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Persons and Patents

. . . it is a story . . . seared into my genetic makeup that this nation is more than the sum of its parts – that out of many, we are truly one.

Barack Obama, Philadelphia, PA, March 18, 2008

In April 2010, Judge Robert Sweet of the Southern District of New York ruled that gene sequences could not be patented.[1] The court also ruled that a medical diagnostic test requiring comparison of a patient's gene with an identified breast cancer gene sequence was not patentable because it was a mental process.[2] These controversial rulings shook the foundations of many global industries engaged in providing medical services based on genetic information. Biotechnological research at university and industry labs faced a paradigm change if Judge Sweet's ruling were upheld. The assumption guiding commercialization efforts and U.S. scientific policy was that patents on gene sequences provided a stable set of legal rights for the development of science and industry in biotechnology.

Although this assumption has been the subject of criticism before and after the U.S. Supreme Court's landmark 1980 ruling in *Diamond v. Chakrabarty*, holding that a genetically modified single-cell organism could be patented,[3] the availability of patents for gene sequences had not been seriously challenged until 2010. There was an expected sigh of relief from the affected industry interests when in July 2011, the Court of Appeals for the Federal Circuit overruled Judge Sweet's ruling with respect to the patentability of a gene sequence.[4] However, the Federal Circuit upheld Judge Sweet's ruling that the diagnostic

[1] The Association for *Molecular Pathology v. United States Patent Office & Myriad Genetics, Inc.*, 702 F. Supp. 2d 181 (S.D.N.Y. 2010).
[2] Idem. at 235–236.
[3] 447 U.S. 303 (1980).
[4] *The Association for Molecular Pathology v. United States Patent Office & Myriad Genetics, Inc.*, 653 F.3d 1329 (Fed. Cir. 2011).

method involving comparing gene sequences was not patentable. On March 26, 2012, the Supreme Court vacated the Federal Circuit's ruling and sent the case back to the appeals court for review in light of the Supreme Court's decision in *Mayo v. Prometheus*.[5] From the perspective of industry groups, scholars, and policy makers, we are living in interesting times for patents and biotechnology.

In 2002, eight years before Judge Sweet's ruling, a start-up company called Nitromed received an initial patent on a prescription drug called BiDil that was designed for treatment of hypertension in "black patients," to adopt the language from the granted patent.[6] Like many pharmaceuticals aimed at hypertension, BiDil was a nitrogen dilator, controlling the amount of nitrogen in the blood. Nitromed obtained a patent on an earlier version of the hypertension drug in the late 1980s. During its clinical trials, testing the effectiveness of the drug on actual people, researchers at the company noticed that a certain combination of compounds was particularly effective on the African-American population. The researchers were not looking to target the African-American population in their trials; they were using a population of veterans. African Americans constituted a large proportion of the veteran population used in the clinical trials as compared to the U.S. population as a whole. The company decided to patent the findings of its researchers as a new compound that would be particularly effective in treating hypertension in the African-American population. In 2005, Nitromed received approval from the U.S. Food and Drug Administration (FDA) for BiDil as a hypertension treatment for African Americans, the first time the agency had approved a drug compound for a particular racial or ethnic group. Although the patent did

[5] See 2012 WL 9861819. The Supreme Court ruled in *Mayo v. Prometheus* that a specific method of personalized medicine was not patentable because it only recited a law of nature without any applications. See *Mayo v Prometheus*, 132 S. Ct. 1289 (2012).

[6] U.S. Patent No. 6465463 (issued Oct. 15, 2002). The first claim reads as follows: "1. A method of reducing mortality associated with heart failure, for improving the oxygen consumption, for improving the quality of life or for improving exercise tolerance in a black patient comprising administering to the black patient a therapeutically effective amount of at least one hydralazine compound of Formula (I) or a pharmaceutically acceptable salt thereof, and at least one of isosorbide dinitrate and isosorbide mononitrate, wherein the hydralazine compound of Formula (I) is wherein a, b and c are each independently a single or a double bond; R1 and R2 are each independently a hydrogen, an alkyl, an ester or a heterocyclic ring; R3 and R4 are each independently a lone pair of electrons or a hydrogen, with the proviso that at least one of R1, R2, R3 and R4 is not a hydrogen" (emphasis added). Claim 2 is a dependent claim that refers to claim 1 but limits it to the case "wherein the black patient has a less active rennin-angiotensin system relative to a white patient." Finally, claim 3 also depends on claim 1 but limits it to the case "wherein the black patient has hypertension." This patent was reissued in 2004 as U.S. Patent No. 6784177 (issued Aug. 31, 2004).

not receive much publicity, the decision of the FDA did, bringing the issue of personalized medicine to the forefront of policy debates.[7]

Judge Sweet's decision in 2010 and Nitromed's patenting and commercialization strategies with respect to BiDil more than half a decade earlier have much in common. They both bring to the forefront the challenging question of patent law's relationship to people who use and rely on patented inventions. This question is the central focus of this book. It may appear that juxtaposing an abstraction like a patent with something concrete and living like a person is just an academic exercise. But developments in the marketplace, society, and legal rules have mixed the realm of the abstract with that of the personal.

