CQ Researcher

90th Anniversary 1923-2013

Published by CQ Press, an Imprint of SAGE Publications, Inc.

www.cqresearcher.com

Patenting Human Genes

Should the Supreme Court uphold patents on human genes?

The Supreme Court is set to decide by the end of June a case challenging a Utah company's patents on two breast-cancer genes that can indicate heightened risks of breast or ovarian cancer. Myriad Genetics has used its gene patents to maintain a monopoly on the lucrative market for genetic testing among women worried about a family history of breast cancer. Backed by patent lawyers and other biotech firms, the company argues that gene-related patents provide financial incentives for medical research, but women's health advocates say Myriad's aggressive use of its patent rights has made it harder and more expensive for women to have genetic testing. The case drew added attention this month when the actress Angelina Jolie revealed that she had undergone a preventive double mastectomy after testing positive for a defective breast cancer gene.

A demonstrator stands outside the U.S. Supreme Court on April 15, 2013, as the justices prepared to hear arguments on the highly charged issue of whether human genes can be patented. Myriad Genetics is defending its patent rights before the court in a closely watched case brought by a coalition of scientists, clinicians, patients and women's health groups.

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Cover: AFP/Getty Images/Mladen Antonov

CQ Researcher

May 31, 2013
Volume 23, Number 20

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CQ Researcher (ISSN 1056-2036) is printed on acid-free paper. Published weekly, except: (March wk. 5) (May wk. 4) (July wk. 1) (Aug. wks. 3, 4) (Nov. wk. 4) and (Dec. wks. 3, 4). Published by SAGE Publications, Inc., 2455 Teller Rd., Thousand Oaks, CA 91320. Annual full-service subscriptions start at $1,054. For pricing, call 1-800-818-7243. To purchase a *CQ Researcher* report in print or electronic format (PDF), visit www.cqpress.com or call 866-427-7737. Single reports start at $15. Bulk purchase discounts and electronic-rights licensing are also available. Periodicals postage paid at Thousand Oaks, California, and at additional mailing offices. POSTMASTER: Send address changes to *CQ Researcher*, 2300 N St., N.W., Suite 800, Washington, DC 20037.

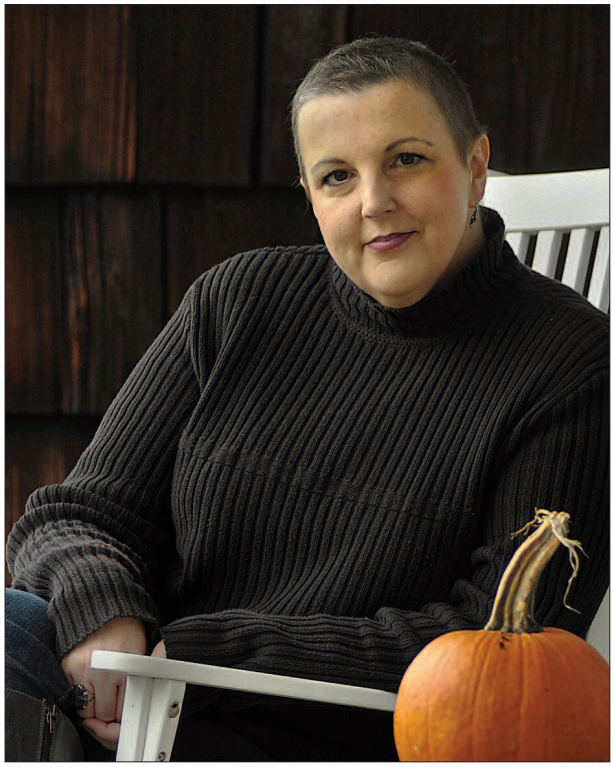
Patenting Human Genes

BY KENNETH JOST

THE ISSUES

Kathleen Maxian has been fighting advanced ovarian cancer for nearly four years and, all the while, blaming a Utah biotechnology company for causing her to fall victim to the disease.

The source of Maxian's anger at the firm can be traced back two decades, when a University of Utah researcher, Mark Skolnick, headed a team that isolated a gene that sometimes carries a mutation linked to heightened risks for breast and ovarian cancer. Myriad Genetics, a biotech company founded by Skolnick, obtained patents on the gene — dubbed BRCA1 for "BreastCancer1" — and the later-discovered gene BRCA2. The patents block other companies from using the genes and thus enable Myriad to control the lucrative market for genetic tests that four years ago showed both Maxian and her younger sister carried the defective gene.



Dan Cappellazzo

Kathleen Maxian, who has advanced ovarian cancer, says her illness could have been prevented if she had had more complete information about her sister's cancer diagnosis. Maxian blames Myriad Genetics for what she construed as a policy blocking her sister from receiving a second genetic screening for breast and ovarian cancer. Myriad denies it had such a policy and is fighting accusations that it has used its human-gene patents to limit genetic research and access to testing.

Myriad is now defending its patent rights before the U.S. Supreme Court in a closely watched case, *Association for Molecular Pathology v. Myriad Genetics*, brought by a coalition of scientists, clinicians, patients and women's health groups represented by the American Civil Liberties Union (ACLU). They contend that the U.S. Patent and Trademark Office (PTO) was wrong to issue patents for human genes and that Myriad has used the patents to limit research on the genes and access to testing. "The government should not be granting private entities control over something as personal and basic to the human body as our genes," the ACLU says on its Web page about the case. [1]

Myriad counters that the discovery of the genes was a scientific breakthrough entitled to patent protection, just like thousands of other gene-related discoveries, and that the company has been at the forefront ever since of promoting research and advancing genetic testing. Patents provide needed incentives, Myriad says, for biotech companies to invest "the hundreds of millions of dollars and decades of time to develop groundbreaking medicines and diagnostics that have saved and enhanced countless lives." Similar arguments were made in supporting briefs filed in the Supreme Court by, among others, trade associations for the biotech and pharmaceutical industries and several patent bar organizations.

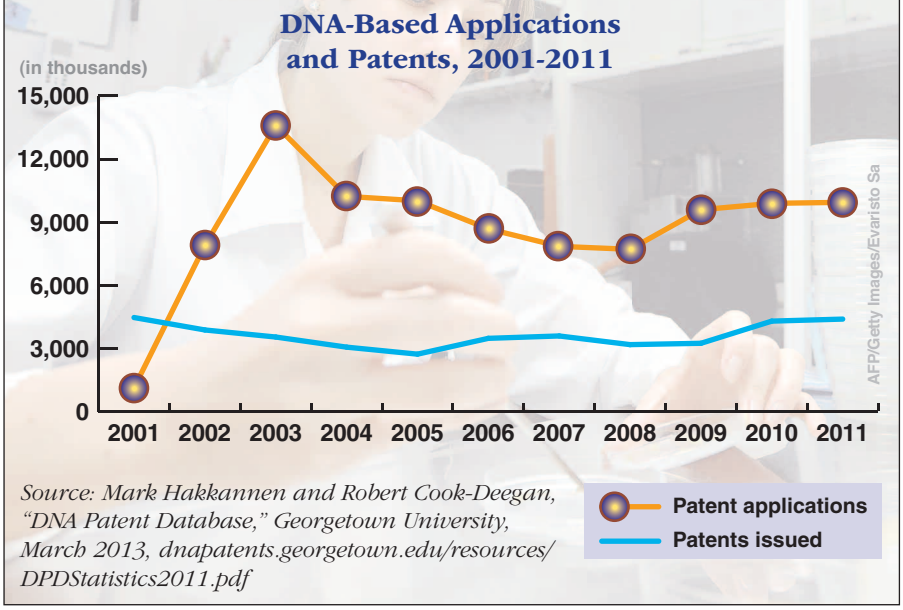
Maxian, who lives near Buffalo, N.Y., with her husband Tom, had never heard of BRCA before her sister, Eileen Kelly, who lives in Atlanta, was diagnosed with breast cancer in 2007 at the relatively young age of 40. Breast cancer at that age is often genetic, so Kelly's doctors suggested genetic testing — but the results were negative.

For Maxian, then 45, the test's failure to find anything dispelled worries that she was genetically at risk of breast or ovarian cancer. Just two years later, however, Maxian was diagnosed with advanced-stage ovarian cancer. When her doctor heard about Kelly's genetic screening, she questioned the results and suggested Kelly be given a second test to look for a separate mutation not covered by the earlier screening.

The second test came back positive. Maxian then followed with her own genetic screening, which likewise was positive for the mutation. Already upset, Maxian became angry when she learned that her sister could have been given the second genetic test earlier but for what she understood was Myriad's rule at the time limiting it to people with a close relative who had had either breast or ovarian cancer. Today, Maxian says she would have had a genetic test earlier herself if she had had more complete information about her sister; with her own results, Maxian says she then would have decided to have a precautionary hysterectomy, as many doctors recommend in such circumstances. "My cancer

DNA-Based Patents Climbing

Of the more than 100,000 DNA-based patent applications submitted to the U.S. Patent and Trademark Office, more than 63,000 have been approved. The numbers of such applications filed and patents issued each year have climbed steadily since 2008 with nearly 4,400 patents issued in 2011. The highest number of DNA-based patent applications filed in one year was 13,603, in 2003.



Source: Mark Hakkannen and Robert Cook-Deegan, "DNA Patent Database," Georgetown University, March 2013, dnapatents.georgetown.edu/resources/DPDStatistics2011.pdf

could have been prevented," Maxian says. She went so far as to call Myriad's customer service line to complain, but said she was told that Kelly had not met the "criteria" in 2007 for the second test.

Myriad spokesman Ronald Rogers says the second test is for patients with a high prevalence of breast or ovarian cancer in their families, but the company never had a policy of declining to offer the second test if requested. [2]

Maxian briefly considered suing Myriad, but a lawyer said she had no basis for a suit since she herself had not been Myriad's patient back in 2007. Two years later, however, the ACLU put the company in a higher-stakes legal fight by filing a federal suit in New York City seeking to invalidate the patents that Myriad had obtained in the 1990s.

The suit filed by the ACLU in May 2009 put Myriad in a defensive posture 180 degrees different from the public acclaim it had gained with the discovery of the first of the breast cancer genes in 1994. The discovery was heralded as opening the door to genetic testing that could alert at-risk women to the need for more attentive cancer screening and reassure others about needless fears of genetic predisposition to the disease. [3] (*See sidebar, p. 478.*)

With a Supreme Court decision in the case due by the end of June, genetic screening made big news in mid-May when actress Angelina Jolie disclosed she had undergone a preventive double mastectomy because she carries the defective BRCA1 gene. Jolie's disclosure in a May 14 op-ed article in *The New York Times* renewed attention to Myriad's control of the test for the gene even as women's health advocates and others discussed the pros and cons of genetic screening and treatment options for women at risk. [4] (*See sidebar, p. 484.*)

The advances in genetic diagnostics trace back to the discovery in the 1940s and '50s of DNA (deoxyribonucleic acid), its structure and its role in heredity.* The U.S. patent office took a lead role in the biotech revolution of the late 20th century after a 1980 Supreme Court decision that first allowed patent protection for bioengineered micro-organisms. [5]

The number of DNA-related patents grew from a trickle in the 1980s to a steady and sometimes surging stream since the late 1990s. An unofficial data base counts more than 63,000 DNA-related patents issued through June 2012.

