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MYRIAD LESSONS LEARNED

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

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* 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.


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.”

The Myriad story began long before the Myriad plaintiffs filed suit in 2009, and even before Myriad and others raced to discover the genes linked to hereditary breast cancer in 1994. In 1980, the Supreme Court in Diamond v. Chakrabarty confirmed the patent eligibility of biological organisms. 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. Discussing the diagnostic testing that she received, Jolie wrote:

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.


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 chromosome16 (“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

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,
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-op-ed_n_3275208.html.
14 GREGOR MENDEL, EXPERIMENTS IN PLANT HYBRIDIZATION (1865). TID 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,

\(^{18}\) 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.


and sequencing genes associated with particular proteins or diseases proved difficult.\textsuperscript{26}
Better markers, known as restriction fragment length polymorphisms (RFLPs),\textsuperscript{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.”\textsuperscript{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.\textsuperscript{29} Breast
cancer, like other cancers, derives from a large number of factors, including genetic and
environmental ones.\textsuperscript{30} However, researchers as early as the 1800s noted that some forms
of breast cancer appeared to have higher incidences within families.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{34} Myriad won the “most impasioned and publicly
visible of all genetic races” when it announced on September 15, 1994, that the company
had isolated and sequenced BRCA1.\textsuperscript{36}

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

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

\textsuperscript{27} \textit{Davies & White}, supra note 25, at 131–33; \textit{Cook-Deegan, Gene Wars}, supra note 23, at 40–44.

\textsuperscript{28} \textit{Davies & White}, supra note 25, at 266. See Declaration of Sir John E. Sulston, Ph.D. at 5–8, Ass’n for

\textsuperscript{29} Natalie Angier, \textit{Fierce Competition Marked Fervid Race for Cancer Gene}, \textit{N.Y. TIMES}, Sept. 20, 1994,
at C1.

\textsuperscript{30} \textit{Davies & White}, supra note 25, at 50; see Bernadine Healy, \textit{BRCA Genes — Bookmaking,

\textsuperscript{31} \textit{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”).

\textsuperscript{32} See Bryn Williams-Jones, \textit{History of a Gene Patent: Tracing the Development and Application of
Commercial BRCA Testing}, 10 \textit{HEALTH L.J.} 123, 131 (2002); see also Ass’n for Molecular Pathology v.

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

\textsuperscript{34} Ass’n for Molecular Pathology, 702 F. Supp. 2d at 201.

\textsuperscript{35} Natalie Angier, \textit{supra} note 29 at C1. See also Miki et al., \textit{supra} note 8; Natalie Angier, \textit{Scientists Identify a
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 \textit{Miki et al.}, \textit{supra} note 8 for a complete listing of
researchers and their affiliations.

\textsuperscript{36} 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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\(^{39}\) Ass’n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2113 (2013).


\(^{42}\) 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. 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. 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. 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.

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. 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. Myriad, as a private company, could support Skolnick’s gene hunting research by attracting capital from private investors. Myriad raised $55 million in this manner in 1992 alone. 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. Private placement offerings raised an additional $8.8 million in March 1993 and $59 million in 1994. The infusion of cash worked wonders, allowing the Myriad team “to work at a superior pace.” In September 1994, as a result of intense search efforts, the team announced that they had sequenced the BRCA1 gene. The sequence for BRCA2 came along in much the same way not long after Myriad became a public company in 1995.

49 Harold M. Schneck, 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 Williams-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.
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.”65 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 BRACAnalysis®, 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 BRACAnalysis® originally included only full sequencing of the patient’s BRCA genes,69 but later added detection of large rearrangements.70 At present, BRACAnalysis® 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


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 BRACAnalysis® 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.
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. In January 1996, OncorMed, Inc., the owner of a competing patent on a BRCA1 sequence, began selling a diagnostic test for BRCA1. 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). 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. GIVF acquiesced to Myriad’s demand, but GDL continued to provide diagnostic testing, claiming a research exemption. In 1997 and 1998, Myriad sued OncorMed for patent infringement, eventually obtaining its patents in a settlement. 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.

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), BRACAnalysis® might detect a mutation known as a “genetic variant of uncertain significance,” or a “VUS,” which presents an unknown cancer risk. With data collected from patients, including ethnicity and family pedigrees, Myriad built a large, proprietary database of information about the BRCA genes. 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. As a result, one study suggests that Myriad likely

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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.


76 See id.; see also Ass’n for Molecular Pathology v. USPTO, 669 F. Supp. 2d 365, 398 (S.D.N.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.