A patent is a grant from the government that allows the patent owner to keep others from making, using, selling, or importing the invention covered by the patent. With this grant, the owner can, in theory, commercialize and sell the invention to the public. Almost all products, from your car to your smartphone to your microwave, are currently covered by a patent or have been covered by a patent in the past. Through the gadgets we use or purchase, patents affect our personal lives. Patents also cover pharmaceuticals and in that way directly affect our health and our ability to live. One of the biggest controversies, still ongoing, is access to medicines in both the developed and the developing worlds. The access-to-medicine debate has many dimensions, and the existence of a patent on these medicines is one of them. A patent is most certainly an abstraction, but it is one that intervenes in the personal sphere in many direct and indirect ways.

The patent at issue in Judge Sweet's decision, owned by Myriad, covered diagnostic techniques to identify a specific genetic sequence linked with the proclivity to breast cancer in women. Anyone using this particular diagnostic and the genetic sequence identified by Myriad would have to deal with the patent. The lawsuit against Myriad that gave rise to Judge Sweet's opinion challenged the patentability of the genetic sequence that was the basis for the diagnostic test. The legal argument was that no one can own a gene, especially when it is part of a person. Myriad's argument was that it did not own a gene as it existed in a person, but a purified, extracted form of the gene as it existed in a laboratory for the purpose of making a medical diagnosis. The distinction would be analogous to distinguishing ownership of a lock of hair from someone's head from ownership of the purified chemical and material

[7] See, e.g., "Getting to the Heart of the Matter," *U.S. News & World Report* 14 (June 15, 2005); "Color-Blind Drug Research Is Myopic; More, Not Less, Study Is Needed on Ways Different Races Respond," *Business Week* 44 (June 27, 2005); "FDA Approves Heart Drug for African-Americans," *The New York Times* C2 (June 24, 2005).

compounds that comprise the lock. Judge Sweet, however, did not entertain such hairsplitting. What Myriad claimed ownership of was not distinguishable from an actual gene as it existed in a human person.[8] Therefore, the patent was invalid. The facts of the case illustrate how our understanding of a patent is related to our understanding of a person.

This point is underscored by the Federal Circuit's decision on appeal. The court held that the patented gene sequence (see Figure 1.1) was different from the one that exists in the person. The patented sequence was not in a natural state, but was rather in a purified state. It had been processed physically by a researcher in a lab to obtain a new composition that could be manipulated and studied. The patented gene sequence was in effect a representation of, and hence different from, the naturally occurring gene.[9] Much like a tree differs from a photograph of a tree, the song of a bird differs from synthesized bird calls, or color and light differ from hues of paint, so the patented sequence is the product of human endeavor. In a similar vein, the Federal Circuit upheld Judge Sweet's ruling that the diagnostic method of comparing two gene sequences is not patentable because the act of comparison constitutes a mental process.[10] The act of comparing occurs inside a person's brain. Processing information occurs inside a person. Allowing patents on mental processes would be tantamount to patenting thoughts. The reach of patent law seems to depend on the boundaries of a person's body and mind. The person so defined by these boundaries is impermeable to patent ownership.

There has been no legal challenge either in the U.S. Patent Office (USPTO) or in the courts to the Nitromed patent. My research has found no evidence that Nitromed has brought legal actions for infringement or has even sought to license the patent – the usual strategies for enforcing one's patent rights. It should also be made clear that there is no genetic component to Nitromed's patent (see Figure 1.2). The patent covers a pharmaceutical compound that is effective for the treatment of hypertension in "black patients." But blackness is not defined in genetic terms. And, of course, it really cannot be. Nitromed is basing its claim on epidemiological and statistical data. The company's researchers found that the compound at issue was effective in treating hypertension as a statistical matter when tested on a group of self-identified black patients. Blackness is a self-identified category, rooted in sociological understandings rather than genetic ones. Whereas the decisions in Myriad suggest that the physical and mental dimensions of a person are not subject to patent

[8] See note 1 to this chapter at 222–227.
[9] See note 3 to this chapter at 1349–1350.
[10] See note 3 to this chapter at 1355–1356.