Myriad's breast cancer gene patents helped it develop genetic tests that grew over time into what is now a $400 million annual business. (*See graphic, p. 480.*) The integrated BRAC Analysis® test — which combines the two previously separated tests that were given to Maxian's sister Eileen — costs about $4,000, according to Myriad's Rogers. The ACLU says Myriad has used its patent to prevent others from offering the test at lower cost.

Myriad in effect says the cost issue is a red herring because most insurance policies cover the cost for eligible patients — those with a family history of breast or ovarian cancer or those like Eileen Kelly diagnosed with breast cancer at an early age. The ACLU maintains, however, that only about 40 percent of the population is eligible for insurance coverage for the testing. The insurance issue may be partly mooted by preventive-care provisions in President Obama's Affordable Care Act that require insurers to cover the

* DNA is the molecular substance that carries genetic information in humans and virtually all other animal and plant life.

cost of genetic breast-cancer screening for women, with no copayment, "if appropriate." [6]

The cost issue is only one of the complaints that critics have been directing at Myriad since the late 1990s. Ellen Matloff, director of cancer genetic counseling at the Yale Cancer Center in New Haven, Conn., recalls that the center began offering the testing at a cost of $1,600 in 1996 but stopped after receiving a cease-and-desist letter from Myriad. More recently, Matloff asked Myriad in July 2011 to include the second breast-cancer gene test in all testing because of missed diagnoses, as in Eileen Kelly's case. Matloff says Myriad never responded, though the company does now test for both mutations in the single comprehensive screening.

"Everybody would agree that Myriad has been quite aggressive in protecting its patent," says Robert Cook-Deegan, a research professor in genome ethics, law and policy at Duke University's Institute for Genome Sciences and Policy in Durham, N.C. "The business model was basically to establish a service monopoly. In the United States, they did just that."

Rogers says Myriad's monopoly has actually helped promote access to the testing. He contrasts breast cancer screening with the far less prevalent genetic screening for colorectal cancer that is offered by 15 companies. "No one provider owns that market and is out there raising awareness and educating both physicians and patients," Rogers says. "No one has enough skin in the game to make that investment."

Myriad's breast-cancer gene patents are set to expire in 2017 and 2018, but Rogers says the company is still vigorously defending the patents because of the importance of the issue for the biotech industry generally. "We think that without a strong patent system to incentivize companies to make those investments, innovation is going to suffer," he says. But the ACLU and other critics say the patents, broadly written and vigorously enforced, actually prevent the kind of research and testing that would advance innovation. "These kinds of patents actually impede innovation," says Joseph Stiglitz, the Nobel Prize-winning economist at Columbia University, who filed an affidavit supporting the ACLU challenge in the trial of the case. (*See "At Issue," p. 489.*)

As all sides on the issues await the Supreme Court's decision, here are some of the questions being debated:

Should human genes be patentable?

The American scientist James D. Watson collaborated in the early 1950s with the British scientist Francis Crick in proposing the now-familiar double-helix structure of DNA, the molecular substance that carries genetic information in all animals and plants. Now in his 80s, Watson is an adamant opponent of patenting human genes.

Human genes are unlike any other "composition of matter" that federal law makes eligible as subject matter for patent protection, Watson argues in a friend-of-the-court brief submitted to the Supreme Court in the Myriad Genetics case. Genes carry the very information that "makes us who we are," Watson explains. "Life's instructions," he continues, "ought not be controlled by legal monopolies created by whim of Congress or the courts."

The ACLU lawyers representing the individuals and groups challenging Myriad's breast-cancer gene patents agree. "About 20 percent of genes have been patented," says Sandra Park, senior staff attorney with the ACLU's Women's Rights Project. The Myriad case illustrates the risks of allowing patent holders to limit research and access to genetic testing, she says. "We all have a stake in ensuring that scientists have the ability to examine and study and examine our genes in order to further understand our susceptibility to diseases and how we might approach treatments."

The critics of Myriad's and other gene-related patents cite the well-established legal doctrine — codified in the first section of U.S. patent law — that "products of nature" are not eligible for patent protection. But Myriad and other biotech companies argue that genetic discoveries are patentable when scientists isolate and modify genes found in the human body.

"We strongly believe that the genes we discover are synthetic chemicals created and discovered by the handiwork of man," says Myriad spokesman Rogers. "These genes do not exist in nature. It required a lot of sophisticated chemistry to discover, isolate and sequence those genes and then create the synthetic molecules that are used for diagnostic purposes."

Patent law expert Christopher Holman, an associate professor at the University of Missouri-Kansas City School of Law, agrees. "For over 100 years, we've understood that you can patent naturally occurring biological molecules by purifying them and coming up with something that has new properties," he says, referring to the patenting of chemically manufactured adrenalin early in the 20th century.

"There are thousands of patents directed to DNA and genetic inventions," says Holman, who formerly worked as a patent lawyer for biotech companies. "In this case, the question is asked: Are human genes patentable? The answer to that literal question is no, but isolated DNA molecules are eligible for patent protection."

Other health advocacy groups echo the ACLU's complaint that gene-related patents can hinder access to diagnostic testing. As one example, Miami Children's Hospital obtained a patent in 1997 covering testing for a genetic mutation linked to Canavan disease, a fatal neurological disorder found disproportionately among Ashkenazi Jews. In a brief filed in the Myriad Genetics

Myriad Genetics Wins Heated Race to Find Breast Cancer Gene

Move to seek patents defended, criticized at the time.

Mary-Claire King had big news to tell on the eve of the American Society of Human Genetics' annual convention in October 1990, so she asked the convention organizers to add her to a previously scheduled cancer symposium.

King, a geneticist already credited with having discovered the close genetic relationship between humans and chimpanzees, had spent 15 years of her professional life looking for a genetic link to breast cancer. In the summer of 1990, King and her colleagues at the University of California-Berkeley School of Public Health succeeded in finding not the gene itself but at the least its location. The elusive gene lay somewhere on chromosome 17, one of the 23 pairs of threadlike structures that carry genetic information inside human cells.

King's presentation of the findings to the genetics convention that fall came late in the evening, but hundreds of scientists were on hand, some of them alerted by a rumor that there would be something worth staying up late to hear. The news spread through the convention the next day, according to the thoroughly reported account by science journalists Kevin Davies and Michael White in their book *Breakthrough: The Race to Find the Breast Cancer Gene.* But it did not reach the public until two months later, after King's report of the finding was published in the journal *Science.* [1]

Without wasting any time, King returned to the quest for the gene itself and formed a collaboration with Francis Collins, the University of Michigan geneticist who had led the discovery of the cystic fibrosis gene in 1989. Other scientists were looking for the gene too: one team in the United Kingdom, another in Japan and another at the University of Utah led by an entrepreneurial-minded geneticist, Mark Skolnick. King's discovery intensified a race that drew increasing attention from scientists and the general public.

Four years after announcing her discovery, King had to swallow her pride and congratulate Skolnick and his team for having isolated the breast cancer gene itself. A Berkeley economics major who moved on to demography and then to genetics, Skolnick had been drawn to Utah because of the huge database available thanks to the Mormon Church's interest in collecting family genealogies.

Skolnick had one breakthrough to his credit already: a study published in 1985 showing a hereditary susceptibility to colon cancer. Through the 1980s, according to Davies and White, Skolnick explored ideas for forming a company to make money out of genetics. King's localization of the breast cancer gene gave Skolnick the focused goal he needed in 1991 to found Myriad Genetics and, with the aid of venture capitalist Kevin Kimberlin, raise $10 million in financing. The pharmaceutical firm Eli Lilly also pumped $1.8 million into the company over three years in return for an agreement to license diagnostic kits and therapeutic products resulting from any discovery.

Skolnick, who resigned from the company in February 2010, was touting the commercial application of the breast cancer

case, the Canavan Foundation notes that the hospital invoked the patent to block its plan to provide free screening for the defective gene. The dispute led to a lawsuit eventually resolved by an out-of-court settlement that allows some licensing to other centers for the genetic testing. [7]

Patent lawyers counter that legal protections for genetic discoveries are needed to give biotech companies financial incentives for the underlying research and subsequent commercialization.

In another brief in the Myriad case, lawyers for the pioneering biotech company Human Genome Sciences (HGS) say patent protections were essential to the company's discovery of new therapies for the immunological disorder lupus and for anthrax infection. "All that HGS achieved would not have been possible had it not been able to patent its gene discoveries," the brief by InHouse Patent Counsel, LLC, states. The brief notes that HGS, founded in 1992, was acquired by the pharmaceutical giant GlaxoSmithKline in 2012 for $3.6 billion.

Despite the patent office's approval of Myriad's patents on the breast cancer genes, the government is now siding with the challengers in urging the Supreme Court to invalidate them. Citing the "product of nature" doctrine, the brief filed by the solicitor general's office argues that "isolated, unmodified" DNA molecules are not patentable. But the brief would allow patents for DNA modified in the laboratory — variously called synthetic DNA or cDNA for "complementary DNA."

Synthetic DNA offers potential for treating diseases with drugs that in effect correct or circumvent genetic defects in the body. Myriad argues in its brief that cDNA is patentable, while the ACLU argues that it is not but that the court need not decide the issue. One patent lawyer who predicts a decision along the lines of the government's position says the impact of such a ruling would be somewhat limited.

A ruling to invalidate patents like Myriad's on isolated DNA molecules would be "bad" for current patentholders, according to Andrew Torrance, a professor at the University of Kansas School of Law in Lawrence, but many of those patents — including Myriad's

gene even before it was found. A press release in April 1994 described genetic testing as "a multi-billion dollar market opportunity for the Company." Over the summer, Myriad moved closer to realizing the opportunity as Skolnick's research team succeeded in identifying a genetic mutation common to families with a high prevalence of breast cancer.

Skolnick submitted a paper with the findings to *Science* on Sept. 2, 1994, but the news did not hold. NBC science reporter Robert Bazell got wind of the discovery and — despite pleas from Skolnick and others to wait — broke the story for the NBC "Nightly News" on Sept. 13. Once newspapers had time to catch up, the story was "plastered" all over the front pages, Davies and White write. [2]

The National Institutes of Health — which had given Myriad $5 million in grants, including more than $1 million specifically earmarked for breast cancer gene research — held a press conference the day after the NBC story to discuss the discovery. Among those in attendance was Collins, by then the director of the National Human Genome Research Institute. "This is a very exciting day," Collins said. King was also gracious when asked for comment later. "This is beautiful work," she was quoted in *Science* as saying. "These guys deserve their success." [3]

Davies and White noted that Myriad's applications to patent the two breast cancer genes, BRCA1 and BRCA2, still pending when their book was published, were controversial. [4] "If it's not patented," Skolnick argued, referring to BRCA1, "you won't get some group to spend money to develop it, and you won't get a high-quality, inexpensive test."

British researchers who had lost the race to find the gene disagreed. "I don't think it is appropriate for [BRCA1] to be owned by a commercial company," Michael Stratton, who was with the Institute of Cancer Research at the time, said. Stratton had collaborated with Skolnick's team in isolating BRCA2, but the partnership dissolved over the patent issue.

A U.S. breast cancer activist also criticized the proposed patents. "Women gave their blood for this research," Fran Visco, then president of the National Breast Cancer Coalition, said. "I know many of these women, and they didn't give blood so some company could make millions of dollars."

