry a steep estoppel provision, making them less desirable for groups like the ACLU to use to challenge individual patents to promote a broad policy agenda the way that the plaintiffs did in the *Myriad* litigation.

After almost thirty years of similar patents issuing from the USPTO to others, *Myriad* held that isolated gene sequences are free for everyone to use and not patent eligible, furthering an important public policy "favoring the full and free use of ideas in the public domain."[310] Policymakers would be wise to consider how the limited ability to challenge the USPTO's policies and the individual patents on Section 101 grounds impacted the development of substantive law in this area through delay.[311]

This aspect of *Myriad* illustrates how marginal growth within one doctrine (like standing to sue in declaratory patent cases) can promote a general policy within the patent laws overall. The Supreme Court in *Lear* and again in *MedImmune* emphasized the importance of encouraging the invalidation of bad patents.[312] That policy seemingly guided Judge Sweet to find standing, despite precedent within the Federal Circuit that might have predicted the *Myriad* plaintiffs could not sue even after *MedImmune* (or at least predicted a close question).[313] This policy also seemingly guided the Federal Circuit to affirm standing on the narrowest of margins in Ostrer's ability to infringe. Although the Federal Circuit's opinion considerably carved down the reach of the lower court's standing decision to just one single plaintiff with sufficient standing to sue, one plaintiff is all it takes to maintain the suit. In an age of patent skepticism, this is not insignificant progress within the law.

C. Promote Progress Means More Than Incentivize

The *Myriad* story also suggests that the traditionally stated goal of patent law to incentivize innovation (or disclosure or commercialization) is just one in a spectrum of goals that arise from the constitutional mandate to promote progress. Of the many theories that have been developed to justify a patent system like the one in the United States, the utilitarian rationale carries the most sway.[314] This rationale suggests that invention, commercialization, and disclosure of new and useful inventions maximize the general welfare of all of us. Thus, to encourage such invention, commercialization, and disclosure of their inventions, the government grants to private actors exclusive rights. Exclusive rights can be valuable, and as such, individuals and firms often seek them to

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[310] Lear v. Adkins, 395 U.S. 653, 673–74 (1969). In *Actavis*, the Court favored antitrust scrutiny of a reverse payment settlement scheme between a generic company and a patent owner pharmaceutical. FTC v. Actavis, Inc., 133 S. Ct. 2223 (2013).

[311] The USPTO could be challenged in litigation for its policymaking. *Myriad* involved a claim against the USPTO for improperly issuing all gene patents as a violation of the constitutional mandate to promote progress, but those claims were dismissed because the district court invalidated all of the claims on Section 101 grounds. *See* Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 237–38 (S.D.N.Y. 2010). Thus, the USPTO's power to grant patents to gene sequences was not an issue in either the Federal Circuit or the Supreme Court. Moreover, historically, courts have been reticent to litigate claims against the USPTO for granting patents erroneously. *See* Animal Legal Defense Fund v. Quigg, 932 F.2d 920 (Fed. Cir. 1991) (concluding that plaintiff animal rights group lacked standing to sue the USPTO).

[312] Lear, 395 U.S. at 673–74.

[313] *See* Benitec Austl., Ltd. v. Nucleonics, Inc., 495 F.3d 1340 (Fed. Cir. 2007). [CITE]

[314] [CITE]

improve profitability in research and development.[315] When patents are sought, we are all better off, so the story goes. Descriptively, the rationale goes a long way—inventors seek patents, and one reason they do so is the potential for supracompetitive profits or some other return on investment as a result of a patent's limited but exclusive rights.[316] Patents also provide public benefits, including increased innovation, commercialization, and disclosure of information to the public.[317] To provide these benefits, the patent system carries large costs: administrative costs at the USPTO,[318] the potential for deadweight loss in the form of output restriction by patent owners, and the potential for patent races between rivals, resulting in considerable expenditures prior to obtaining patent protection, both important societal costs.[319] When the patentability requirements, including Section 101, are met, the patent balance sheet assumes that the benefits are greater than the costs, and thus technological progress is promoted.[320]