US005693473A

United States Patent [19]
Shattuck-Eidens et al.

[11] **Patent Number: 5,693,473**
[45] **Date of Patent: Dec. 2, 1997**

[54] **LINKED BREAST AND OVARIAN CANCER SUSCEPTIBILITY GENE**

[75] Inventors: **Donna M. Shattuck-Eidens**, Salt Lake City, Utah; **Jacques Simard**, Quebec; **Francine Durocher**, Ste-Foy, both of Canada; **Mitsuuru Emi**, Tokoyo; **Yusuke Nakamura**, Yokohama, both of Japan

[73] Assignees: **Myriad Genetics, Inc.**, Salt Lake City, Utah; **Centre de Recherche du Chul**, Sainte-Foy, Canada; **Cancer Institute**, Tokyo, Japan

[21] Appl. No.: **480,784**

[22] Filed: **Jun. 7, 1995**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 409,305, Mar. 24, 1995, abandoned, which is a continuation-in-part of Ser. No. 348,824, Nov. 29, 1994, abandoned, which is a continuation-in-part of Ser. No. 308,104, Sep. 9, 1994, abandoned, which is a continuation-in-part of Ser. No. 300,266, Sep. 2, 1994, abandoned, which is a continuation-in-part of Ser. No. 289,221, Aug. 12, 1994, abandoned.

[51] **Int. Cl.**[6] **C12Q 1/68**; C12P 19/34; C07H 21/04; C07H 21/02

[52] **U.S. Cl.** **435/6**; 435/91.2; 536/23.1; 536/24.3; 536/24.33

[58] **Field of Search** 435/6, 91.2; 536/23.1, 536/24.3, 24.33

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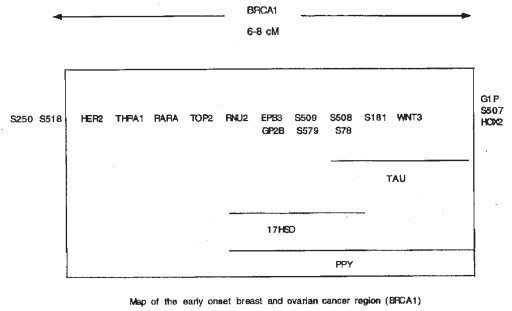
[57] **ABSTRACT**

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast and ovarian cancer predisposing gene (BRCA1), some mutant alleles of which cause susceptibility to cancer, in particular breast and ovarian cancer. More specifically, the invention relates to germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer. The present invention further relates to somatic mutations in the BRCA1 gene in human breast and ovarian cancer and their use in the diagnosis and prognosis of human breast and ovarian cancer. Additionally, the invention relates to somatic mutations in the BRCA1 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA1 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA1 gene for mutations, which are useful for diagnosing the predisposition to breast and ovarian cancer.

14 Claims, 18 Drawing Sheets



Map of the early onset breast and ovarian cancer region (BRCA1)

FIGURE 1.1. First page of one of Myriad's patents.

(57) **ABSTRACT**

The present invention provides methods or treating and preventing mortality associated with heart failure in an African American patient with hypertension and improving oxygen consumption, quality of life and exercise tolerance by administering a therapeutically effective amount of at least one hydralazine compound and at least one of isosorbide dinitrate and isosorbide mononitrate, and, optionally, one or more compounds, such as, for example, a digitalis, a diuretic compound, or a compound used to treat cardiovascular diseases. In the present invention, the hydralazine compound is preferably hydralazine or a pharmaceutically acceptable salt thereof. Preferred methods of the invention comprise administering hydralazine or a pharmaceutically acceptable salt thereof and isosorbide dinitrate.

FIGURE 1.2. Abstract from the Nitromed patent.

ownership, the Nitromed patent on BiDil suggests that the sociological conception of a person is susceptible to patenting.