— Kenneth Jost

[1] J. M. Hall, *et al.*, "Linkage of early-onset familial breast cancer to chromosome 17q21," *Science*, vol. 250, 1990, pp. 1684-1689, cited in Kevin Davies and Michael White, *Breakthrough: The Race to Discover the Breast Cancer Gene* (1996), p. 5. Other background also drawn from book.

[2] The findings were published in two papers in *Science*, vol. 266, 1994: Y. Miki, *et al.*, "A strong candidate for the breast and ovarian cancer susceptibility gene BRCA," pp. 66-71, and A. Futreal, *et al.*, "BRCA1 mutations in primary breast and ovarian carcinomas," pp. 120-122. Davies and White, *op. cit.*, cite front-page stories in *The Boston Globe*, *The New York Times* and *The Philadelphia Inquirer*. See p. 298.

[3] See R. Nowak, "Breast cancer gene offers surprises," *Science*, vol. 265, 1994, pp. 1796-1799.

[4] Davies and White, *op. cit.*, pp. 224-226.

— are set to expire after 20-year terms in the near future. Patents for synthetic DNA are more important, he explains. "The real action today," Torrance says, "is in synthetic biology."

Should the U.S. patent office have stricter rules for issuing DNA-based patents?

Despite approval from the U.S. patent office, Myriad Genetics ran into trouble when it applied for a similar patent for the breast cancer genes in Europe. The European Patent Office (EPO) initially approved the application in 2001, but revoked it on the basis of opposition from research institutes and genetics societies that complained of Myriad's restrictions on research and testing. After seven years of litigation, the EPO reinstated the patent, but only after significantly narrowing it. [8]

The EPO's action was in line with European patent experts' long-held view that the U.S. Patent and Trademark Office had been "over-generous" in granting gene patents in the 1990s. [9] Supreme Court Justice Elena Kagan voiced the same thought during the April 15 arguments in the Myriad Genetics case when she described the PTO as "patent-happy."

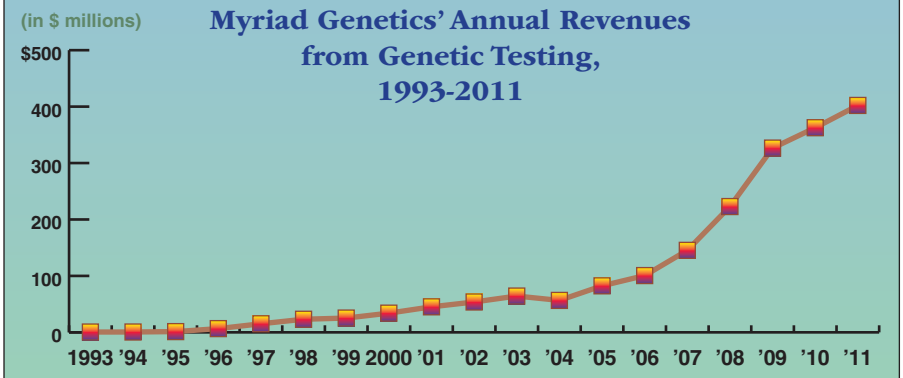
Many U.S. lawyers and experts agree. "I do think the USPTO is patent-happy," says Kali Murray, an assistant professor at Marquette University Law School in Milwaukee, who filed a brief supporting the challengers in the Myriad Genetics case. "I think most people who cover the USPTO think that. They have a sort of institutional bias toward patenting."

Others, however, think the PTO has been faithfully following patent law. Holman, the Missouri law professor, notes that the Supreme Court has endorsed the broad phrasing that patents can extend to "anything under the sun that is made by man." * "The PTO has been following the rules that they believe exist," Holman says. "The PTO

* P. J. Federico, the longtime head of the patent office, used the now familiar phrase in testimony before Congress during the 1952 overhaul of the Patent Act. The Supreme Court cited it in its precedential decision, *Diamond v. Chakrabarty* (1980), approving patents for bioengineered micro-organisms.

Myriad Genetics' Revenues Soar

Utah-based Myriad Genetics generated more than $400 million in revenue from genetic testing in 2011, more than a 700-fold increase from 1993. Medical associations, doctors and patients have sued the company over what they contend are invalid patents on genes related to breast and ovarian cancer.



Source: Lane Baldwin and Robert Cook-Deegan, "Constructive Narratives of Heroism and Villainy: Case Study of Myriad's BRACAnalysis® Compared to Genentech's Herceptin®," Genome Medicine, January 2013, genomemedicine.com/content/5/1/8

has been reluctant to be a policy-making body."

Despite some differences on the Myriad Genetics case itself, several experts say today that the PTO gave too little consideration in the 1980s and '90s to the scope and the likely impact of the gene-related patents it was approving. "There wasn't much hesitation in allowing patents on genetic discoveries until quite late in the day," says Rebecca Eisenberg, a professor at the University of Michigan Law School in Ann Arbor. "These patents flew under the radar for a long time."

The PTO thought the patents were "relatively noncontroversial" at first, according to Cook-Deegan, the Duke professor. The patent office "was not only granting patents, they were granting broad claims."

Patent claims are the operative provisions that patent-holders employ to police the use of their inventions. Myriad's breast-cancer gene patents, for example, have a total of more than 500 claims, according to spokesman Rogers, but only nine of those are before the Supreme Court. In their brief, however, the ACLU lawyers contend that Myriad's claims on the genes themselves "reach all possible uses of the claimed genes," including research by other scientists.

Cook-Deegan echoes the concerns about further research. The disputed claims are "extremely broad," he says. "In effect, they say you can't study these genes." Rogers disputes the accusations, pointing to the thousands of articles about the BCRA genes found on the medical journal data base *Pub Med*. "These are the most studied genes in history," says Rogers. "Any allegation that we have blocked research is just false."

The ACLU's decision to attack Myriad's patents on so-called "subject matter" grounds means that the specific claims in the patents have not been litigated. "None of the claims has been 'construed,' " says Arti Rai, a Duke law professor, using patent law jargon. "There are gene-related patents that shouldn't have been granted as broadly as they should have been," Rai adds.

Rai, who served as the PTO's administrator for policy and external affairs in 2009-2010, points to the Europeans' decision to narrow Myriad's patents. "In Europe, they restrict the scope to the particular mutation that Myriad found," Rai explains. "That makes the patent much less threatening."

Should holders of gene patents be required to license their use by others?

Francis Collins was already a successful gene hunter when he and researchers at Toronto's Hospital for Sick Children succeeded in 1989 in discovering a gene linked to cystic fibrosis (CF). Collins, then a professor at the University of Michigan in Ann Arbor, obtained a patent on therapy derived from the discovery, assigned it to the university and, along with his collaborators, insisted the discovery be available to any laboratory interested in offering testing.

Collins, now director of the National Institutes of Health (NIH), has continued to argue for wide availability of genetic discoveries throughout his career. "You don't want to put toll booths on basic science," Collins said in a talk in 1999. In his book *Language of Life*, published in 2009, Collins contrasted his decision regarding the CF gene with Myriad's decision to challenge any laboratory that wanted to offer testing for the breast cancer gene. [10]

Under current U.S. law, patent holders have virtually complete freedom in deciding how widely to "practice" their patents — the term used in the field — or to license them for others to use. Federal law has a few "compulsory license" provisions allowing the government to require a patent holder to license a patent for others to use, but the only one directly relevant to the gene patent debate has never been enforced.

The so-called "march in" provision of the Patent and Trademark Law

Amendments of 1980 — commonly called the Bayh-Dole Act, after its principal Senate sponsors — allows a federal agency that has helped fund research resulting in a patent to require the patent holder to license it to others. The government can exercise the power only if at least one of four criteria is met, including failure to satisfy health needs of the patent holder's customers. NIH has been asked to exercise that power four times, and each time it has declined. [11]

Myriad's policy of refusing to license its breast cancer gene patents for testing by other labs prompted several European countries to enact or expand compulsory license provisions. A Swiss law, enacted in 2004, allows a court to grant a compulsory license if the patent holder is guilty of anticompetitive practices. The Belgian law, enacted in 2005, allows the government to grant a license for use of a patent-protected invention "in the interest of public health." [12]

Any broad compulsory licensing provision in U.S. law would require action by Congress. As part of a rewrite of patent law in 2011, Rep. Debbie Wasserman Schultz, D-Fla., a breast cancer survivor herself, sponsored a provision that would have required genetic diagnostic labs, such as Myriad, to license their diagnostic-related patents to other labs to provide "confirmatory" or second-opinion testing. The proposal was backed by women's health groups, but Wasserman Schultz withdrew it after the ACLU complained it was too weak. Instead, the law — the America Invents Act — includes a provision requiring the PTO to study the impact of patents on genetic diagnostics. [13]

Some patent law experts say Congress should consider compulsory licensing provisions. "It's a policy option that ought to be on the table," says Cook-Deegan, the Duke professor. "It does create a bargaining chip in the licensing process. It's a point of pushback against really egregious business practices."

Myriad Genetics

A Myriad Genetics researcher in Salt Lake City analyzes DNA samples. Myriad says its discovery of the BRCA1 and BRCA2 breast cancer genes was a scientific breakthrough entitled to patent protection. Critics argue that the U.S. Patent and Trademark Office erred in issuing patents for human genes.

Myriad officials say the provision is both unnecessary and unwise. "There's no evidence whatsoever that a solution as dramatic as compulsory licensing is anywhere near necessary, warranted or desirable on any level," says Benjamin G. Jackson, Myriad's senior director for legal affairs. In any event, Myriad says it has licensed the breast-cancer gene test to one private company, LabCorp, and seven universities for confirmatory testing, but that the demand for second-opinion testing is low.

PTO officials heard both sides of the issue in public sessions in 2012 and 2013 but are now almost a full year late in submitting the report that Congress ordered. Any legislation to require companies to license patent-protected genetic testing, however, would certainly face strong opposition from biotech companies. "That's a nonstarter with the biotechnology industry," says Eisenberg, the Michigan professor. ■

BACKGROUND

Patenting Life

The Constitution gives Congress the power "to promote the progress of science and useful arts" by "securing" to inventors "the exclusive right to their . . . discoveries" for a limited period of time. From its earliest days, the law has authorized patent protection for "any

new and useful" devices, compositions or processes. Patents were awarded for living organisms as early as the 19th century and for isolated human hormones in the 20th century. Those patents, and the judicial decisions upholding them, came to be viewed as precedents for the granting of gene-related patents as the field of molecular genetics was being born in the late 20th century. [14]

The French scientist Louis Pasteur is credited with having received the first U.S. patent on a living organism in 1873 when what was then called the Patent Office awarded him ownership of a strain of yeast used in beer-making.* The patent drew little attention at the time, and the head of the Patent Office in the 1930s voiced doubt that it should have been granted. [15] In its historical overview, the congressional Office of Technology Assessment (OTA) says therapeutic patents in biotechnology were issued as early as 1895. [16]

The patentability of substances found in the human body received its first full examination early in the 20th century after Jokichi Takamine, a Japanese chemist working in the United States, isolated the hormone produced by the adrenal gland and called it "Adrenalin." The Patent Office granted him a patent in 1903. The pharmaceutical firm Parke-Davis acquired the patent and established a lucrative market for the product; other companies followed, and a patent infringement suit ensued. The suit was tried in federal court in New York City before a then recently appointed judge, Learned Hand, later recognized as one of the century's greatest jurists.

In the crucial passage upholding the patent, Hand wrote in 1911 that the extracted hormone "became for every practical purpose a new thing commercially and therapeutically." The decision, according to Brooklyn Law School patent expert Christopher Beauchamp, was "a watershed in both biomedical research and in patent practice."