Even the most vocal critics of gene patents (and of Myriad's business model that exploited them) remained on the legal sidelines. Why? Courts typically equate a patent's exclusive rights with the desirable "encouragement of investment-based risk."[321] This incentive-centric approach to patent law characterizes licensing and exploitation, and by extension the right to exclude others, as necessary to achieve the constitutional goal of promoting progress in implementing a patent system.[322] Accordingly, the U.S. patent system accepts limited access to patented good or services and higher prices as standard harms that might arise from patenting—claims about access and prices are important, to be sure, but they are also worries that courts prefer to leave for Congress to handle.[323] Patents are explicitly exclusive—the consequences of exclusivity that fall short of antitrust violations or patent misuse are accepted as a matter of course.[324] Perhaps the ACLU's pessimistic view of its chance of success in *Myriad* was driven, in part, by its recognition that concerns about Myriad's business model might not be persuasive enough to move the needle on a stable doctrine like patent eligibility.

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[315] [CITE]

[316] [CITE, maybe Berkeley entrepreneurial study]

[317] JAMES BESSEN & MICHAEL J. MEURER, PATENT FAILURE: HOW JUDGES, BUREAUCRATS, AND LAWYERS PUT INNOVATORS AT RISK 216 (2008).

[318] 35 U.S.C. §§ 1, 2 (2006).

[319] On the some of the costs of output restriction, see T. Randolph Beard et al., *Quantifying the Cost of Substandard Patents: Some Preliminary Evidence*, 12 YALE J. L. & TECH. 240 (2009) (examining some of the deadweight losses that result from granting substandard patents). On the costs of races to invent, see Yoram Barzel, *Optimal Timing of Innovations*, 50 REV. ECON. & STAT. 348 (1968) (modeling competition among firms for patent rights as inefficient races to invent that dissipate social surplus).

[320] Over time, technology has progressed—from the cotton gin, to the telegraph, to the light bulb, to the airplane, to the smart phone—and that could be directly caused by the patent system. Or, it could be caused by the passage of time, scientific advancements, and other factors. That question—not whether technology has progressed, but how much has it progressed as a result of the patent system—may be unanswerable. [CITE]

[321] Patlex Corp. v. Mossinghoff, 758 F.2d 594, 599–600 (Fed. Cir. 1985) (quoting Smith Int'l, Inc. v. Hughes Tool Co., 718 F.2d 1573, 1577–78 (Fed. Cir.), *cert. denied*, 464 U.S. 996 (1983)).

[322] *Id.*

[323] *See* [CITE].

[324] For a discussion of antitrust violations in the context of patent owner conduct, see Nobelpharma AB v. Implant Innovations, Inc., 141 F.3d 1059 (Fed. Cir. 1998). For an explanation of the patent misuse defense, see Princo Corp. v. Int'l Trade Comm'n, 616 F.3d 1318 (Fed. Cir. 2010); see generally Mark A. Lemley, *The Economic Irrationality of the Patent Misuse Doctrine*, 78 CAL. L. REV. 1599 (1990).

The *Myriad* story could start an entirely new conversation—not about gene patents, but about whether patent law should take into account a wider group of values that inform both patent eligibility and the scope of a patent's rights.[326] A multi-valence approach to patent law could improve upon an incentive-centric one by allowing courts and policymakers (including Congress and the USPTO) to consider other factors that promote progress outside of the traditional utilitarian rationale, including traditional notions of fairness, equity, and economic concerns like access and price.