As I explain in Chapter 3 the use of the term "black patient" creates a tenuous foundation for the patent, certainly more tenuous than Myriad's claim to the "breast cancer gene." Nonetheless, the Nitromed patent, like the Myriad patent, illustrates how the abstraction of a patent is used to intersect with understandings of the human person. The motivation is one of commercialization, which opens up the salient question of the relationship between markets and persons – another focus of inquiry for this book. Furthermore, there have been nearly a thousand patents in the wake of the Nitromed patent that purport to cover inventions aimed at particular self-identified racial and ethnic groups, such as Asian Americans and Latinos. The Myriad and Nitromed patents are useful twins, one covering genetic understanding of the person, the other sociological. Of course these two understandings might intersect. In the European Union, for example, Myriad has a patent covering a special form of the breast cancer gene as it exists in Ashkenazi-Jewish women.[11]

[11] Sabine Steimle, "Critics Question BRCA2 Patent Decision in Europe," 97 (18) *Journal of the National Cancer Institute* 1326 (Sept. 21, 2005).

The quote by President Obama that begins this chapter shows how the genetic and sociological views of identify can easily be elided. When he refers to his "genetic makeup," President Obama is not speaking literally. The quote is from his famous speech in which he distanced himself from the racialist views of his minister, Reverend Jeremiah Wright. The brilliance of the speech was to highlight the historical and cultural contingencies of race. President Obama simultaneously questioned the use of race as a fixed, immutable category and emphasized the reality of race in framing the historical reality of race that shapes contemporary relations. His use of the phrase "genetic makeup" highlights this contingency. President Obama is not saying there is such a thing as a "black gene," a phrase that confuses the sociological with the biological. Instead, the genetic makeup is a reference to a litany of contingencies. Who we are genetically depends on who our parents are, and their meeting and joining was not inevitable. Conception and fetal development are also subject to accidents, with the early stages of cellular division having several possible pathways. But the final accumulation of these contingencies produces an identity that we take as natural and, at some level, unchanging. The danger, of course, is that some may read a phrase like "genetic makeup" literally, and this book attempts, in part, to prevent dangerous conclusions like that.

My goal is to provide a more coherent framework for assessing the types of patents illustrated by my two starting examples of Myriad and Nitromed. I am not suggesting that such patents should be forbidden. In my opinion, Judge Sweet overstated the case in his decision. My concern is with the casual intrusion of patent law into the realm of personal identity. I am troubled by this intrusion partly because we do not fully understand it. For example, it is too easy conceptually to start reducing a person to one's genes. As history has shown, this conceptual move is particularly pernicious when a person's racial or ethnic identity is viewed as genetic.[12] At the same time, we are beginning to understand that the gene itself is not fixed and unchanging and can be shaped by environmental factors. Furthermore, certain diseases are more prevalent in certain groups. It is important that scientific and medical communities address these differences. Otherwise, disease prevention will focus solely on the majority. The goal of this project is to open options for improving the lives of persons in a responsible and thoughtful manner. With this goal in mind, this book should be read as the starting point for a discussion, rather than as the final word in it.

[12] Victoria F. Nourse, *In Reckless Hands: Skinner v. Oklahoma and the Near Triumph of American Eugenics* (New York: W.W.Norton & Co., 2008) 124–126.

WHY PATENTS?

I have described patents as an abstraction, but patents can have tangible and concrete effects. Under current usage, a patent is a grant from a national government to an individual or a group of individuals that allows the patent owner to prevent others from making, using, selling, or importing an invention. But patents have deep historical roots. Patents were at one point granted by the sovereign, namely the monarch, on any item. There were patents on different spices, on playing cards, on gaming devices. A grant of land was also referred to as a patent. The key meaning of the word "patent" follows from its Latin roots. A patent is and was an "open" grant, as opposed to a secret one.[13] The sovereign made a pronouncement and the individual received this exclusive set of rights, protected by the crown. In 1624, with growing concern over the monopoly and market privileges bestowed by patents and general discontent with the power of the monarch, the English parliament enacted the Statute Against Monopolies, designed to limit the power of the crown to grant the privileges of patents for the manufacture and selling of particular products. The Statute limited these grants to those covering inventions and grants related to copyrights, or the printing privilege. It is from the Statute of Monopolies that the relationship between patents and inventions originates in the Anglo-American legal tradition.[14] As this brief history suggests, patents are abstractions, essentially sovereign pronouncements, but they have economic and political implications.

With the formation of nation-states and the development of democratic market economies, the understanding of patent law changed from a strict grant from the sovereign to a property right for which an inventor would apply with a respective government agency that had the responsibility to ensure that property rights were granted to appropriate inventions.[15] The agency, or the patent office, would enforce the patent statute that provided the legal requirements for an invention. While there are slight differences across countries in these legal requirements, they generally reduce to five:[16] (1) patentable subject matter, or the product of some useful art or industry; (2) utility, or having some practical application; (3) novelty, or not previously existing;

[13] Erich Kaufer, *Economics of the Patent System* 1 (1989).
[14] Idem. at 8–9.
[15] Suzanne Scotchmer, *Innovation and Incentives* (Cambridge, MA: The MIT Press, 2004) 11–14.
[16] Shubha Ghosh et al., *Intellectual Property: Private Rights, the Public Interest, and the Regulation of Creative Activity* (St. Paul: Thomson West, 2010) 258–260.

