Features

Wrangling Genes

As the law changes and new medical frontiers open, the dispute over genetic patents intensifies

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Lisbeth Ceriani
Photo by Webb Chappell/
Wonderful Machine

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After being diagnosed with an aggressive type of breast cancer, Lisbeth Ceriani had a double mastectomy last year followed by chemotherapy that caused her hair to fall out in clumps.

Just when she thought the worst was over, she learned that some of the genes in her body that led to the cancer were patented.

Myriad Genetics, based in Salt Lake City, holds patents on two genes and their mutations that have been linked to hereditary forms of breast and ovarian cancer. As a result, the private biotech company offers the only genetic screening tests for the diseases.

Ceriani, a 43-year-old single mother who works part time and lives in a Boston suburb, needs to know whether she is at risk for ovarian cancer and should have her ovaries removed. But she can't afford the $3,200 genetic test.

"When I found out there was a patent on the gene and not on the test, it was quite astonishing," Ceriani says. "My life is absolutely at risk. There is a potential time bomb ticking inside of me, and I just have to wait and see unless I get this test done."

As scientists break barriers in understanding genetic links for various diseases, the law is trailing close behind, raising questions about whether the fundamental building blocks of life should be patented. The answers will have lasting impacts for patients, doctors and the burgeoning biotech sector.

"The nature of patenting genes pre-empts research over an entire body of knowledge," says Chris Hansen, senior national staff counsel for the American Civil Liberties Union in New York City. "Some of the patent claims are really claims over ideas, not over things or discoveries."

The ACLU filed a federal lawsuit in May against Myriad Genetics and the U.S. Patent and Trademark Office on behalf of several women's health groups and four professional organizations that represent more than 150,000

geneticists, pathologists and laboratory personnel. The plaintiffs, who are being represented by Hansen, include Ceriani and three other cancer patients.

Filed in the U.S. District Court for the Southern District of New York, the suit is the first patent case in the ACLU's nearly 90-year history and is considered the first of its kind in challenging the patenting of genetic information.

The suit seeks to overturn Myriad's patents on the BRCA1 and BRCA2 genes, and it claims the patents increase patient costs, eliminate the possibility of second opinions on test results and stymie scientific research on the genes. The suit also claims Myriad's patents violate patent law and the First and 14th Amendments because the patents represent abstract ideas or basic human knowledge.

Richard Marsh, general counsel for Myriad Genetics, did not respond to requests for comment.

If the ACLU wins, the ruling could undermine thousands of patents on genetic information. Nearly 20 percent of the more than 23,000 genes in the human body are already patented, including genes associated with Alzheimer's disease, asthma and some forms of colon cancer and muscular dystrophy, the ACLU reports.

Some biotech patents also are under attack at the U.S. Court of Appeals for the Federal Circuit. In its dramatic decision in *In re Bilski* last October, the court's 9-3 en banc opinion gutted a decade of its own precedents on patents relating to processes. Many business methods, including numerous genetic-based diagnostic tools, are processes that don't rely on particular machines. Those patents are now on shaky legal ground because *Bilski* requires that a process involve a machine or a transformation of something into a different state.

Bilski could threaten thousands of biotech patents that have been approved over several decades, says David Resnick, a partner at Nixon Peabody in Boston who leads the firm's biotechnology team.

"Our concern is that for a lot of patents that have been filed in the past, there is a cloud over them. There is a chance they could be invalid," he says. "I think a lot of these patents are going to be subject to attack. No ifs, ands or buts."

DEBATE GETS PERSONAL

Dr. Roger Klein
Photo by Seville Media Photography

Whether that is a good or bad thing depends on whom you ask.

Dr. Roger D. Klein, the director of molecular oncology at the BloodCenter of Wisconsin in Milwaukee, says *Bilski* is very good news. Scientific research has been stalled because of patents on many biomarkers, he says. Biomarkers often contain genetic information that can reveal hereditary links to certain diseases or help predict which patients will respond to drug treatments.

"Every time a marker is discovered, someone files a patent on it. Suddenly, the genetic relationships are patented," says Klein, who holds a law degree from Yale in addition to his medical degree from Case Western Reserve University. "That type of patent in my view not only doesn't encourage innovation, it is negative and destructive."

Klein says many gene patents aren't inventions or even true discoveries. "They are simply biological relationships," he says. "It's not different than drawing a blood level for glucose and saying this is correlated with diabetes."

