Despite Gene Patent Victory, Myriad Genetics Faces Challenges

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Myriad Genetics retained its monopoly on a lucrative genetic test for breast cancer risk when a federal appeals court recently upheld the company's patents on two human genes — and the validity of gene patents in general.

Kathleen Maxian of Pendleton, N.Y., with a group that is planning ovarian cancer awareness events in western New York. She says a supplemental test may have helped her fight her cancer.

But it is only a matter of time before the company's business faces severe challenges, some experts say, because that $3,340 test is technologically outmoded, incomplete and too costly.

"Science has moved beyond what these folks do," said Mary-Claire King, a professor of genome sciences and medicine at the University of Washington. "It's not good for the science and it's not good for the patients and their clinicians if they cannot have the most complete, up-to-date information."

Myriad sequences the two patented genes, known as BRCA1 and BRCA2, for mutations that raise the risk of a woman getting breast and ovarian cancer.

But newer DNA-sequencing techniques are far faster and only a fraction of the cost of the 1990s technology that Myriad uses. Indeed, it will soon be possible to sequence a person's entire genome, all 22,000 or so genes, for less than Myriad charges for just two genes.

Executives at Myriad say they are preparing for changes. Although its major patents start expiring in 2014, the executives say the company's patent protection should last until at least 2018.

They say that will give the company time to adopt new technology and to diversify beyond the breast cancer test, which accounted for $353 million, or 88 percent, of Myriad's $402 million in revenue in the fiscal year that ended in June.

The company also plans to rely less on patents and more on trade secrets. Because it has done so much more testing than anyone else, Myriad has more information on which of the thousands of possible mutations in the two genes actually raise the risk of getting cancer.

Myriad used to share such information with a public database maintained by the National Institutes of Health, and it cooperated with academic scientists trying to analyze the mutations. But a few years ago, the company quietly stopped contributing and cooperating, in favor of building its own database.

An academic consortium, relying on data from European labs or from individual patients, is trying to catch up, but "it's kind of slow going," said Sean Tavtigian, a former Myriad scientist who is now an associate professor of oncological sciences at the University of Utah and is involved in the consortium.

Myriad, which is based in Salt Lake City, is hoping to use that advantage first in Europe, where it will open a testing laboratory next year.

"If I had my druthers, I would not want to go into a new market in a heavy-handed fashion, trying to enforce patents," Peter D. Meldrum, Myriad's chief executive, told analysts in January. Instead, he said the company would exploit its quicker turnaround time for testing and its "vastly superior information."

Myriad executives have said that when a European laboratory finds a mutation in either of the two genes, 20 to 40 percent of the time it does not know if the mutation raises the cancer risk. They say that Myriad's rate of uncertain findings is just 3 percent.

Daniel B. Vorhaus, a New York lawyer and editor of the Genomics Law Report, a Web site, said there were ethical questions about whether Myriad should be withholding the mutation information, important for public health, that it has gathered by dint of its patents to essentially extend its monopoly beyond the life of the patents.

Mark C. Capone, the president of Myriad's laboratory division, said in an interview that the company had invested heavily in characterizing the various mutations. He said that the company became uncomfortable sharing its information with a public database when it realized the information might be used to compete against it.

Ever since Myriad and its partner, the University of Utah, beat other researchers, including Professor King of the University of Washington, in identifying the BRCA1 gene in 1994, Myriad has been the target of those opposed to the patenting of genes.

In 2009, the American Civil Liberties Union and the Public Patent Foundation filed a lawsuit challenging Myriad's patents on behalf of various medical researchers, medical societies and patients.

A federal district judge last year said genes could not be patented. But his decision was reversed in late July by a 2-1 decision from the Court of Appeals for the Federal Circuit. The plaintiffs are considering appealing to the Supreme Court.

The lawsuit contends that the patents, by giving Myriad a monopoly, have limited testing options for patients and led to lower-quality tests.

