Endgame. A hearing on Myriad Genetics's *BRCA* gene patents drew protesters.

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INTELLECTUAL PROPERTY

Supreme Court Rules Out Patents on 'Natural' Genes

Myriad Genetics, the Salt Lake City firm that built a $450-million-a-year business on gene analysis, lost a big patent fight on 13 June. The U.S. Supreme Court gutted five of its intellectual property claims on the *BRCA1* and *BRCA2* genes, whose DNA sequences company scientists analyze to find mutations that raise a woman's risk of developing breast and ovarian cancer.

Few doubt that Myriad will survive the blow, but the 9–0 ruling against Myriad more broadly overturned 3 decades of U.S. support for human gene patents, rattling patent lawyers and biotech executives. The opinion, written by Justice Clarence Thomas, said that, "Myriad did not create anything. To be sure, it found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention." Raw DNA sequences like these cancer genes, even if "isolated" from tissue, are a "product of nature," according to the court. They are not patentable.

It's the same argument put forward by Myriad's opponents, a coalition of doctors and researchers who wanted to break the company's 15-year monopoly on *BRCA* testing. (Myriad charges more than $3000 per test.) The challengers received legal help from the American Civil Liberties Union and an advocacy group called the Public Patent Foundation in New York City.

But the decision was not all in the coalition's favor. The court also ruled that human genes in the lab-made format known as complementary DNA, or cDNA, should remain patentable. The mixed signal seemed to confuse the stock market: On the morning of the decision, Myriad's stock shot up more than 11%. In the afternoon, it fell below the starting point and has remained there. Myriad still has the means to protect its investment, though: It holds 24 valid patents around *BRCA* testing, notes spokesperson Ronald Rogers, and it is entitled to sue anyone who infringes them.

Last week's ruling drew mixed responses from researchers and business leaders. Jim Greenwood, CEO of the Biotechnology Industry Organization in Washington, D.C., praised the allowance of cDNA patents. But he deplored the main outcome as a "departure from decades of judicial and Patent and Trademark Office precedent supporting the patentability of DNA molecules." Greenwood added that it could "create business uncertainty for a broader range of biotechnology inventions."

Some closely following the long-running case speculated that the court's explanation for banishing patents on "isolated DNA" might undercut inventors' legal claims on isolated cells. In a blog, cell biologist Paul Knoepfler of the University of California (UC), Davis, School of Medicine, suggested that "[i]t is quite possible" that in the future patents on human embryonic stem cell (hESC) could be invalidated. Robert Cook-Deegan, a genetics policy expert at Duke University in Durham, North Carolina, agrees that "the logic of the ruling" clearly applies to stem cells. In his reading, embryonic stem cell patents would be out, while those on induced pluripotent stem cells would be in because they're actively created by adding genes.

The Supreme Court's rationale is "troublesome," says Carl Gulbrandsen, managing director of the Wisconsin Alumni Research Foundation, the nonprofit in Madison that holds the first hESC patents on behalf of the university. "It wouldn't surprise me if we got challenged on this." He argues that hESCs are not naturally occurring because they can be sustained only in carefully managed lab cultures. If they are unpatentable, Gulbrandsen says, the same logic would rule out patents on human insulin, human cell receptors, warfarin, enzymes, bacteria, microbes, and many other biological entities.

Many clincians and scientists have been energized by the Supreme Court's logic. "It's a great decision," says Haig Kazazian Jr., a geneticist at Johns Hopkins University in Baltimore, Maryland, who provoked Myriad's ire a decade ago by testing the *BRCA* status of women worried about breast cancer, without seeking its permission. Myriad threatened to sue for infringement and "shut us down" in 1999, he says.

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Although Myriad sued a number of private outfits, the lab under Kazazian and Arupa Ganguly, both then at the University of Pennsylvania (Penn), was the rare operating academic lab that it sought to halt. But Myriad also sent a warning to geneticist Harry Ostrer, formerly at New York University and now at the Albert Einstein College of Medicine in New York City, who had planned to do *BRCA* sequencing. Ostrer was sending specimens from his office to Penn for testing.

Ostrer received a warning letter from Myriad in 1999, according to court records, and stopped. In 2009, he signed up to sue Myriad over its *BRCA* patents and became the sole plaintiff in the case that went to the Supreme Court. Ostrer's "thrilled" with the outcome and says he is again planning to offer *BRCA* testing. The court has made it clear, he says, that, "inventors are going to have to really invent and not just extract."