(4) nonobviousness, or a substantive step beyond previous inventions; and (5) enablement, or the requirement that the invention be described to the public. At a very simplistic level, a patent is still a grant from the sovereign, but modern patent grants occur in a technically and legally rich environment of administrative review and decision making. Furthermore, this grant is supported by a judicial system that serves to oversee both the function of the agencies and the enforcement of the patent owner's rights as defined under the patent statute and its judicial interpretation.

As part of a legislative enactment, the modern patent has many justifications. A common one is that of the quid pro quo: the inventor discloses the invention to the public in exchange for legal protection of rights in the invention from those who make, use, sell, or import the invention without the patent owner's permission.[17] Under this justification, the public benefits from the incremental knowledge, and the patent owner is free to make the disclosure without the concern of having the invention be misappropriated. Another contemporary justification for a patent is as a reward for invention.[18] Under this view, the promise of a patent motivates inventors to apply their labor to produce whatever the legislature has deemed worthy of a patent. Once the inventor produces something that meets the requirements of a patent, the resulting grant of legal rights rewards the inventor for his or her efforts. The final justification for a patent is as a tool for commercialization.[19] Once an inventor obtains a patent on an invention, the exclusive rights allow the inventor to commercialize the invention and thereby disseminate it to the public. Referred to as a prospecting theory of patents, this justification emphasizes not only the reward that comes to the patent owner in the form of profits from commercialization, but also the benefit to the public that arises from commercial dissemination.

These three modern justifications for patent law – disclosure, reward, and prospecting – frame the legislative debates over the enactment and reform of patent statutes and doctrines. It is possible for each of these separate justifications to be valid. For example, with respect to patents on genetic sequences, the disclosure theory would justify patents as a means of educating the relevant research audience about identified genetic sequences. The reward theory would support such patents as an incentive for research on genetic sequences.

[17] *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 161 (1989). The Court called it the "congressionally mandated price for disclosure" paid by the public. Idem. at 152.

[18] See note 14 to this chapter at 98–99.

[19] Edmund W. Kitch, "The Nature and Function of the Patent System," 20 *J.L. & Econ.* 265, 267–271 (1977).

Finally, the prospecting theory would justify these patents as tools to aid in the commercialization of the invention, such as through the creation of diagnostic tools like the ones marketed by Myriad.

Although the three justifications may differ little in the practical implications for patents, they can differ in justifying the scope and details of patent rights. The disclosure justification would focus on patent rules that promote the dissemination of the teaching of the invention. The reward justification would support a sufficient scope that would provide the appropriate reward for the invention. Finally, the prospecting theory would support fairly broad and strong patent rights so as to allow the patent owner to earn a return from as many commercial applications of the invention as possible. Perhaps the one point of patent law on which all three justifications would converge is the time limitation for the rights. Unlike other property rights, such as for land, water, or personal items, each of which recognizes rights that last forever, the patent right is time limited to reflect the fact that ultimately the public is the beneficiary of the invention. So, under the disclosure justification, the teaching falls into the public domain for anyone to use after some time. Similarly, under the reward justification, the patent right expires so that the inventor has the incentive to move on to create other inventions. Finally, the prospecting justification also supports time-limited patent rights so that new inventions can come into the market and supplant the old one. In their unique ways, each justification for patent law promotes invention and progress in society and in the marketplace.

The abstraction of patent law has concrete applications and implications for how society is structured and how progress is deemed to occur. But even these concrete implications betray an antihumanistic bias. Innovation and progress are big concepts, hard to bring to human scale. But there is a humanistic side to patent law that informs the policy debates over the scope and limits of patent rights. Judge Sweet implicitly invokes this humanistic element in rejecting patents on genetic sequences as effectively creating property rights in a person. Even the Federal Circuit, which overruled Judge Sweet's decision in part, recognized the humanistic side of patents in disallowing patents for mental processes, for what goes on in a human mind. The battles over BiDil and personalized medicine, as we will see, also evince the humanistic side of patents by demonstrating the incidence of disease among different demographic groups.

Two broader theories of patent rights encompass the three justifications for patents discussed earlier and also inform a humanistic understanding of inventions and patent law. The first broad theory is the labor theory, which