Patents for other isolated hormones followed — most notably, insulin, in 1923. By the 1930s, patents for hormones were well established, according to Beauchamp, even though the Patent Office became stricter in other contexts in applying the "product of nature" rule to reject patent applications. Hand's opinion, little noticed at the time, was to become a century later a focal point of the legal debate over patenting human genes. [17]

The science of genetics dates back to the study of heredity in plants and animals by the mid-19th century Austrian monk Gregor Mendel; it advanced step by step in the early 20th century as researchers turned to studying heredity in humans. The study of molecular biology resulted in two crucial advances in mid-century. In 1944, three scientists at the Rockefeller Institute in New York — Oswald Avery, Colin McLeod and Maclyn McCarty — demonstrated the role of DNA in carrying inherited genetic information. A decade later, in 1953, Watson and Crick proposed DNA's double-helix structure. Their work set the stage for understanding how genetic instructions are passed from generation to generation through copying of the DNA molecule. Crick later wrote that he and Watson speculated about determining the full sequence of DNA but concluded — wrongly, as it turned out — that the task would take "centuries." [18]

Watson and Crick were asked at the time whether they could patent their discovery, but they thought they could not meet the patent law requirement to show it was useful. [19] Two decades later, in 1974, however, biochemists Stanley Cohen at Stanford University and Herbert Boyer at the University of California-San Francisco (UCSF) applied for a patent for their method of splicing DNA molecules from different organisms — "recombinant DNA technology," as it came to be known. The application provoked debate in the scientific community and beyond, but the PTO finally approved the patent on Dec. 2, 1980. Historian Sally Smith Hughes describes it as the first major patent in the new biotechnology. [20]

For Stanford and UCSF, the patent proved to be a gold mine. Over the 17-year life of the patent, Stanford granted 468 licenses for commercial application of the technique, generating more than $255 million in revenue for the two schools. For Boyer, it provided the opening to team with venture capitalist Robert Swanson in forming the first major biotech company: Genentech — short for genetic engineering technology. Still, Watson, a critic of patent policies, praises Cohen and Boyer for making the gene-splicing technology widely available at a low cost and for donating part of their share of the proceeds to their schools. [21]

Six months before the issuance of the Cohen-Boyer patent, the Supreme Court had made its own seminal contribution to biotechnology law by upholding for the first time a patent for a genetically modified living organism. Working for General Electric, microbiologist Ananda Chakrabarty developed a bacterium capable of breaking down crude oil — useful in combating oil spills. The PTO approved Chakrabarty's patent claims for the processes he developed for producing the bacterium but refused to allow a patent for the bacterium itself because it was a "product of nature." In a 5-4 decision, however, the Supreme Court ruled that the micro-organism itself could be patented. For the majority, Chief Justice Warren E. Burger explained that Chakrabarty had created "a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility." [22]

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* The Patent Office was renamed the Patent and Trademark Office as of Jan. 2, 1975.

Chronology

1900-1970

Patents allowed for human hormones; DNA discovered.

1911
Federal judge upholds patent for manufactured adrenalin.

1944
Rockefeller Institute scientists demonstrate role of DNA in carrying genetic information.

1953
American James D. Watson and Briton Francis Crick propose double-helix structure of DNA, tie it to transmission of genetic data.

1970s-1980s

Supreme Court rules genetically modified microorganisms eligible for patents.

1974
California biochemists Stanley Cohen and Herbert Boyer apply for patent for gene-splicing method ("recombinant DNA technology"); patent granted in 1980, but technology liberally licensed.

1976
Genentech, pioneering biotechnology company, founded by Boyer and venture capitalist Robert Swanson.

1980
Supreme Court upholds patent for genetically modified organism used to combat oil spills. . . . Patent and Trademark Law Amendments Act allows universities, small businesses and nonprofits to obtain patent rights for inventions made from federally funded research.

1987
Project to map the human genome is launched; Watson is chosen in 1989 to head it.

1989
Cystic fibrosis gene is isolated by researchers from University of Michigan, Toronto children's hospital.

1990s

Clash over patenting human genes; breast-cancer genes isolated, patented.

1990
U.S. geneticist Mary-Claire King locates breast cancer gene on chromosome 17; researchers step up race to isolate gene.

1991
National Institutes of Health (NIH) biologist files application to patent gene fragments. . . . University of Utah geneticist Mark Skolnick founds Myriad Genetics with plans to commercialize genetic testing.

1992
Watson is forced out as genome project director in dispute over gene patents. . . . Patent office rejects patents for gene fragments.

1994
Skolnick's research team in Utah confirms isolation of breast cancer gene (BRCA1); company applies for patents for BRCA1 and later-discovered BRCA2.

1997, 1998
U.S. patent office approves Myriad Genetics patents for BRCA1/2.

2000-Present

Breast cancer gene patents challenged in court; Supreme Court ruling awaited.

2000
President Bill Clinton, British Prime Minister Tony Blair announce human genome has been mapped.

2001
U.S. Patent and Trademark Office (PTO) reaffirms patent eligibility for human genes if new and useful purpose is shown.

2007
Science fiction novelist Michael Crichton argues against patenting human genes in op-ed essay.

2009
Coalition of scientists, physicians, patients and others, represented by American Civil Liberties Union, files federal suit challenging Myriad's breast cancer gene patents; plaintiffs win ruling by federal district court in 2010, lose at U.S. Court of Appeals for Federal Circuit in 2011, again in 2012.

2010
Federal advisory committee recommends testing, research exemptions for gene-related patents; three members dissent.

2011
America Invents Act directs U.S. PTO to study effect of patents on second-opinion genetic testing.

2013
Supreme Court hears arguments in Myriad Genetics case (April 15); decision due by end of June. . . . Actress Angelina Jolie discloses that she had preventive double mastectomy after testing positive for defective breast cancer gene.

Angelina Jolie's Revelation Stirs Praise, Caution

"People should not be quick to say, 'I should do like she did.' "

Angelina Jolie, the actress, director and goodwill ambassador for the U.N. High Commissioner for Refugees, watched helplessly as her mother, Marcheline Bertrand, struggled against advancing ovarian cancer for a decade until she died early in 2007 at the age of 56.

With that family history in mind, Jolie decided earlier this year to have a genetic screening. The results showed that she carries the defective BRCA1 gene, indicating a high likelihood of developing breast cancer and a 50/50 chance of developing ovarian cancer.

Armed with that information, Jolie, 37, decided to have her breasts removed in a preventive double mastectomy. The surgery was performed on Feb. 16 at the Pink Lotus Breast Center in Beverly Hills, Calif., with reconstructive procedures over the next two months ending on April 27. Barely two weeks later, an actress known worldwide for beauty and femininity told the world about what she called her "strong choice" to have the operation.

"My chances of developing breast cancer have dropped from 87 percent to under 5 percent," Jolie wrote in a 950-word op-ed in *The New York Times*. "I can tell my children that they don't need to fear they will lose me to breast cancer." Jolie is raising six adopted children with her partner, fellow actor Brad Pitt. She said Pitt had been with her "every minute of the surgeries." [1]

Jolie's candid story moved instantly to the top of television newscasts and online news sites. Other women followed with their own accounts of the wrenching decisions to have their breasts removed in order to prevent a disease that claims about 40,000 women's lives in the United States each year. At week's end, *People* magazine hit the newsstands and grocery store checkout displays with a cover promising to take readers inside Jolie's "brave choice." [2]

Breast-cancer advocates helped lead the chorus of praise for Jolie's decision to go public with her story. But some advocates, experts and physicians who joined in the coverage also raised concerns that the news could help fuel a trend toward unnecessary mastectomies. "Angelina's situation is very unique," Dr. Isabelle Bedrosian, a surgical oncologist at M.D. Anderson Cancer Center in Houston, told *The New York Times*. "People should not be quick to say, 'I should do like she did,' because you may not be like her." [3] Other preventive steps include more frequent mammograms or MRIs.

Only about 5 percent of the estimated 220,000 newly diagnosed breast cancer cases each year are attributable to one of the two defective BRCA genes, according to experts. The

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Patent Races

Both Congress and the PTO adopted policies beginning in the 1980s aimed at commercializing the scientific discoveries being made in university and corporate labs, sometimes with federal funding. Patents played a major role in the biotech industry's explosive growth; they became a major source of work at the patent office and later a source of costly, high-stakes litigation in the courts. Critics in the scientific and public-interest communities opposed the widening scope of so-called life-form patents. As the new century opened, however, the PTO issued guidelines reaffirming the patentability of human genes if they were isolated from the body and new uses were specified and disclosed.

Congress set the tone for the era by passing the Bayh-Dole Act to allow universities, small businesses and nonprofits to retain ownership of patents obtained through federally funded research. Lawmakers were told that the previous practice of awarding patents to the sponsoring federal agency had resulted in only limited application or commercialization of scientific breakthroughs. President Ronald Reagan issued an executive order in 1987 that allowed larger businesses as well to obtain patents for their federally funded research. The law's "march-in" provision allowing the government to force patent holders under some conditions to provide access to the invention drew little attention at the time. [23]

The race for genetic discoveries accelerated after the government threw its weight and resources behind the project that Watson and Crick had deemed impossible in the 1950s: mapping the human genome. The project, funded by NIH and the Department of Energy, was launched in 1987 and declared complete in 2000 in a joint announcement in Washington by President Bill Clinton and British Prime Minister Tony Blair. From early on, the international project operated under policies for public disclosure of the genetic mapping information; the so-called Bermuda rules, adopted in 1996, called for labs to submit DNA sequencing information to the publicly accessible GenBank within 24 hours of discovery.

The tension between patent protection and public disclosure flared early in the 1990s when J. Craig Venter, a biologist at NIH, proposed the patenting of thousands of human gene fragments called "expressed sequence tags" or ESTs. Supported by NIH director Bernadine Healy, Venter submitted a patent application in 1991 that grew to cover

U.S. Preventive Services Task Force, an independent panel of experts sponsored by the federal Agency for Healthcare Research and Quality, recommends breast cancer gene screening only for women "whose family history is associated with an increased risk for deleterious mutations" — meaning a mother, sister or other close relative with the disease. The task force's guidelines specifically recommend against genetic counseling or screening for women without such a family history. [4]

In her account, Jolie described surgical advances in the procedure, including steps that save the nipples and reduce scarring and disfigurement. Once implants have been placed, she said, "the results can be beautiful." Jolie said she plans later to have her ovaries removed.

AFP/Getty Images/Lucy Nicholson

Actress Angelina Jolie, right, and her mother, Marcheline Bertrand, attend a premiere of Jolie's film "Original Sin" in 2001. Bertrand, an actress and producer, died in 2007 at age 56 from ovarian cancer. With her mother's death in mind, Jolie decided this year to have a genetic screening and found she carried the BRCA1 gene, indicating a high likelihood of developing breast cancer and a 50/50 chance of developing ovarian cancer. In February Jolie underwent a preventive double mastectomy.

Jolie said she hoped her account would encourage other women to have genetic testing and let them know of their options if they were at high risk. "Life comes with many challenges," she wrote in closing. "The ones that should not scare us are the ones we can take on and take control of."

— Kenneth Jost

[1] Angelina Jolie, "My Medical Choice," *The New York Times*, May 14, 2013, p. A25.