Klein, who isn't part of the Myriad Genetics suit, believes the development of new drugs that require massive expenditures on research and clinical trials are worthy of patent protection, along with complex genetic tests that rely on multiple biomarkers. He notes he is expressing his views, not those of the BloodCenter of Wisconsin.

Gordon Arnold, chair of the ABA Section of Intellectual Property Law, says patent claims involving genes shouldn't be approved when they simply describe natural phenomena. But he says there is "zero evidence" that patents or the patent system are hindering scientific research.

"I think that over time we will find that is a worry that was created by academics without evidence, and patents have never discouraged innovation," he says. "A lot of people who want to copy other people's inventions would like to have a weaker patent system and have certain areas of technology unpatentable."

Bilski will affect more than just business methods and will make it difficult to draft patent claims for many legitimate inventions in the biotech sector and other fields, Arnold says. An invention may be new, not obvious, and very useful, but it will first have to meet a "linguistic test" to comply with *Bilski*, says Arnold, a partner at Arnold & Knobloch in Houston.

"What is going to happen is [that] hurdles are being put up in front of a good, robust examination on the merits," he adds.

Part of the scientific frontier is personalized medicine, which uses information about a patient's specific genetic makeup to tailor individualized medical care.

"We think personalized medicine is going to transform health care," says Edward Abrahams, executive director of the Personalized Medicine Coalition in Washington, D.C. "By bringing precise diagnostics for future therapies, it will change the ways that medicine will be practiced."

The Supreme Court opened the door to the patenting of living organisms with its 1980 decision in *Diamond v. Chakrabarty*, which found that a genetically engineered bacterium could be patented. The bacterium could break down crude oil, making it useful in treating oil spills.

The manmade bacterium possessed new properties that didn't exist in any naturally occurring bacteria, so the patent avoided the U.S. Supreme Court's exclusions for laws of nature and natural phenomena. It is a crucial difference from many current biotech patents that describe genetic information in its natural state.

Ceriani couldn't get Myriad Genetics' test for ovarian cancer fully covered by her health insurance from MassHealth, a form of Medicaid. MassHealth was willing to pay half of the $3,200 cost for the test, but Myriad Genetics wasn't willing to reduce its reimbursement rate, she says.

Ceriani is working part time for an au pair agency, but her medical bills have wiped out her savings. She is now living in a house owned by her mother, and her sisters have paid some bills to support her and her 8-year-old daughter. She doesn't want to ask for more money from family or friends to pay for the genetic test.

"It's part of your body. Nobody is allowed to look at your genes other than this company, and then you have to pay them for the privilege," she says. "It's like putting a patent on blood or gold out of a mountain."

Bilski is a key development in patent law. Essentially, the case has nothing to do with the biotech industry, but its fallout certainly does.

Bernard L. Bilski and Rand A. Warsaw developed a mathematical model for hedging risks in commodities trading. Filed in 1997, the patent application has been rejected in every appeal, which may not bode well if the Supreme Court decides to hear the case after a cert petition was filed in January.

"If you look at the cases that the Supreme Court has decided lately, they aren't very patent-friendly," says Resnick. "With their recent decisions, they are sort of smacking patents down. I'm confident that any decision relating to *Bilski* will not be good news [for patent seekers]."

In June the court decided to take a look and granted petition to the case. *Bilski v. Doll* will be heard during the term starting in October.

TELLING DISSENTS

Three Supreme Court justices gave a hint of their views in an oft-cited 2006 dissent in *Laboratory Corp. of America Holdings v. Metabolite Laboratories Inc*.

That case involved a patent dispute over a discovery that high levels of an amino acid correlate with two vitamin B deficiencies. The patent covered not only the amino acid test but also the correlation between the amino acid and vitamin B levels.

LabCorp had argued that Metabolite's patent was invalid because natural phenomena are not patentable. On a 5-3 vote, the court dismissed the writ of certiorari as improvidently granted. The court left the Federal Circuit decision in place that upheld the patent along with damages against LabCorp for patent infringement.

Justice Stephen G. Breyer, joined by Justices John Paul Stevens and David H. Souter, dissented, citing Supreme Court precedents from 1948 to 1981 stating that laws of nature, natural phenomena and abstract ideas are not patentable.

“The reason for the exclusion is that sometimes too much patent protection can impede rather than ‘promote the progress of science and useful arts,’ the constitutional objective of patent and copyright protection,” Breyer wrote.