Myriad was a rich Section 101 case with many competing values bound to the question of whether Myriad deserved exclusive rights associated with the isolated gene sequences claimed in its patents. At the oral arguments, the justices questioned the parties about the impact of its ruling on incentives for biotechnology companies and inventors.[327] The question on everyone's mind appears to be: if patent protection is weakened in some way by a ruling, what is the impact on the patent system's ability to incentivize? In his dissent of the Court's denial of certiorari in *Lab. Corp. v. Metabolite Laboratories*, Justice Breyer explains, "Patent law seeks to avoid the dangers of overprotection just as surely as it seeks to avoid the diminished incentive to invent that too little protection can threaten. One way in which patent law seeks to sail between these opposing and risky shoals is through rules that bring certain types of invention and discovery within the scope of patentability while excluding others."[328] In other words, Section 101 helps the progress promotion balance sheet stay in the black, the traditional goal of patent law.

When it considered the eligibility question, the *Myriad* Court purportedly weighed the important incentives awarded by isolated gene patents, especially in fledgling industries like biotechnology, against the preemption of others' uses of these genes for society's benefit.[329] In other Section 101 cases, the Court similarly focuses on incentives versus preemption (which presumably provides incentives for future inventors by preserving the use of products of nature, abstract ideas, or natural laws for all). The Court does not consider other values like access, affordable prices, or even the "gruesome parade of horribles" raised in *Chakrabarty*.[330] Incentivizing invention (and the resultant commercialization of technologies valuable to society) appears to be the only goal considered when tinkering with patent law doctrines, including eligibility. The promotion of progress has been distilled to this goal alone. Section 101, the most abstract of the patentability requirements, allows for a more robust policy discussion than the other patentability statutes, including Section 102's novelty, Section 103's non-obviousness, and Section 112's disclosure requirements, and still, the Supreme Court has not indicated any interest in its Section 101 cases, including *Myriad*, to consider the effort expended for discovery, nor the effect on access or pricing.[331] This is not to suggest that a multi-valence analysis should always render the patent not eligible for patenting. On the

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[326] *See* Simone A. Rose, *The Supreme Court and Patents: Moving Toward a Postmodern Vision of "Progress"?*, 23 FORDHAM INTELL. PROP. MEDIA & ENT. L. J. 1197 (2013). Rose argues that the Supreme Court's Section 101 jurisprudence, in particular, fails to recognize "equally important measures of progress" like improved public health and access to basic research tools. *Id.* at 1198.
[327] Transcript of Oral Argument, *supra* note 173, at 11, 12, 52, 58.
[328] Lab Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 128 (2006) (Breyer, J., dissenting).
[329] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2116 (2013).
[330] Diamond v. Chakrabarty, 447 U.S. 303, 316 (1980).
[331] The *Myriad* Court makes this clear.

contrary, it would simply invite a more robust conversation about patenting and the impact of exclusivity on patent owners and the public. As Malcolm Gladwell said of Myriad in 1995, "If you can get a patent for building a better mousetrap, it is very hard to argue that you don't deserve a patent for decoding the mysteries of breast cancer."[332] Careful consideration in some industries might indicate rewarding discovery does create more benefits to society as a whole than the avoidance of preemption.

Myriad represents one kind of overprotection, where a field of invention obtains patents that are later invalidated as a category not eligible for patenting under Section 101. Overprotection also might occur when the USPTO makes a simple mistake in examination, or when a court interprets a rule of patentability narrowly compared to an earlier broad interpretation. *Myriad* concerns itself with correcting overprotection by characterizing the patenting of isolated gene sequences as an error under its *Chakrabarty* doctrine. As Part III.A explains, however, maybe this was not in error, but a second best decision made with the knowledge available at the time and later replaced with another second best decision based on new knowledge about genes and how they work. *Myriad* does not seem to acknowledge that overprotection (and underprotection) are relative concepts tied to the laws for obtaining patent protection. The costs of overprotection—those costs the patent system purports to account for in balance with the private and public benefits provided by the patent—are borne by society, and accepted lock, stock, and barrel, once the decision to grant the patent has been made. What made *Myriad* such a polarizing case is that not only did it involve an allegation of traditional patent harms stemming from a single-provider monopoly,[335] but an allegation that the patents interfered with patients' medical care decisions and treatment.[336] From the time that its patents were granted, Myriad enforced them against others when it needed to, and used them defensively to deter entrants to its diagnostic testing market. Myriad also looked the other way when researchers used the sequences, worked to expand insurance coverage of its test so that more people could afford it, and used feedback from patients and others to improve the quality of its tests. Invalidation rendered Myriad's isolated gene sequence claims invalid, as well as all other claims drawn to isolated gene sequences (and other claims that might fall within the product of nature exception explained in *Myriad*), but it did not undo any of the gains made by Myriad or other patent owners in the interim that resulted from exclusivity guaranteed by the patents. *Myriad* represents one example of how overprotection not only results in exclusivity where there should be none, but exclusivity that endures even once the overprotection is corrected.