[2] See Michelle Tauber, "Angelina Jolie: 'I Made a Strong Choice,' " *People*, May 27, 2013 (forward dated), pp. 67ff. Some medical background also drawn from article.

[3] Denise Grady, Tara Parker-Pope and Pam Belluck, "Jolie's Disclosure of Preventive Mastectomy Highlights Dilemma," *The New York Times*, May 15, 2013, p. A1.

[4] "Genetic Risk Assessment and BRCA Mutation Testing for Breast and Ovarian Cancer Susceptibility," U.S. Preventive Services Task Force, www.uspreventiveservicestaskforce.org/uspstf/uspsbrgen.htm.

nearly 7,000 gene fragments. Watson, who had been chosen to head the National Genome Project, strongly opposed what he called "speculative patenting." Other scientists and much of the biotech industry similarly warned against locking up the information developed by the genome project.

Watson's clash with Healy helped lead to his forced resignation from the project in April 1992. In August, the PTO rejected the application on, among other grounds, vagueness, and a new NIH director, Harold Varmus, abandoned the application in 1994. By then, Venter had left NIH, taking a team of researchers with him, and continued to seek patents for gene fragments as he moved first to a nonprofit organization and then to what became the biotech company Celera Genomics. Biotech companies continued to apply for patents for gene fragments despite continued resistance from many scientists. The PTO sought to resolve the issue with guidelines, issued on Jan. 5, 2001, that directed examiners to grant patents on gene fragments only if the application had sufficient detail to "identify a specific and substantial utility." In commentary, however, the PTO reaffirmed that naturally occurring DNA compounds are eligible for patents "when isolated from their natural state and purified." [24]

Well before the gene-fragment controversy, the PTO had begun issuing patents for gene-related discoveries that heralded a new day in medicine and health. In one of the first major breakthroughs, Genentech, the company that Boyer had helped found, announced in 1978 that it had used recombinant DNA technology to clone a human insulin gene. The discovery was licensed to Eli Lilly, which won Food and Drug Administration (FDA) approval in 1982 to market recombinant human insulin. Genentech developed its own market for recombinant drugs, notably, human growth hormone, approved in 1986 for treating children with a form of dwarfism. [25]

The discovery of the breast cancer gene in 1994 made front-page news in coverage that emphasized its financial potential for Myriad. A *New York Times* story that described the intensely competitive race between a dozen laboratories over a four-year period noted that Myriad had filed for a patent on the gene. The discovery represented "a bonanza" for the company, the story noted. [26]

With financial stakes so high, litigation was the inevitable result of the patent races. "This is exactly what you would expect in a high-tech innovative industry," says Daniel Kevles, a patent expert at Yale Law School. In its 1989 report, the Office of Tech-

nology Assessment noted litigation already under way over, among other discoveries, human growth hormone (HGH). Genentech was to be locked in a court fight through the 1990s with UCSF over competing accounts of the source of the discovery. UCSF scientists had obtained the patent, and the university had sued Genentech for alleged infringement in marketing its HGH drug Protropin. Without admitting infringement, the company settled the suit in 1999 by agreeing to pay $200 million — with $85 million to the scientists involved and the rest to the university. [27] As Watson would later write, biology had clearly become "a big-money game." [28]

Patent Examinations

Myriad's exploitation of its breast-cancer gene patents helped stoke a growing debate over gene-related patents from the late 1990s on. Some in Congress embraced the opposition from many in the scientific community and proposed bills to bar the patenting of human genes, but they never advanced. The PTO continued to approve gene patents, but lower courts and the Supreme Court appeared to become more skeptical of patents for claimed inventions related to the human body. The ACLU's heavily publicized court challenge to Myriad's breast-cancer gene patents kept the debate going and set the stage for the Supreme Court's first full airing of the issue of patenting human genes.

The human gene patenting debate drew its most publicly recognizable participant perhaps when the best-selling science fiction writer Michael Crichton took to the editorial pages of *The New York Times* in February 2007 to oppose the practice. Crichton cited Myriad's breast-cancer gene patents as one of several approved by an "underfinanced and understaffed" patent office that patent holders had used to "halt research, prevent medical testing and keep vital information from you and your doctor." *The Times* published six letters to the editor a week later: Four seconded Crichton's views, while two others — one by a patent law attorney and the other by a noted patent law professor — disagreed. [29]

AP Photo/*The Virginian-Pilot*/Stephen M. Katz

Lisa Lane holds her 5-year-old daughter Sadie as blood is drawn for a genetic test at Children's Hospital of the King's Daughters in Norfolk, Va., on May 26, 2010. Sadie suffers from an extremely rare chromosome disorder that has led to heart troubles and an intellectual disability. The science of genetics dates back to the study of heredity in plants and animals by the mid-19th century Austrian monk Gregor Mendel.

The gene patenting debate played out as the Supreme Court and the Federal Circuit engaged in a prolonged back-and-forth about the scope of patent law. In a series of cases, the Supreme Court acted to rein in the Federal Circuit's seeming bias toward broad patent protections. In one decision that was to play a role in the Myriad case, the court in March 2012 reversed a Federal Circuit decision that had upheld a private laboratory's patent for a method of controlling medication dosage to patients with certain autoimmune diseases. Torrance, the Kansas law professor, cites the decision as one example of a general trend toward disapproving patents related to the human body. "The closer that a biotechnology is to the human body, whether it takes place within the human body or is injected into the human body, the less likely that such patents are patentable subject matter," he says. [30]

Critics of human gene patenting tried several times during the decade to limit or even prohibit the practice. Bills introduced in 2000 and 2002 would have allowed use of gene patents for research and diagnostics. A broader measure, which Crichton endorsed in his op-ed essay, would have barred patents altogether for genes found in human nature. None of those bills were

brought up for formal consideration. The gene patenting issue surfaced again in the multiyear review of the patent system that culminated with passage of the America Invents Act in September 2011. Wasserman Schultz's original proposal to exempt "confirmatory testing" from liability for patent infringement ended as merely a mandate to the PTO to study "effective ways to provide independent, confirming genetic diagnostic test activity where gene patents and exclusive licensing for primary genetic diagnostics exist." The provision went unnoticed in general news coverage of the act. [31]

The Myriad case meanwhile was making its way up and down the federal court system toward a full-scale argument before the Supreme Court. In the first court ruling, U.S. District Court Judge Robert Sweet agreed with the ACLU lawyers in ruling most of Myriad's patent claims invalid. "DNA's existence in an 'isolated' form alters neither [the] fundamental quality of DNA as it exists in the body nor the information it encodes," he wrote at the start of a 152-page opinion issued on March 29, 2010. In a footnote, Sweet minimized the possible financial impact on the biotech industry, but biotech executives and patent lawyers all warned of dire consequences from the ruling. Myriad suffered a second jolt in the fall when the government switched sides and — in a clash with the patent office — argued on appeal that patents could be allowed for synthetic DNA but not for naturally occurring DNA even when isolated from the body. [32]

Despite the government's new position, the U.S. Court of Appeals for the Federal Circuit — a Washington-based court with exclusive jurisdiction over appeals in patent cases — ruled for Myriad and upheld the breast cancer gene patents. In a 2-1 ruling issued on July 29, 2011, the appeals court sided with Myriad in concluding that its patent claims "cover molecules that are markedly different . . . from molecules that exist in nature." The court rejected Myriad's patents for the method of isolating the gene, however, saying it entailed only "abstract mental steps."

On ACLU's appeal, the Supreme Court sent the case back to the Federal Circuit for reconsideration in the light of a separate decision that appeared to rule out patents for natural processes. The Federal Circuit reaffirmed its earlier decision, however, setting the stage for the ACLU to appeal again. The Supreme Court agreed to hear the case on Nov. 30. By the time of argument, more than 40 friend-of-the-court briefs had been filed, divided roughly equally between Myriad's supporters and opponents. [33] ■

CURRENT SITUATION

Patent Office Study

The patent office is awaiting review by other government agencies of a long overdue report mandated by Congress on the impact of gene-related patents on the ability of patients to check the results of genetic screening.

PTO officials gathered sharply conflicting views on the issues in three public sessions, most recently in January, before completing a draft report within the past few months. A PTO spokesman says the report is currently going through interagency clearance. Congress had asked for the report to be finished by June 2012 when ordering the study in the 2011 patent law overhaul known as the America Invents Act.

Breast cancer activists, including the congressional sponsor of the study provision, testified in public hearings that Myriad's restrictions on screening by other laboratories prevent women from getting a second opinion if Myriad's test shows a positive result for the defective breast cancer gene. "No one should ever have to go through this experience without the comfort and the confidence of a second opinion," Rep. Wasserman Schultz said in a video played at both hearings, held Feb. 16 at PTO headquarters in Alexandria, Va., and March 9 in San Diego.

Wasserman Schultz had a double mastectomy and an oophorectomy — removal of the ovaries — after testing positive for the defective gene, but said she had no opportunity to confirm the result before deciding to undergo the procedure. The Florida Democrat said exclusive patents also limit diagnostic testing for other genetically related diseases.

Richard Marsh, Myriad's executive vice president and general counsel, countered at the San Diego hearing that allowing other laboratories to conduct "confirmatory testing" would result in a "gray market" for initial testing by unauthorized labs. That could "effectively eviscerate the exclusive provider's patent position," he warned.

Marsh also contended that insurers are unlikely to reimburse the cost of confirmatory testing. In any event, the Myriad official insisted that patients who test positive for the defective gene are more likely to want a second opinion about what to do with the results than a repeat of the test to confirm the results. [34]

Four PTO officials participated in the two public sessions, including the then-deputy director, Teresa Stanek Rea. In both sessions, Rea described the time frame for the study as "very short." Rea became acting director after David Kappos resigned effective Feb. 1.

Myriad's defense of exclusive patent rights to control genetic testing drew support from patent lawyers and other biotech companies, including a lawyer

representing the Southern California-based trade association BIOCOM. "Without robust patent protection or the ability to control licensing of their innovations, most BIOCOM member companies would never be able to financially recoup their upfront costs," San Diego attorney Leonard Svensson testified.

From the opposite side, Mary Williams, executive director of the Association for Molecular Pathology, testified at the Alexandria hearing that exclusive patent rights on genetic information "discourage rather than encourage the widespread provision of genetic testing services." "It's time for a change in policy," she said, "so that [other labs] can develop tests . . . and so that patients can fully access needed testing."

The issue got a full examination early in 2010 in a report by an advisory committee to the U.S. Department of Health and Human Services (HHS). The report by the Secretary's Advisory Committee on Genetics, Health and Society concluded that patents on genetic discoveries are unnecessary as incentives for either basic genetic research or the development of genetic tests. It also found that patents had had the effect of limiting the availability of testing or independent second-opinion testing.

The report recommended, among other steps, an exemption from liability for patent infringement for anyone making, using or selling a genetic screening test. In a dissent, three members of the advisory committee said any modification of the patent system "would be more harmful than helpful to patient access and to the quality of innovative genetic diagnostics." [35]

Six months past the original deadline, PTO officials held a third public session on Jan. 10. Rea opened the so-called roundtable by saying that officials wanted more information in order to "produce the best study possible," according to notes taken by Krista Cox, a staff attorney with the advocacy group Knowledge Ecology International. [36]

Getty Images/*Chicago Tribune*/MCT/Nancy Stone

Lindsay Avner, shown here on March 7, 2013, had a preventive double mastectomy at age 23 and has since started Bright Pink, an organization that aims to help young women facing choices about breast and ovary health. About 5 percent of the estimated 220,000 newly diagnosed breast cancer cases each year are attributable to one of the two defective BRCA genes.