81 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 So & Joly, supra note 72, at 104. 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.
88 See Ass’n for Molecular Pathology v. Myriad Genetics, Inc., 133 S.Ct. 2107, 2111 (2013).
91 U.S. CONST. art. I, § 8, cl. 8.
93 U.S. CONST. art. I, § 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”) 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). Because this commonly accepted rationale for granting patents in the first place implicates incentives to would-be inventors—incentives to invent, disclose, commercialize, etc.—participants at every level of the patenting process prefer uniformity and predictability in the law. After all, uncertainty in the law makes for qualms about ex ante investment. 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. Before *Chakrabarty* and after, activists protested the patenting of life forms and expressed concerns about the privatization of life itself. Despite generating scholarly, media, and policy discussion, these activists did not successfully change patent policy. Fifteen years after Myriad filed its first patent applications, the ACLU decided to challenge Myriad’s BRCA gene patents. 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.”

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.” Section 101, the present statute, reads similarly: “Whoever invents or

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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."

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

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).


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.


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.\footnote{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.\footnote{116} An inventor whose invention lies out of bounds
obtains no patent, regardless of any extraordinary expense or ingenuity in his
endeavors.\footnote{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 \textit{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.”\footnote{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.”\footnote{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.\footnote{120}

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

\begin{quote}
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.”
\end{quote}


\footnote{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).

\footnote{117} See \textit{Myriad}, 133 S. Ct. at 2117.

\footnote{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).

\footnote{119} Merck, 253 F.2d at 162.


\footnote{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

\(^{122}\) *Id.* at 134–35.


\(^{124}\) *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)).


\(^{127}\) *Id.*

\(^{128}\) See *id.* at 134.


\(^{131}\) *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.” But it does not embrace every discovery, excluding “[t]he laws of nature, physical phenomena, and abstract ideas.” 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.’”

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. 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.” 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.”

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. 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. As one newspaper reported, “The decision opened a floodgate.”

Biotechnology companies filed patent applications at a record pace. Employment and better lives for our citizens.”

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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.
143 Id.
The Chakrabarty vision embraced by biotechnology companies underscored the role of human intervention in patent eligibility, but it did not say anything about the eligibility of isolated genomic sequences. 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 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).

By this time, the Federal Circuit had come into existence, charged with injecting patent law with consistency and uniformity across the country. 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.” Without questioning eligibility, the Federal Circuit held that the patent’s disclosure failed to enable such a broad array of sequences without undue experimentation. 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. As researchers filed patent applications on these gene

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).


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
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 or purified products, even if they originated in nature prior to being isolated or purified, are patent eligible under Section 101.”


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. 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 York’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.” 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. 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.

The breadth of the district court’s opinion surprised even patent law experts. (Even the *New York Times* reported, “The decision invalidating the gene patents stunned many lawyers who follow such issues.” Of course, Myriad appealed to the Federal Circuit, which reversed the trial court’s decision as to the composition of matter claims. 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*. Tellingly, however, the panel members were divided as to both outcome and reasoning. 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).


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. Judge Moore, concurring in part, agreed about eligibility, but couldn’t agree that isolation, alone, sufficed to find the claims patent eligible. 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. Judge Bryson, dissenting, concluded that isolated gene sequences are not patent eligible. 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. 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.

Unlike the startling district court opinion, the Federal Circuit’s opinion drew more tempered reactions. 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.

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. During oral arguments, the Justices actively asked questions and created humorous hypotheticals to help sort out its characterization of isolated gene sequences. 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.

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. 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. 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. 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.

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. 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. 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, the ACLU’s mission to “[ensure] people’s rights to bodily integrity, human dignity, and scientific freedom” pushed it to bring the litigation anyway. 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. Recognizing that Section 101 could be “an important lever to help advance the public interest,” 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. 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. 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. The *Myriad* plaintiffs included “an assortment of medical organizations, researchers, genetic counselors, and patients,” all claiming harm from Myriad’s use of the patents “to prevent [the] plaintiffs from engaging in clinical analysis of the BRCA1 and BRCA2 genes, from informing women about testing options other than by Myriad, and the public interest in patent law.”

185 Park, supra note 99, at 524.  
186 Id. at 520.  
187 Id. at 524–25.  
188 Id. at 527.  
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.\footnote{Ass’n for Molecular Pathology, 669 F. Supp. 2d 365, 386 (S.D.N.Y. 2009).}

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.”\footnote{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. \textit{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. \textit{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.} 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 . . . .”\footnote{Id. at 387. In fact, such a requirement, Judge Sweet continued, would be inconsistent with the Supreme Court’s \textit{MedImmune} opinion, requiring that “all the circumstances” be considered in these cases. \textit{Id.} at 388.} 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.\footnote{Id. at 378–79.} Myriad also filed two suits, which either settled or were dismissed without prejudice.\footnote{Id. at 379.} The eleven-year-old letters, standing alone, might not support standing in a declaratory patent case.\footnote{See \textit{Avante Int’l Tech., Inc. v. Hart Intercivic, Inc.}, No. 08-832, 2009 WL 2431993, at *3 (S.D. Ill. July 31, 2009).} 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.\footnote{Ass’n for Molecular Pathology, 669 F. Supp. 2d at 390.}