Accordingly, in addition to considering additional values when making a decision on eligibility (whether a patent should be granted in the first place), the *Myriad* case might also hint that the patent's strong property right to exclude others could be adapted to mitigate the possibility of overprotection in the first instance. Currently, patent law does not police patent owner conduct other than in the limited defense of patent misuse for infringement defendants. Antitrust law does some policing, but most patent owner

[332] Gladwell, *supra* note 266, at 122.

[335] [CITE suggests that Myriad's pricing structure eliminated one typical monopoly harm, the deadweight loss.]

[336] Kane, *supra* note 244, at 835, 851–52.

conduct is immune from antitrust liability.[337] If some policing of conduct were to occur that takes into account the importance of preserving the incentive to innovate as well as other values important to the public interest, the decision to grant a patent in the first place could result in fewer harms like those identified in *Myriad* as problematic over time, regardless of later invalidation.

IV. CONCLUSION

Maybe the most important lesson that can be learned from cases like *Myriad* (ones in which the legal problems are complex) is a subtle one: the big picture is complicated. After all, if every case were easy to resolve on the merits, all lawyers and judges would be out of jobs quickly. Technology is complex, also. This results in a tendency (maybe even a compulsion) among patent attorneys and courts deciding patent cases to analogize to other areas of the law, to shoehorn fact into narrow doctrines, or otherwise to do things that reduce the case and the technology at issue into smaller and smaller, easy to digest components. This method of tackling complexity merits commendation—it has been described as an evolutionary cognitive process.[338] However, over time, within legal doctrines, simplification that aids in categorizing and predicting outcomes for future cases may result in an unintended consequence that resonates in patent law—too much stability. Policymakers might fail to appreciate that complexity in a case could bring richness and nuance to our understanding of doctrines, especially those built upon complexity like patent law.

Patents had been granted on genes for twenty-five years and this enabled policy makers to review the consequences of gene patents over that long period of time when considering the eligibility question in *Myriad*. Collecting data is good—it provides for a richer view of the incentives rationale and perhaps supports different rationales for protecting patents in the first place—but what about the intervening twenty-five years of enforcement actions, license agreements, and unquestioning adherence to the patent eligibility model set forth in *Chakrabarty*? The incentive story that supports the *Chakrabarty* model of Section 101 dominates how courts view questions of eligibility and enforcement, and this causes courts to ignore other values, including both positive and negative externalities resulting from the issuance of patents. Because these externalities implicate not just technological progress but overall societal welfare, courts should be cautious in reducing eligibility and enforcement questions to logical deductions revolving around *ex ante* incentives to inventors. Instead, courts should embrace the possibility of progress within and across doctrines to move patent law toward an ultimate goal like welfare maximization, inestimable (and invaluable) as it may be. Stable doctrines and entrenched status quos provide a safe avenue for courts and certainly avoid messy departures into analyses with no absolute truths. Perhaps the lasting legacy of *Myriad* is that growth within the law is possible, but multi-valence scrutiny may be necessary to promote that kind of progress.

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[337] *See* FTC v. Actavis, Inc., 133 S. Ct. 2223, 2231 (2013).
[338] [Tversky? Judgment under Uncertainty?]