Breyer found that Metabolite’s patent was invalid because it “simply described the natural law at issue in the abstract patent language of a ‘process.’ ” He argued that the Supreme Court should have heard the case to address patents that can cause undue restrictions on research.

“The problem arises from the fact that patents do not only encourage research by providing monetary incentives for invention,” Breyer wrote. “Sometimes their presence can discourage research by impeding the free exchange of information, for example by forcing researchers to avoid the use of potentially patented ideas, by leading them to conduct costly and time-consuming searches of existing or pending patents, by requiring complex licensing arrangements, and by raising the costs of using the patented information, sometimes prohibitively so.”

Breyer took a big swipe at the Federal Circuit’s precedents, which had established the court’s own test for business method patents, starting with the 1998 decision in *State Street Bank & Trust Co. v. Signature Finance Group Inc.*

“Neither does the Federal Circuit’s decision in *State Street Bank* help respondents,” Breyer wrote. “That case does say that a process is patentable if it produces a ‘useful, concrete and tangible result.’ But this court has never made such a statement and, if taken literally, the statement would cover instances where this court has held to the contrary.”

The ACLU’s arguments in the Myriad Genetics suit mirror Breyer’s dissent in many respects.

“For a long time, the Federal Circuit was trending toward being very protective of patents and affirming a lot of patents that were in dispute,” says Hansen from the ACLU. “I think the dissent is a sign that at least some justices of the Supreme Court think the Federal Circuit has gone too far.”

The Federal Circuit’s lenient test in *State Street Bank* unleashed a flood of business method patent applications across numerous industries, including biotechnology. More than 40,000 applications were filed over the past decade, and more than 15,000 patents were issued in the business method category, according to statistics cited in *Bilski*.

“I think the Federal Circuit is trying to react to criticism and clamp things down,” says Richard Meyer, a patent attorney and head of East Coast litigation at Townsend and Townsend and Crew in Washington, D.C. “Typically, what happens is the pendulum swings too far one way. Then instead of getting a nice correction, the pendulum swings too far back the other way.”

TIDE HAS TURNED

Breyer’s dissent had a profound impact on legal thinking about business method patents, including many diagnostic tools used in personalized medicine, Resnick says.

“That dissent put the bug in everybody’s ear that this is a great way to attack these patents and certain district courts have agreed, and now these cases are starting to percolate their way up to the Federal Circuit,” he says.

Breyer’s dissent also was cited by the Federal Circuit in *Bilski*. In a stunning move, the court fell on its own sword and dispatched its own precedents, including *State Street Bank* and *AT&T Corp. v. Excel Communications Inc.*, which established that a process can be patented if it produces a “useful, concrete and tangible result.” The court found that its test is “insufficient to determine whether a claim is patent-eligible” and “was certainly never intended to supplant the Supreme Court’s test.”

In *State Street Bank*, the Federal Circuit ruled that a data processing system for managing mutual fund assets was patentable because mathematical calculations applied in a practical way can produce “a useful, concrete, and tangible result.”

In *Bilski*, the court reached a very different conclusion and found that mathematical calculations for hedging risks in commodities trading represent an abstract idea that isn't eligible for a patent. Under *Bilski*, a process now must be "tied to a particular machine or apparatus" or transform "a particular article into a different state or thing."

That machine-or-transformation test seeks to work with the Supreme Court's patent exclusions for laws of nature, natural phenomena and abstract ideas. The Federal Circuit pulled the test largely from the 1972 Supreme Court decision in *Gottschalk v. Benson*.

In that case, the Supreme Court denied a patent application for a computer program that converted binary-coded decimal numbers into pure binary numbers because the process was just a series of calculations that represented an abstract idea. "Transformation and reduction of an article 'to a different state or thing' is the clue to the patentability of a process claim that does not include particular machines," the decision stated.

No machine, no transformation, no patent.

The cert petition in *Bilski* argues that the Supreme Court never declared the machine-or-transformation test was mandatory for process patents.

"The Federal Circuit has essentially confined all process patents to manufacturing methods, using a test that may have been appropriate during the Industrial Age but no longer fits our modern information-based economy," the petition states. "The decision has disrupted the settled expectations of patent owners and cast doubt on tens of thousands of issued patents."

While Breyer's dissent was pressing down from above, the Federal Circuit also was catching heat from below. When the patent application at issue in *Bilski* reached the Board of Patent Appeals and Interferences in 2006, the board teed off not only on that business model but on the huge number of business method patent applications.