After the verdict came down, many labs said they may add *BRCA* genes to the list of those they check, because it's less likely that Myriad will sue. These include, among others, groups at Penn; the University of Washington, Seattle; Quest Diagnostics; GeneDx; and Ambry Genetics (whose website carries an image of the Supreme Court with the banner, "Your Genes Have Been Freed").

On another front, Robert Nussbaum, a geneticist at UC San Francisco, is asking clinics around the world to send him and his colleagues the results of *BRCA* mutation analyses that they've ordered for patients over the years. He plans to put the anonymous details about mutations—originally provided to clients by Myriad—in a database to be shared on the Internet; he has already received 4000 submissions. The Genetic Alliance, a patient advocacy group, aims to create a medical outcomes database with input from patients who were tested for *BRCA* genes.

Francis Collins, director of the National Institutes of Health and a champion of free access to DNA data, was ebullient. "Our position all along has been that patenting DNA in its natural state does not provide any benefit to the public," Collins said. "We can breathe a big sigh of relief that [lawsuits] will no longer threaten to inhibit the progress of DNA research."

But Myriad found something to be happy about, too. Company spokesperson Rogers called last week's ruling "a very positive decision." That's because it gives new legal support to gene patents based on cDNA, which is a standard format for describing genes in most labs. Although the genetic sequence may be exactly the same, the court ruled that cDNA is patentable because it is lab-made, whereas DNA is not.

"We feel we are in a good position," says Myriad's Rogers, because the company still has 500 valid claims related to *BRCA* gene testing. "These won't go away" as a result of the ruling, Rogers says.

Because the primary *BRCA* patents are due to expire in any case in 2 years, Myriad was already getting ready to revamp its testing. The firm will discontinue its patented BRACAnalysis product and wrap the *BRCA* genes into a screening service that looks at an array of 25 risky genes.

Some patent attorneys, however, were discouraged. The U.S. patent system is the envy of the industrialized world but is "under attack," says Mercedes Meyer, a Ph.D. virologist and patent attorney for Drinker Biddle & Reath in Washington, D.C. "It is not broken," but is being turned into "Swiss cheese" thanks to decisions like the court's ruling on DNA. Meyers thinks that the legal situation on what is patentable for biotech firms has only become "muddier."

If that's correct, at least the patent lawyers have something to look forward to: more biotech litigation.

–ELIOT MARSHALL

With reporting by Michael Price.

Myriad and U.S. Patent Law

Early 1980s	U.S. Patent and Trademark Office begins to issue patents on human genes
1994–1995	Myriad Genetics files for patents on *BRCA1* and *BRCA2*
1997–1998	U.S. patents on *BRCA* genes awarded to Myriad
1998–1999	Myriad warns other labs not to do unlicensed *BRCA* testing
2009	Association for Molecular Pathology, Kazazian, Ostrer, and others sue Myriad
2010	New York federal court rules Myriad's *BRCA* patents invalid
2011	Appeals court validates Myriad's *BRCA* gene patents but not its methods patents
2012	U.S. Supreme Court asks for a re-review; appeals court affirms its decision
2013	U.S. Supreme Court rules that human DNA is unpatentable

HUMAN GENETICS

Agency Nixes deCODE's New Data-Mining Plan

The controversial company known for mining the DNA of Iceland's population to find links between genes and diseases, deCODE genetics, has hit another rough patch. A national agency that oversees data privacy in Iceland has rejected a request from deCODE to allow it to apply computational methods to the country's genealogical records to estimate the genotypes of 280,000 Icelanders who have never agreed to take part in the company's research and link the data to hospital records. The Data Protection Authority (DPA) ruled that the company must first obtain individuals' informed consent.

The 28 May ruling, which deCODE is challenging, revives concerns about the practices of the company, which has pioneered population studies that link genes to risks for common diseases. A decade ago, an Icelandic court ruled that the company could not create and mine a database of the entire country's medical records without getting consent from individuals. With its latest research, the company appears to once again be trying to expand its studies to the entire population, this time by linking real or estimated genotypes for all 320,000 Icelanders to selected health records it is acquiring. DPA's decision has also raised questions about several papers that the company has recently published using the strategy, and the company is taking heat in the Icelandic media.

Led by founder and CEO Kári Stefánsson, deCODE set out in 2006 to combine Iceland's extensive genealogical records, which it put into a database, with genetic data and also health records for all citizens. Unless individuals explicitly asked to opt out, all Icelanders would be included, making it one of the largest such biobanks in the world. The company would collect DNA from con-

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