Among 19 participants, 10 had not testified in the earlier hearings, including representatives of two government agencies: NIH and the National Institute of Standards of Technology. The two government witnesses noted the availability of the "march-in" provision to force licensing of patented diagnostics, according to Cox's account, but also appeared to acknowledge the need for incentives for private companies to develop genetic testing.

Supreme Court Case

The Supreme Court is due to hand down by the end of June its first ever direct ruling on the patentability of human genes after several justices appeared skeptical during oral arguments of Myriad's broadest patent rights claims.

Justices grappled with the science and the law during the hour-long argument on April 15, but several seemed skeptical of allowing a patent for a gene naturally found in the human body even if scientists had to work to isolate it. Other justices, however, voiced concerns that researchers needed the prospect of patent protections to provide economic incentives for their work. [37]

Opening the arguments for the plaintiffs, ACLU attorney Christopher Hansen challenged Myriad's right to claim any invention at all. "What exactly did Myriad invent?" Hansen asked. "The answer is nothing." Myriad "deserves credit," he continued, for having unlocked "the secrets of two human genes," but not a patent.

For the government, Solicitor General Donald Verrilli agreed that DNA isolated from the body is not patentable. Allowing the patent, he warned, "would effectively preempt anyone from using the gene itself for any medical or scientific purpose."

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Should the Supreme Court uphold Myriad Genetics' breast cancer gene patents?

BENJAMIN G. JACKSON
SENIOR DIRECTOR, LEGAL AFFAIRS, MYRIAD GENETICS

WRITTEN FOR *CQ RESEARCHER*, MAY 2013

Yes

Opponents of so-called "gene patents," and Myriad and the BRCA (breast cancer gene) patents specifically, allege they cause various harms, including inhibiting innovation and harming patient access to quality health care. These allegations have been passed along without proof or concern whether they are true. All available evidence shows them to be false.

Numerous studies have failed to find any evidence gene patents do anything other than spur innovation. In *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, University of Missouri-Kansas City law professor Christopher Holman wrote, "The paucity of documented examples in which the fears surrounding gene patents have manifested themselves is striking, particularly when one considers the high level of public concern and the extraordinary nature of the proposed legislative fix."

Beyond merely doing no harm, gene patents help more patients get access to life-saving medical technology than they otherwise would. Myriad Genetics has invested hundreds of millions of dollars and two decades in delivering the highest quality genetic testing to the most patients possible. This kind of investment by an exclusive genetic testing provider simply does not happen, and patients ultimately suffer, when there are multiple providers.

Comparing hereditary breast and ovarian cancer syndrome (HBOC) with Lynch syndrome (colorectal cancer) suggests patients may in fact be harmed when there are multiple providers. Despite HBOC and Lynch having equivalent prevalence and associated cancer risk, over the last three years more than 4.5 times more patients were tested for the BRCA genes by Myriad than were tested for the Lynch genes by 15 providers.

Comparing BRCA gene testing in the United States versus Europe confirms these findings. Each year, between two and eight times more U.S. patients get BRCA testing by Myriad than are tested by the 25 providers offering such testing in five major European countries. And in both HBOC versus Lynch and U.S. versus Europe, Myriad's test is of dramatically better quality at the same or a better price.

A million patients have benefited from the BRCA patents, and countless other Lynch and European patients have suffered for lack of a patent-incentivized standard-bearer. In the words of Linda Bruzzone, the head of Lynch Syndrome International and a Lynch syndrome mutation carrier, "Many of us with Lynch Syndrome wish there had been a patent in place for us. It would have protected us and perhaps protected the lives of our loved ones."

SANDRA PARK
SENIOR STAFF ATTORNEY, AMERICAN CIVIL LIBERTIES UNION WOMEN'S RIGHTS PROJECT

WRITTEN FOR *CQ RESEARCHER*, MAY 2013

No

The patent system was designed to safeguard true inventions in order to incentivize innovation. But as we argued before the Supreme Court, human genes are not inventions. Gene patent holders did not invent the genes' sequence, their function or significance; these qualities were determined by nature and inherited from our parents. And these patents stand in the way of innovation by granting monopolies to fundamental elements of our bodies. For these reasons, the U.S. government, American Medical Association, geneticists and a wide range of patent advocacy groups have spoken out against gene patents.

Myriad Genetics holds patents on two genes, mutations of which are associated with a high risk of breast and ovarian cancer. Myriad claims that it invented the BRCA genes once they "isolated" them. But isolation simply refers to removing the genes from the cell and body. Because it is the first step for any examination of these genes, scientists cannot "invent around" the patents like they can with a patented drug or test. The patents give Myriad the exclusive right to offer genetic testing on the genes and determine what research is done on the genes. Although other labs want to offer more affordable testing using different, advanced methods, the patents ensure that Myriad is the only game in town.

This has had devastating effects for women who rely on these tests before they make life-changing decisions. Some can't afford the tests at all. Others have no option for a second opinion before they make serious medical choices.

Kathleen Maxian in Buffalo, N.Y., is an example. Kathleen's sister tested negative for a mutation initially, and Kathleen thought she was in the clear. What Kathleen and her family weren't told was that Myriad does not include many mutations in its standard test, but instead looks for these mutations in a separate test that costs $700 more. When Kathleen contracted ovarian cancer, her sister was retested using the more comprehensive testing, and this time she tested positive. Had Kathleen's sister been able to obtain a full analysis or second opinion from one of the many geneticists who would like to offer testing, Kathleen would have removed her own ovaries to prevent cancer. Now she is fighting Stage 4 ovarian cancer.

The Supreme Court has held for 150 years that you cannot patent laws or products of nature. For example, you can patent the method for extracting iron from rock, but you can't patent the element of iron itself. The same rules should apply to human genes. All of us who care about medical advancement deserve no less.

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Representing Myriad, attorney Gregory Castanias drew a contrasting picture for the justices as he began his argument. "What inventors created in this circumstance was a new molecule that had never before been known to the world," he said. Myriad's "human ingenuity," he later told the court, directly benefits patients. "They didn't have the BRCA1 isolated gene before the Myriad invention," he said.

Chief Justice John G. Roberts Jr. was among those who appeared to minimize Myriad's claimed inventiveness. "What's involved is snipping," he said to Castanias. "You've got the thing there, and you snip — snip off the top, and you snip off the bottom — and there you've got it."

Justice Sonia Sotomayor also challenged Myriad's lawyer on the point. "I find it very, very difficult to conceive how you can patent a sequential numbering system by nature," she told Castanias.

Earlier, Justices Elena Kagan and Anthony M. Kennedy had put Hansen on the defensive on the issue of economic incentives for genetic research. "Could you tell me what you think the incentives are for a company to do what Myriad did?" Kagan asked.

Hansen skirted the question by pointing to the intense competition to discover the breast cancer gene and the government funding behind some of the research. He continued by saying that the "enormous recognition" from discoveries were sufficient, but Kennedy found his answers unsatisfactory. "I just don't think we can decide the case on the ground, oh, don't worry about investment, it'll come," Kennedy said.

Hansen used his rebuttal time at the end, however, to emphasize the danger of using patent law to limit genetic research. "The government has given Myriad the authority to stop research on every one of our genes," he said. "That simply can't be right."

Roberts closed the argument, as usual, with no substantive comment. "The case is submitted," he said. The court finished hearing oral arguments at the end of the next week, facing the customary deadline of finishing the term's decisions before breaking for summer recess at the end of June.

While waiting for the Myriad decision, biotech companies took some encouragement from an unrelated ruling in a suit by Monsanto against an Indiana farmer for infringing the company's patent on a herbicide-resistant soybean. The May 13 ruling upheld a damage award of nearly $85,000 that Monsanto had won against Vernon Bowman for having repeatedly replanted soybean crops from commercially available soybeans that included some of Monsanto's so-called RoundupReady seeds. Kagan explained that Monsanto's patent "would provide scant benefit" if farmers were able to obtain the herbicide-resistant seeds from commercial sources instead of from the company. [38] ■

Getty Images/David Levenson

American geneticist James D. Watson, who collaborated in the early 1950s with British scientist Francis Crick in proposing the double-helix structure of DNA, strongly opposes patenting human genes. Genes carry the information that "makes us who we are," he says in a friend-of-the-court brief in the Myriad case before the Supreme Court. "Life's instructions ought not be controlled by legal monopolies created by whim of Congress or the courts."

OUTLOOK

Brave New World?

With human genetics racing ahead at seemingly breakneck speeds, many experts foresee a not-too-distant future when obtaining a full analysis of one's own DNA will be routine and will cost as little as $1,000. Already, prominent geneticists are serving as guinea pigs for this brave new world and publicly reporting what they have learned from their personal genomes.

As one example, NIH director Collins learned that he had elevated risks of, among other conditions, adult-onset diabetes and age-related macular degeneration, a common cause of blindness in the elderly. Recounting the results in his book, Collins said he was glad to learn that he is at reduced risk of Alzheimer's disease. [39]

Earlier, the grandfather of DNA science,

Watson, had his own DNA analyzed. He learned that he has heightened sensitivity to drugs used to control blood pressure and responded by changing the medication from daily to weekly. Watson said he learned very little else, however. And he specifically asked not to be told about his potential susceptibility to Alzheimer's disease because, with no cure or treatment, there was nothing he could have done with the information. [40]

Collins is an enthusiast for what he calls the "revolution" in personalized medicine, but he also acknowledges the caution voiced by scientists and others that much of the information in a DNA analysis may be difficult to interpret. In fact, the two private firms that analyzed Collins' DNA disagreed on whether his risk of prostate cancer was higher or lower than normal.

Kevin Noonan, a molecular biologist-turned-patent lawyer, notes that a personal genome is useful only to the extent that it discloses variations from a standard genetic structure and that many variations are themselves of unknown significance. "If you don't know what the information means, I don't know what the value is," he says.

"The era of personalized medicine is going to be harder than anybody thought it was going to be, and it's going to be longer than anybody thought it was going to be," Noonan continues. "It's not going to happen anytime soon."

For now, the patent office and the courts are weighing how best to apply U.S. patent law to gene-related discoveries so as to advance rather than delay that hoped-for future. The debate continues even as Supreme Court justices work behind closed doors writing what may turn out to be majority and dissenting opinions in the Myriad case.

Writing in *The Wall Street Journal*, Kevin Kimberlin, the venture capitalist who helped raise Myriad's initial financing, argued that gene patents are essential to attract needed investment in genetic research. "The Supreme Court must uphold the ability to patent isolated DNA to keep this innovation engine going at full speed," Kimberlin wrote.

One day later, *Washington Post* columnist Ruth Marcus summarized the competing arguments before coming down against Myriad's patent. "No one should have a monopoly on BRCA sequences," the op-ed page editors wrote in a headline summarizing Marcus' conclusion. [41]

Myriad officials insist they are not overly concerned about the court's eventual ruling. "We do not expect a decision that goes either way to have a material effect on our business operations," spokesman Rogers says. Even if the patent on the gene itself is invalidated, Rogers says the company believes its claims on the test for the gene would be "valid and enforceable."