The latest controversy concerns a supplemental test that Myriad is offering.

In 2006, Professor King and colleagues published a paper showing that Myriad's test, known as the Comprehensive BRACAnalysis, actually failed to detect a significant number of genetic alterations in the two genes.

Myriad then developed a test for these alterations. But instead of incorporating it into its main product, it offered it as a supplemental test at a price of $700. Many insurers do not pay for it, and therefore many women do not get it.

Myriad's data shows that for Latina women in particular, 20 percent of all mutations found are detectable only by the supplemental test.

"The comprehensive testing they are advertising is not really comprehensive," said Ellen T. Matloff, director of cancer genetic counseling at Yale, who is also a plaintiff in the patent lawsuit. "This would not happen in a competitive market. It simply would be unacceptable."

More than 200 doctors, genetic counselors and other health care professionals have signed an open letter to Myriad urging it to incorporate the supplemental testing into the main test.

Kathleen Maxian says that if that had been done earlier, she might not be fighting for her life against ovarian cancer.

Her sister developed breast cancer at age 40 about five years ago, but tested negative for mutations on Myriad's main test. She was not offered the supplemental test.

Two years ago, Ms. Maxian developed ovarian cancer. It turned out that both she and her sister had genetic alterations that were detectable only by the supplemental test.

"If my sister had had that test and had gotten a positive result, I would have gone to a genetic counselor and have been tested," said Ms. Maxian, who is 49 and lives in Pendleton, N.Y., near Buffalo. She would then have had the option of having her ovaries removed to avoid getting ovarian cancer.

"I don't want to see this happen to anyone else," she said. "Women should have this test."

Mr. Capone of Myriad said the company kept the test separate because insurers would not pay for it. The company has now compiled the data necessary to arrange for reimbursement and is moving to incorporate that testing into its main product.

He said only 1 percent of women over all would have a mutation detected only by the supplemental test.

The future challenge for Myriad is from new sequencing machines and techniques. Last year, Professor King and colleagues published a paper on a technique that can test

BRCA1 and BRCA2, as well as 20 other genes that contribute to breast cancer risk, and at a cost much lower than Myriad's.

Some companies like Knome already offer sequencing of a person's full genome. Prices are still high — Illumina, for instance, charges $9,500 — but are dropping rapidly. Others, like GenomeQuest, are developing software tools to analyze the genetic information.

Lawyers say it is not clear if sequencing a person's whole genome and then providing information on mutations in the BRCA genes would violate Myriad's patents on the isolated genes.

Mr. Capone said that full genome sequencing did not yet meet the requirements for accuracy required of a medical diagnostic test. And the reported cost of sequencing a human genome does not include the significant cost of analyzing the data.

"It will probably take four years or more before whole genome sequencing can be done clinically," Mr. Capone said. By then, Myriad will have developed its test using new sequencers that will judge the risk of all hereditary cancers, not just hereditary breast and ovarian cancers.

Many analysts like the stock, though Isaac Ro of Goldman Sachs rates it a sell, saying the price of the breast-cancer risk test is unsustainable.

For now, sales of the breast cancer risk test continue to grow, rising 10 percent in the last fiscal year. Mr. Capone said that many women who were eligible for testing under medical guidelines were still not getting tested, leaving a large untapped market.

Myriad is also trying to diversify. It sells seven other tests, including one for the risk of inherited colon cancer and one that helps guide prostate cancer treatment by gauging a tumor's aggressiveness.

It has at least 13 other tests in development and is moving into so-called companion diagnostics, which are tests to show whether a particular drug is appropriate for a particular patient.

But so far, the other tests pale beside the one for breast cancer. Professor Tavtigian said Myriad insiders refer to the company's product portfolio as Snow White and the Seven Dwarfs.

www.nytimes.com/2011/08/25/business/despite-gene-patent-victory-myriad-genetics-faces-challenges.html?pagewanted=all