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.\footnote{Id. at 391.} Judge Sweet distinguished the \textit{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.”\footnote{Id. But cf. \textit{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); \textit{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.’”).} The non-researcher plaintiffs (patients and members of medical organizations) alleged a risk of

\begin{footnotesize}
\item[\footnote{193}]{\textit{Ass’n for Molecular Pathology, 669 F. Supp. 2d 365, 386 (S.D.N.Y. 2009).}}
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\item[\footnote{196}]{\textit{Id.} at 378–79.}
\item[\footnote{197}]{\textit{Id.} at 379.}
\item[\footnote{198}]{\textit{See \textit{Avante Int’l Tech., Inc. v. Hart Intercivic, Inc.}, No. 08-832, 2009 WL 2431993, at *3 (S.D. Ill. July 31, 2009).}}
\item[\footnote{199}]{\textit{Id.} at 391.}
\item[\footnote{200}]{\textit{Id. But cf. \textit{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); \textit{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.’”).}}
\end{footnotesize}
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

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
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 re framing 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. 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.

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. This proceeding allowed for invalidation of claims “on the basis of prior art patents or printed publications,” not on patent eligibility grounds. 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. 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.” 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. 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. 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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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.


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.


of the third party.\textsuperscript{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.\textsuperscript{220} However, the Federal Circuit recently held that a consumer interest group, like several of the plaintiffs in \textit{Myriad}, did not have the requisite standing to appeal an adverse decision in a reexamination.\textsuperscript{221}

Thus, USPTO alternatives may present a compounding problem for folks like the \textit{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 \textit{Myriad}, standing remains a substantial barrier to bringing challenges to patent policies like the USPTO’s interpretation of Section 101.

\subsection*{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 \textit{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.\textsuperscript{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.”\textsuperscript{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.”\textsuperscript{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,\textsuperscript{225} but its early enforcement likely affected day-to-day practices in clinics and laboratories nationwide.\textsuperscript{226} Research,

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\textsuperscript{220} 35 U.S.C. § 141(c) (2012).
\textsuperscript{221} Consumer Watchdog v. Wis. Alumni Research Found., 753 F.3d 1258, 1263 (Fed. Cir. 2014).
\textsuperscript{223} Id. at 383.
\textsuperscript{224} Carbone et al., \textit{supra} note 76, at 785.
\textsuperscript{225} So & Joly, \textit{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.”)
\textsuperscript{226} Carbone et al., \textit{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.\textsuperscript{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.\textsuperscript{228} Myriad even offered its testing
to researchers at a discounted rate.\textsuperscript{229}

The impact of gene patents on innovation remains unclear.\textsuperscript{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.”\textsuperscript{231} Patent scholars also conclude there is no evidence to support
patent problems as a result of human gene patents.\textsuperscript{232} In the area of diagnostic testing, however, Myriad’s exclusivity resulted in some empirical evidence supporting concerns
about research impact.\textsuperscript{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.”\textsuperscript{234} Others reported that, especially within the diagnostic testing
markets, “university researchers [became] more secretive and less willing to share
research results or materials.”\textsuperscript{235}

When it comes the impact of gene patents on clinical availability, evidence is
more conclusive.\textsuperscript{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.\textsuperscript{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.\textsuperscript{238} Myriad explains that second opinion testing does

\textsuperscript{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.

\textsuperscript{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.

\textsuperscript{229} Tom Reynolds, NCI-Myriad Agreement Offers BRCA Testing at Reduced Cost, 92 J. NAT’L CANCER INST. 596, 596 (2000).

\textsuperscript{230} Caulfield, supra note 160, at 978 (describing innovation impact as “a complex and rather muddled picture.”)


\textsuperscript{233} Id. at 299–300.

\textsuperscript{234} Robertson, supra note 217, at 384.

\textsuperscript{235} Caulfield et al., supra note 226, at 1092.

\textsuperscript{236} Robertson, supra note 231, at 385–86.

\textsuperscript{237} Id. at 386.