Meanwhile, some patent law experts worry that the Supreme Court's decision may be less clear than advocates on either side would like. "I would be extremely surprised if the Supreme Court decision brings greater certainty to this area," says Eisenberg, the Michigan law professor. Duke geneticist Cook-Deegan agrees. "We're going to still have some lingering uncertainty" after the decision, he says. ■

Notes

[1] The case is *Association of Molecular Pathologists v. Myriad Genetics, Inc.*, 12-398, U.S. Supreme Court, www.supremecourt.gov/Search.aspx?FileName=/docketfiles/12-398.htm. SCOTUSblog has a comprehensive compilation of legal materials and news coverage: www.scotusblog.com/case-files/cases/association-for-molecular-pathology-v-myriad-genetics-inc/?wpmp_switcher=desktop. Briefs quoted in the remainder of this report are listed with links on the SCOTUSblog case page. The ACLU website page on the case is at www.aclu.org/fight-take-back-our-genes; Myriad's general commentary on the case is at www.myriad.com/common-myths-about-gene-patents/.

[2] The ACLU prepared a video that includes excerpts of an interview with Maxian; see "The Fight to Take Back Our Genes," www.aclu.org/free-speech-womens-rights/fight-take-back-our-genes. For coverage, see Elizabeth Cohen, "When breast cancer tests get it wrong," CNN, Oct. 27, 2011, www.cnn.com/2011/10/27/health/brca-genetic-testing-ep.

[3] See Natalie Angier, "Scientists Identify a Mutant Gene Tied to Hereditary Breast Cancer," *The New York Times*, Sept. 15, 1994, p. A1.

[4] For background, see these *CQ Researcher* reports: Marcia Clemmitt, "Genes and Health," Jan. 21, 2011, pp. 49-72; Barbara Mantel, "Breast Cancer," April 2, 2010, pp. 289-312; Mary H. Cooper, "Human Genome Research," May 12, 2000, pp. 401-424; Craig Donegan, "Gene Therapy's Future," Dec. 8, 1995, pp. 1089-1112.

[5] The case is *Diamond v. Chakrabarty*, 447 U.S. 303 (1980). For discussion, see Background, infra.

[6] See "FAQs about Affordable Care Act Implementation Part XII," U.S. Department of Labor, Feb. 20, 2013 (Question 6), www.dol.gov/ebsa/faqs/faq-aca12.html.

[7] The case is *Greenberg v. Miami Children's Hospital Research Institute, Inc.*, 264 F.Supp.2d 1064 (S.D.Fla. 2003). For background, see Aaron Zitner, "Whose DNA Is it, Anyway?" *Los Angeles Times*, July 18, 2003, p. 1.

[8] Nayanah Siva, "Myriad wins BRCA1 row," *Nature Biotechnology*, Vol. 27, No. 1, January 2009, p. 8, www.nature.com/nbt/journal/v27/n1/pdf/nbt0109-8a.pdf; "Myriad Genetics wins European patent appeal," Bloomberg, Nov. 20, 2008.

[9] See Thomas Baldwin, "Ethics and Patents for Genetic Diagnostics Tests," in Geertrui van Overwalle (ed.), *Gene Patents and Public Health* (2007), p. 52. Baldwin, a professor of philosophy at the University of York, attributed the view to the so-called Nuffield Council report entitled "The Ethics of Patenting DNA" (2002), which he helped write.

[10] Francis S. Collins, *The Language of Life: DNA and the Revolution in Personalized Medicine* (2009), pp. 110-113; Collins' earlier quote is from Ken Garber, "Homestead 2000: The Genome," *Signals*, March 3, 2000, www.signalsmag.com/signalsmag.nsf/657b06742b5748e888256570005cba01/fd168fb6c42acf6e882568950015e2d0?OpenDocument. Signals is an online magazine for biotech executives.

[11] For summaries of the four cases, with links

to citations, see the discussion of "march in" provisions in the Wikipedia entry for Bayh-Dole Act, http://en.wikipedia.org/wiki/Bayh%E2%80%93Dole_Act.

[12] Compulsory license provisions in France, Switzerland and Belgium are described in separate articles in Van Overwalle, *op. cit.*, pp. 121-209.

[13] Alex Philippidis, "Myriad, Prometheus Continue to Defend Diagnostic Patents while Others Urge More Licensing," *GEN: Genetic Engineering and Biotechnology News*, March 19, 2012, www.genengnews.com/keywordsandtools/print/3/26481/.

[14] The constitutional provision is Art. I, sec. 8, cl. 8. Historical background drawn in part from Office of Technology Assessment, *New Developments in Biotechnology: Patenting Life* (1989), pp. 51-65. See also Christopher Beauchamp, "Patenting Nature: A Problem of History," *Stanford Technology Law Review*, Vol. 16, No. 2, April 2013, pp. 257-312, http://stlr.stanford.edu/pdf/patentingnature.pdf.

[15] See Pasquale J. Federico, "Louis Pasteur's Patents," *Science*, Oct. 8, 1937, cited in brief of the *American Medical Association, in Association of Molecular Pathology v. Myriad Genetics, Inc.*, U.S. Supreme Court, 12-398, www.americanbar.org/content/dam/aba/publications/supreme_court_preview/briefs-v2/12-398_pet_amcu_ama-etal.authcheckdam.pdf.

[16] *Patenting Life*, *op. cit.*, p. 51.

[17] The case is *Parke-Davis & Co. v. H.K. Mulford & Co.*, 189 F.95 (S.D.N.Y. 1911). Beacuhamp's account is in "Patenting Nature," *op. cit.*, pp. 129-139; his discussion of the insulin patent is at pp. 141-143.

[18] Quoted in Stephen A. Merrill and Anne-Marie Mazza (eds.), *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* (2006), p. 33. Background also drawn from Robert Cook-Deegan, *The Gene Wars: Science, Politics, and the Human Genome* (1994), pp. 28-47.

[19] See James D. Watson, *DNA: The Secret of Life* (2003), p. 58.

[20] See Sally Smith Hughes, "Making Dollars Out of DNA: The First Major Patent in Biotechnology and the Commercialization of Molecular Biology," *Isis*, Vol. 92, 2001, pp. 541-574. *Isis* is the journal of the History of Science Society; Hughes, now retired, was a specialist in the history of science at the University of California-Berkeley. For briefer references, see "Cohen-Boyer and Recombinant DNA," Center for Public Genomics, Duke University, www.genome.duke.edu/centers/cpg/case-histories/seminal-genomic-technologies/cohen-boyer/; "The Cohen-Boyer patents," Life Sciences Foundation, www.lifesciencesfoundation.org/events-The_CohenBoyer_patents.html.

[21] See Watson, *op. cit.*, pp. 120-121.

[22] The decision is *Diamond v. Chakrabarty*, *op. cit.* For discussion, see *Patenting Life*, *op. cit.*, pp. 51-54. The case reached the Supreme Court on an appeal by Patent and Trademark Commissioner Sidney Diamond of the decision upholding the patent by what was then the U.S. Court of Customs and Patent Appeals, predecessor to the U.S. Court of Appeals for the Federal Circuit.

[23] See *Patenting Life*, *op. cit.*, p. 8; "Patent Law Amendments," *CQ Almanac* (1980). The Senate sponsors were Birch Bayh, D-Ind., and Bob Dole, R-Kan.

[24] "Utility Examination Guidelines," United States Patent & Trademark Office, 666 Fed. Reg. 1092, Jan. 5, 2001, www.uspto.gov/web/offices/com/sol/notices/utilexmguide.pdf. For coverage, see "U.S. Issues Stiffer Regulations on Frivolous Patenting of Genes," Reuters, Jan. 5, 2001, published in *The New York Times*, Jan. 6, 2001.

[25] See *Reaping the Benefits*, *op. cit.*, pp. 47-48.

[26] Natalie Angier, "Fierce Competition Marked Fervid Race for Cancer Gene," *The New York Times*, Sept. 20, 1994, p. C1.

[27] Marcia Barinaga, "Genentech, UC Settle Suit for $200 Million," *Science*, November 1999, p. 1655, www.biology.iupui.edu/biocourses/Biol540/pdf/UCSFvsGenetech.pdf.

[28] Watson, *op. cit.*, p. 118.

[29] See Michael Crichton, "Patenting Life," *The New York Times*, Feb. 13, 2007, p. A23. The letters were published under the headline "Whose Genes Are They Anyway?" Feb. 19, 2007, p. A14.

[30] The decision is *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. — (2012).

[31] See Alex Philippidis, "USPTO Tasked with Evaluating Impact of Gene Patents on Second-Opinion Testing," *Genetic Engineering & Biotechnology News*, Dec. 15, 2011, www.genengnews.com/keywordsandtools/print/3/25345/. For general coverage of the bill, see Edward Wyatt, "Fighting Backlog in Patents, Senate Approves Overhaul," *The New York Times*, Sept. 9, 2011, p. B4; Jia Lynn Yang, "Senate passes patent bill, says measure will spur job creation," *The Washington Post*, Sept. 9, 2011, p. A25.

[32] The decision is *Association for Molecular Pathology v. Myriad Genetics*, U.S. Dist. Ct.-S.D.N.Y., March 29, 2010, available at www.genomicslawreport.com/wp-content/uploads/2010/03/Myriad-SJ-Opinion.pdf. For coverage, see John Schwartz and Andrew Pollack, "Cancer Genes Cannot Be Patented, U.S. Judge Rules," *The New York Times*, March 30, 2010, p. B1. For coverage of the government's change in position, see Andrew Pollack, "In a Policy Reversal, U.S. Says Genes Should Not Be Eligible for Patenting," *The New York Times*, Oct. 30, 2010, p. B1.

[33] The Federal Circuit's second decision, issued Aug. 16, 2012, is *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 689 F.3d 1303 (Fed. Cir. 2012), www.cafc.uscourts.gov/images/stories/opinions-orders/10-1406.pdf. For coverage, see Tom Harvey, "Utah's Myriad wins another round in gene-patent case," *The Salt Lake Tribune*, Aug. 18, 2012. For coverage of the earlier ruling, see Andrew Pollack, "Ruling Upholds Gene Patent in Cancer Test," *The New York Times*, July 30, 2011, p. B1.

[34] Transcripts of the two hearings are on the PTO web site: www.uspto.gov/aia_implementation/120216-genetic_transcript.pdf (Feb. 16); ttp://www.uspto.gov/aia_implementation/120309-genetic_transcript.pdf (March 9). A complete index of witnesses and commenters,

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with links to testimony or statements, is at www.uspto.gov/aia_implementation/genetic-testing-comments.jsp.

[35] See "Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests: Report of the Secretary's Advisory Committee on Genetics, Health, and Society," U.S. Department of Health and Human Services, April 2010, http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_patents_report_2010.pdf. The report, released in February, drew little attention in general circulation news media, but an industry group held a news conference to criticize it. See "US HHS advisory group SACGHS' proposals to limit gene patent draws fire from industry," *thepharma letter*, Feb. 8, 2010, www.thepharmaletter.com/file/68022/us-hhs-advisory-group-sacghs-proposals-to-limit-gene-patent-draws-fire-from-industry.html.