"The bounds of patentable subject matter are increasingly being tested," the unanimous decision stated. "Many of these applications are referred to as so-called business methods, but claims to methods of meditation, dating, physical sports moves, etc., are also presented."

In a bold move, the patent board bypassed the Federal Circuit's precedents and applied the Supreme Court's machine-or-transformation test in its *Bilski* decision. The board implied that it would be doing more of the same in the future.

"In questionable cases, we feel that the public interest is best served by making a rejection," the board de- cision stated. "The Federal Circuit cannot address rejections that it does not see."

But the Federal Circuit definitely saw *Bilski* coming. After oral arguments in 2007, the court sua sponte ordered an en banc review instead of issuing a panel decision. The full court issued its 132-page decision last October, with three separate dissents and one concurring opinion in a case that attracted 38 widely diverging amicus briefs.

Despite the potentially dire consequences from *Bilski*, the decision isn't the end of the world for patents on business methods or diagnostic tools in personalized medicine, Resnick says.

Software that detects a biomarker could be considered a new machine because it enhances a computer's functions, and a genetic test kit sold to a doctor's office also may qualify as a new device, Resnick says. The measuring of changes in protein levels caused by an antibody in a patient's blood sample could be claimed as a transformation, he adds.

"At least now we know what we're dealing with, and we have methods for dealing with *Bilski*," he says.

SEEKING A MIDDLE GROUND

The federal government and some companies are trying to find a middle road that promotes scientific research but also offers incentives for companies holding patents on biomarkers or other advances in personalized medicine. Launched in 2006, founding members of the public-private Biomarkers Consortium include the National Institutes of Health, the Food and Drug Administration and the Pharmaceutical Research and Manufacturers of America.

Companies that share their intellectual property won't lose it, but new research developed by the consortium will be open to scientists and subject to shared licensing agreements among consortium members. That level of

cooperation requires trust, but the consortium operates under the theory that a rising tide raises all boats, says Shawnmarie Mayrand-Chung, the NIH program director for the Biomarkers Consortium. She spoke in April at the ABA's Intellectual Property Law Conference in Arlington, Va.

The recession may help the consortium because fewer companies can afford to do large-scale research on their own, Mayrand-Chung says. "There is an advantage with working with people," she says. "I think it's the industry folks who have to decide whether it's better or not for them to put it in the public domain."

Another option is patent pools. In February, GlaxoSmithKline announced it would create a patent pool with more than 500 of its patents to promote research on 16 neglected tropical diseases, including malaria, cholera, leprosy and dengue fever.

Glaxo, the second-largest drug maker in the world, wants other companies and foundations to join the patent pool. Glaxo plans to grant licenses to third-party researchers to develop new tropical disease treatments in 50 of the world's least-developed nations.

Many patents in personalized medicine aren't as controversial as gene patents and aren't threatened by *Bilski*. New drugs such as the successful breast cancer treatment Herceptin are on solid ground, along with inventions of diagnostic machines and treatments that modify existing genes.

The problems start when patents descend to the genes themselves, says Dr. John Ball of Chicago, executive vice president of the American Society for Clinical Pathology, one of the plaintiffs in the ACLU suit against Myriad Genetics.

"Basically what we think is having the patent on the gene makes research less likely, makes innovation less likely," he says. "If 20 percent of the genes in my body can be patented, what about my arm or my finger? When does it stop?"

The Federal Circuit noted the difficulties in keeping the law at pace with the onrushing speed of technology and warned that Bilski may soon be behind the times.

"We agree that future developments in technology and the sciences may present difficult challenges to the machine-or-transformation test, just as the widespread use of computers and the advent of the Internet has begun to challenge it in the past decade," the decision stated. "Thus, we recognize that the Supreme Court may ultimately decide to alter or perhaps even set aside this test to accommodate emerging technologies."

RESEARCH HOLDS THE KEY

While she recovers from breast cancer, ceriani still worries about the future because she can't afford the Myriad Genetics test for ovarian cancer. She also worries about the effects of gene patents for other women suffering from breast or ovarian cancer and those with a hereditary risk for the diseases.

Government-funded research has resulted in many genetic discoveries, but private companies were allowed to patent them, Ceriani says. "I think it's insane. I hope to live to see the day when the policy is changed," she says.

Holding breast cancer walkathons will only help so much because scientific research holds the key, she says.

"How are we supposed to screen for breast cancer when you can't research the frigging gene?" she asks. "It's like putting handcuffs on the scientists. They can't move forward in 20 years. That's how long patents last, and that's a long time for science to stop."

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