\textsuperscript{238} Complaint, supra note 7, at 11.
and can occur at its facilities and as verification from other facilities.\textsuperscript{239} Yet there is still discussed 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{242} 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.\textsuperscript{243} Myriad describes its own BRACAnalysis\textsuperscript{®} test as “the standard of care in identification of individuals with hereditary breast and ovarian cancer.”\textsuperscript{244} This test utilizes full sequencing, which as noted earlier, may miss some large rearrangements or deletions, an observation confirmed in several studies.\textsuperscript{245} In response, Myriad developed BART\textsuperscript{®} to identify some of these missed rearrangements or deletions when a patient tests negative using BRACAnalysis\textsuperscript{®}.\textsuperscript{246} However, Myriad limits the availability of the BART\textsuperscript{®} test to a small fraction of the patients seeking BRCA testing as a concurrent test at no additional cost.\textsuperscript{247} Others may buy BART\textsuperscript{®} for an additional fee of $650.\textsuperscript{248} 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.\textsuperscript{249} Professor Eileen Kane describes this as a public health issue, with which patent law is “not formally burdened.”\textsuperscript{250} Notably, patent law allows for third party policing of

\textsuperscript{239} Myriad Genetics, Inc., Written Comments on Genetic Diagnostic Testing Study 8–9 (2012).


\textsuperscript{241} See id. at S23–24. “[C]ompetition does little to affect price overall.” Robertson, supra note 222, at 387.

\textsuperscript{242} Id. at 388.

\textsuperscript{243} Eileen M. Kane, Patent-Mediated Standards in Genetic Testing, 2008 UTAH L. REV. 835, 852 (2008). “[M]yriad 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)).

\textsuperscript{244} 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).

\textsuperscript{245} Id. at 9.

\textsuperscript{246} Id. at 10.

\textsuperscript{247} Id.

\textsuperscript{248} Id. at 10–12.

\textsuperscript{249} See id. at 852.
patent invalidity. Patent law does not effectively police patent owner conduct except in the extreme cases of antitrust liability.

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. 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. 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. 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.

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. 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 BRCA1). 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.
interest in preserving patent rights will not always trump other considerations, especially when public health issues are at stake.\textsuperscript{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.\textsuperscript{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,\textsuperscript{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.\textsuperscript{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.\textsuperscript{265} 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—


\textsuperscript{261} See Kane, supra note 244, at 853 (describing efforts to establish a research exemption for the use of diagnostic gene patents).


\textsuperscript{265} 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.\textsuperscript{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.\textsuperscript{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).\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 science, technology, not a

\textsuperscript{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.

\textsuperscript{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).


\textsuperscript{273} Ass’n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2120 (2013).

\textsuperscript{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
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
doctines all of the time in ways that leave winners and losers. 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. 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. 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. 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. Years later, explaining that unaltered isolated sequences (as compared to
cDNA sequences) are more informational than chemical, the Myriad Court emphasized

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.

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.

\(^{290}\) 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.


\(^{293}\) *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

²⁹⁵ This is not a novel idea. See Bernand & 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).


²⁹⁷ *CARDOZO, supra* note 6, at 62.

²⁹⁸ *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, *Jurisprudential 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 Jurisprudential 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.

³⁰⁰ *Id.* 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.

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.

³⁰⁳ *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.”\textsuperscript{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.\textsuperscript{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.

\textbf{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,\textsuperscript{307} something none of the plaintiffs realistically could have proven.\textsuperscript{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

\textsuperscript{305} CARDOZO, supra note 6, at 84.

\textsuperscript{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). 

\textsuperscript{307} See Gen-Probe, 359 F.3d 1376.

\textsuperscript{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.”

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.

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. 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). 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. 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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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.\textsuperscript{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.\textsuperscript{316} Patents also provide public benefits, including increased innovation, commercialization, and disclosure of information to the public.\textsuperscript{317} To provide these benefits, the patent system carries large costs: administrative costs at the USPTO,\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.”\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.

\textsuperscript{315} [CITE]

\textsuperscript{316} [CITE, maybe Berkeley entrepreneurial study]

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


\textsuperscript{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).

\textsuperscript{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]


\textsuperscript{322} Id.

\textsuperscript{323} See [CITE].

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.\textsuperscript{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.\textsuperscript{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.”\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{331} This is not to suggest that a multi-valence analysis should always render the patent not eligible for patenting. On the

\textsuperscript{326} See Simone A. Rose, The Supreme Court and Patents: Moving Toward a Postmodern Vision of “Progress”? , 23 FORDHAM INT’L. 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.

\textsuperscript{327} Transcript of Oral Argument, supra note 173, at 11, 12, 52, 58.


\textsuperscript{329} Ass’n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2116 (2013).


\textsuperscript{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.”

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, but an allegation that the patents interfered with patients’ medical care decisions and treatment. 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.
333 [CITE suggests that Myriad’s pricing structure eliminated one typical monopoly harm, the deadweight loss.]
334 Kane, supra note 244, at 835, 851–52.
conduct is immune from antitrust liability. 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. 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-va-lence scrutiny may be necessary to promote that kind of progress.

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338 [Tversky? Judgment under Uncertainty?]