[36] Rea quoted in Krista Cox, "KEI notes on USPTO roundtable on genetic diagnostic testing," Knowledge Ecology International, Jan. 14, 2013, http://keionline.org/node/1638; Cox is a staff attorney with KEI. No independent news coverage of the roundtable was found. The PTO website includes a list of 10 roundtable participants, with links to their prepared statements: www.uspto.gov/aia_implementation/comments_genetic_testing_roundtable_20130110.jsp. See also Anna Schwamlein Howard, *et al.*, "P.T.O. Reopens Public Hearing on Genetic Diagnostic Testing," DrinkerBiddle, Jan. 31, 2013, www.drinkerbiddle.com/resources/publications/2013/P-T-O-Reopens-Public-Hearing-on-Genetic-Diagnostic-Testing-; DrinkerBiddle is a law firm with an intellectual property practice.

[37] The transcript is on the Supreme Court's web site: www.supremecourt.gov/oral_arguments/argument_transcripts/12-398-2n8y.pdf. For coverage, see David G. Savage and Chad Terhune, "Patented Human Genes in Jeopardy," *Los Angeles Times*, April 16, 2013, p. B1; Adam Liptak, "Court Mulls Patents on Human Genes," *The New York Times*, April 16, 2013, p. A13.

[38] The decision is *Bowman v. Monsanto Co.*, 569 U.S. — (2013). SCOTUSblog has comprehensive materials on the case: www.scotusblog.com/case-files/cases/bowman-v-monsanto-co/?wpmp_switcher=desktop. For coverage, see Richard Wolf, "Supreme Court rejects 'blame the bean' defense," *USA Today*, May 14, 2013, p. 2B; Adam Liptak, "Supreme Court Supports Monsanto in Seed-Replication Case," *The New York Times*, May 14, 2013, p. B3.

[39] See Collins, *op. cit.*, pp. xviii-xxiv.

[40] See Rob Stein, "Scientists See Upside and Downside of Sequencing Their Own Genes," NPR, Sept. 19, 2012, www.npr.org/blogs/health/2012/09/19/160955379/scientists-see-upside-and-downside-of-sequencing-their-own-genes. The story was one in a series of stories Stein reported in September and October 2012.

[41] Kevin Kimberlin, "Gene Patents Drive Medical Innovation," *The Wall Street Journal*, May 21, 2013, p. A15; Ruth Marcus, "Our Genes, Ourselves," *The Washington Post*, May 22, 2013, p. A19.

FOR MORE INFORMATION

American Civil Liberties Union, 125 Broad St., New York, NY 10004; 212-549-2500; www.aclu.org. Represents plaintiffs in the case challenging Myriad Genetics' breast cancer gene patents.

American Intellectual Property Law Association, 241 18th St. South, Suite 700, Arlington, VA 22202; 703-415-0780; www.aipla.org. National bar association for companies and individuals in the practice of patent, trademark and copyright law.

American Society of Human Genetics, 9650 Rockville Pike, Bethesda, MD 20814; 301-634-7300; www.ashg.org. Primary professional membership organization for human genetics specialists worldwide.

Association for Molecular Pathology, 9650 Rockville Pike, Suite E133, Bethesda, MD 20814; 301-634-7939; www.amp.org. Advances molecular diagnostic medicine through education and training of practitioners, physicians, laboratory and industrial scientists, and health care professionals.

Biotechnology Industry Organization (BIO), 1225 I St., N.W., Suite 400, Washington, DC 20005; 202-962-9200; www.bio.org. Advocates for favorable policies for the biotechnology industry.

FORCE (Facing Our Risk of Cancer Empowered), 16057 Tampa Palms Blvd. W., PMB #373, Tampa, FL 33647; 866-288-7475; www.facingourrisk.org. Web-based community dedicated to improving the lives of those affected by hereditary breast and ovarian cancer.

Myriad Genetics, 320 Wakara Way, Salt Lake City, UT 84108; 801-584-3600; www.myriad.com. Biotechnology company at center of Supreme Court case on the legitimacy of gene-related patents.

National Breast Cancer Coalition, 1101 17th St., N.W., Suite 1300, Washington, DC 20036; 202-296-7477; www.breastcancerdeadline2020.org. Grassroots advocacy organization working to improve public policies on breast cancer research and treatment.

Public Patent Foundation, Inc., 1375 Broadway, Suite 600, New York, NY 10018; 212-796-0570; www.pubpat.org. Nonprofit legal services organization working to limit perceived abuse in the U.S. patent system.

U.S. Patent and Trademark Office, 401 Dulany St., Alexandria, VA 22314; 571-272-1000; www.uspto.gov. Agency within Commerce Department responsible for issuing patents to inventors and trademark registration to owners of intellectual property.

Note: A complete list of organizations that filed amicus briefs in *Association for Molecular Pathology v. Myriad Genetics* can be found on the Supreme Court's website: www.supremecourt.gov/Search.aspx?FileName=/docketfiles/12-398.htm. For other breast cancer-related organizations, see Barbara Mantel, "Breast Cancer," *CQ Researcher*, April 2, 2010, p. 309.

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Books

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The book details the highly competitive race in the 1990s between scientists on three continents to identify the gene linked to hereditary susceptibility to breast and ovarian cancer. Includes notes. Davies, now editor of *Bio-IT World*, is also author most recently of *The $1,000 Genome: The Revolution in DNA Sequencing and the Era of Personalized Medicine* (Free Press, 2010); White, a British writer now living in Australia, is author of numerous books about science as well as several novels.

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The report by the National Academies of Science traces the history of the molecular biology era and examines the effect of the granting and licensing of genetic-related patents on research and innovation. The report recommends adapting the patent system to changes in genomics and facilitating researchers' access to patent inventions.

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The book examines arguments for and against DNA patenting and recommends government regulation and policies to minimize harmful effects of patenting while promoting beneficial ones. Includes notes, 20-page list of references. Resnik, formerly a professor at the Brody School of Medicine, East Carolina University, is now at the National Institutes of Health.

Articles

Baldwin, A. L., and Robert Cook-Deegan, "Constructing Narratives of Heroism and Villainy: Case Study of Myriad's BRACAnalysis® Compared to Genentech's Herceptin®," *Genome Medicine*, Vol. 5, January 2013, http://genomemedicine.com/content/5/1/8.

Business practices rather than patents explain why Myriad Genetics is criticized for its breast cancer genetic screening policies while Genentech is praised for its patented advance in treating breast cancer. Baldwin is a graduate student and Cook-Deegan a professor and director of genome ethics, law and policy at the Duke Institute of Genome Sciences and Policy.

Cook-Deegan, Robert, "Gene Patents," in Mary Crowley (ed.), *From Birth to Death and Bench to Clinic: the Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns*, Hastings Center, 2008.

The briefing paper provides an overview of gene-patent issues along with useful resources.

Gold, E. Richard, and Julia Carbone, "Myriad Genetics: In the Eye of the Policy Storm," *Genetics in Medicine*, 2010, pp. S39-S70, www.nature.com/gim/journal/v12/n1s/full/gim2010142a.html.

The case study examines the background to and context of Myriad's breast-cancer gene patent practices and the policy, research and business responses to them. Gold is a professor at McGill University, Carbone a professor at Duke Law School.

Kevles, Daniel J., "Can They Patent Your Genes?" *The New York Review of Books*, March 7, 2013, www.nybooks.com/articles/archives/2013/mar/07/can-they-patent-your-genes/.

A patent law expert at Yale University provides a thorough backgrounder on the Myriad Genetics case, in advance of the Supreme Court arguments, from a viewpoint favoring those challenging the company's patent on the breast cancer genes.

Reports and Studies

"Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests: Report of the Secretary's Advisory Committee on Genetics, Health, and Society," U.S. Department of Health and Human Services, April 2010, http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_patents_report_2010.pdf.

The committee recommends exempting genetic testing and research from liability for infringing gene-related patents. Three members dissented.

Dekker, Marcel, "New Developments in Biotechnology: Patenting Life," Office of Technology Assessment, April 1989, http://ota.fas.org/reports/8924.pdf.

The report provides a good historical account of the origins of patent protections for life forms. Includes text of patent law, detailed glossary.

On the Web

The Supreme Court blog *SCOTUSblog* has a comprehensive compilation of materials on the Myriad Genetics case: **www.scotusblog.com/case-files/cases/association-for-molecular-pathology-v-myriad-genetics-inc/?wpmp_switcher=desktop**. Two general blogs on patent law also include information or commentary about the case and gene-related patents in general: *PatentlyO*, **www.patentlyo.com**; and *PatentDocs*, **www.patentdocs.org**.

The Next Step:

Additional Articles from Current Periodicals

Gene Patenting

Darnovsky, Marcy, and Karuna Jaggar, "Who Should Own DNA? All of Us," *Los Angeles Times*, April 12, 2013, p. A17, articles.latimes.com/2013/apr/12/opinion/la-oe-darnovsky-breast-genes-patents-20130412.

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Products of nature, such as human genes, should not be eligible for patent protection, says a White House science adviser.

Rosenfeld, Jeffrey A., and Christopher E. Mason, "Who Owns Your DNA? Not Who You Think," *The Washington Post*, April 7, 2013, p. A21, articles.washingtonpost.com/2013-04-05/opinions/38307541_1_gene-patents-myriad-s-polio-vaccine.

Forty-one percent of genes in the human genome have patents belonging to companies or institutions.

Genetic Screening

Alltucker, Ken, "Genetic Tests Start to Inflate Nation's Health-Care Bill," *The Arizona Republic*, March 18, 2012, p. D5.

The United States spends about $5 billion annually on genetic and molecular tests, but the figure could reach $25 billion within a decade, says health care provider UnitedHealth.

Brown, Eryn, "Not Every Woman Should Get the BRCA Gene Test, U.S. Task Force Says," *Los Angeles Times*, April 1, 2013, articles.latimes.com/2013/apr/01/news/la-heb-brca-breast-ovarian-cancer-testing-20130401.

Women may not benefit from genetic screening for breast cancer unless they have a family history that makes them susceptible to harmful mutations, says the U.S. Preventive Services Task Force.

McCullough, Marie, "Center Promotes Awareness, Testing for Diseases That Affect Ashkenazi Jews," *The Philadelphia Inquirer*, July 20, 2011, p. A3, articles.philly.com/2011-07-20/news/29794575_1_carrier-screening-tay-jewish-genetic-diseases.

The Einstein Medical Center in Philadelphia has a center dedicated to testing Ashkenazi Jews for 19 rare diseases that are more common in Jews of Eastern European descent.

Myriad Genetics

Kolata, Gina, "DNA Project Aims to Make Public a Company's Data on Cancer Genes," *The New York Times*, April 13, 2013, p. A14, www.nytimes.com/2013/04/13/health/dna-project-aims-to-make-companys-data-public.html?pagewanted=all&_r=0.

Myriad Genetics has created a $500 million database that tells which changes in DNA can increase breast cancer risk and by how much.

Pollack, Andrew, "Justices Weigh Issue of Patents on Human Genes," *The New York Times*, April 15, 2013, p. A3, www.nytimes.com/2013/04/15/business/as-court-considers-gene-patents-case-may-overlook-relevant-issues.html?pagewanted=all.

Invalidating gene patents would undermine efforts to develop biotech drugs and DNA-based vaccines, say supporters of Myriad Genetics.

Wolf, Richard, "Justices Skeptical of Patent on Genes," *USA Today*, April 16, 2013, p. B2, www.usatoday.com/story/news/nation/2013/04/15/genes-patents-supreme-court-breast-cancer-ovarian/2084335.

Several Supreme Court justices say Myriad Genetics' patenting of breast cancer genes equates to the patenting of works of nature rather than works of invention.

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