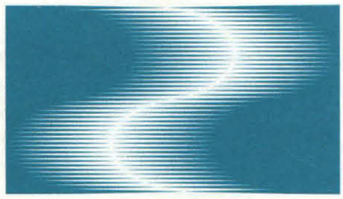
BIOTECHNOLOGY PATENTS

The Battle Over *BRCA1* Goes To Court; *BRCA2* May Be Next

What began a decade ago as a race to find the genes that increase a woman's risk for breast cancer (*BRCA1* and *BRCA2*) has evolved into a bitter court battle over who owns the right to exploit these genes commercially. Over the past month, two U.S. genetic testing companies have sued each other for patent violations. The legal jousting once again raises questions about the value of gene patents and threatens to stir up old grievances in the field—including some researchers' belief that *BRCA2* data were "leaked" from one team to another before they were published.

ONCORMED



MYRIAD

Rivals. Both OncorMed and Myriad seem likely to end up with patents on *BRCA1* sequences.

The two competing companies—OncorMed Inc. of Gaithersburg, Maryland, and Myriad Genetics of Salt Lake City, Utah—have filed suit in separate federal courts. Each holds patent rights from independent research teams, and each sells genetic tests that are used to estimate a woman's risk of getting breast or ovarian cancer. So far, the litigation involves only *BRCA1*, but observers expect *BRCA2* to become involved, too, if a U.S. patent on it is issued—which could happen in the next year.

More is at stake than commercial use of genetic data. The credibility of the U.S. Patent and Trademark Office (PTO) may also be on the line, because it has stoked the dispute by allowing two patents for what appears to be the same use of *BRCA1*, one to OncorMed and one to Myriad. It's a decision one geneticist calls "just crazy."

The details of the initial discovery of *BRCA1* do not seem to be in dispute. A team of researchers led by Myriad's Mark Skolnick, working with groups at the University of Utah and at the National Institutes of Health (NIH)—including Andrew Futreal and Roger Wiseman—won a fierce race to identify the gene. Their work built on years of data collection by others, notably Mary-Claire King, then at the University of California (UC), Berkeley, and now at the University of Washington, Seattle. The Utah-NIH group published its results in *Science* on 7 October 1994 (p. 66), filed for a patent on the gene and several harmful mutations in it, and licensed the rights to Myriad. However, King's genetic linkage markers were licensed by UC to OncorMed.

OncorMed subsequently filed for a patent on what it describes as a "consensus sequence" of the *BRCA1* gene, which the company's researchers obtained by analyzing DNA from five normal persons whose families had no history of breast or ovarian cancer. The company claims that by analyzing these *BRCA1* genes, it was able to identify seven harmless genetic variations and determine the most common nucleotide at each point in the sequence. The result was what it calls "the most likely *BRCA1* sequence to be found in the majority of the normal population." This, OncorMed claims, is significantly different from Myriad's original *BRCA1* sequence. OncorMed was granted its patent on 5 August, well ahead of Myriad, which had withdrawn its application and refiled it to take advantage of new rules that award patents for 20 years rather than 17.

OncorMed thus was in a position to fire the first shot in the legal battle. On 17 November, it sued Myriad in Washington, D.C.'s federal district court, accusing its Utah competitor of violating its *BRCA1* patent (U.S. Patent 5,654,155). OncorMed asked the court to stop Myriad's alleged misuse of its *BRCA1* data in genetic tests.

Myriad waited until the morning of 2 December to fire its counterblast. On that day, it received its own partial patent coverage of *BRCA1* from the PTO (U.S. Patent 5,693,473). The patent covers 47 harmful *BRCA1* mutations, including two that appear often in the Ashkenazi Jewish population. It does not cover the normal form of *BRCA1*, for Myriad's claim on the full sequence is still working its way through the system. But, according to Myriad, the PTO did give "notice of allowance" on the complete *BRCA1* sequence, meaning that the patent has cleared all but the last technical hurdles. On the basis of this news, Myriad raced into federal court in Salt Lake City, accusing OncorMed of violating its new patent and seeking an injunction to stop OncorMed's genetic tests.

Neither company would comment on its patent claims now that the litigation has begun. Researchers familiar with the race to find breast cancer genes, however, say they are not surprised that the two commercial competitors wound up in court. Geneticist Ray White of the University of Utah, Salt Lake City, says he can't understand why the PTO would grant two patents on two slightly different versions of *BRCA1*. If every newly discovered allele can be secured by a separate patent, he says, "that would destroy the entire point of patenting." He feels that "patents would have no value" if they fail to give the first discoverer of a new gene adequate compensation in the form of exclusive and fairly broad property rights. Another researcher who had been involved in the discovery of *BRCA1*, speaking on condition of anonymity, was scornful of all the jockeying to control breast cancer genes. In his view, the legal battle for priority is just one of many "little games companies play" for investors.

This legal tussle over *BRCA1* could be just a warm-up for an equally bitter fight over *BRCA2*. Geneticist Mike Stratton of the Institute of Cancer Research in Sutton, United Kingdom, Futreal, who is now at Duke University, and their colleagues were the first to isolate the *BRCA2* sequence and file patents on it in 1995. But a day before their paper was published in *Nature*, Myriad researchers announced that they, too, had isolated *BRCA2*. In its competing patent applications, Myriad claims that its version of *BRCA2* is superior for genetic testing because it is more complete. Britain's patent office has already issued a patent on *BRCA2* to the Stratton-Futreal teams, which have licensed their rights to OncorMed. Myriad and OncorMed are still waiting to see who will get priority on *BRCA2* from the U.S. PTO.

If it does go to court, the *BRCA2* fight could get nasty. One senior geneticist says there is a suspicion among his colleagues that Myriad learned about the Futreal-Stratton *BRCA2* sequence through the "jungle drums" in the genome research community before the data were published—an allegation Myriad has denied in the past. Guy Heathers, head of business development for Britain's Cancer Research Campaign Technology (CRCT), which funded Stratton's work, says several scientists have called him to express this view. Heathers isn't planning to leap into the fray, however, because CRCT can't afford the U.S. legal fees. "I will sit back and watch what the courts make of this," he says.

–Eliot Marshall