LAW

Gene patents in the dock

As US Supreme Court justices prepare to hear arguments in Myriad Genetics case, observers are debating the impact of the outcome on personal genomics.

BY HEIDI LEDFORD

When Daniel Weaver pitches Genformatic to potential investors, he feels obliged to note a future legal uncertainty. The two-year-old company, based in Austin, Texas, offers whole-genome sequencing and analysis to researchers and physicians, with plans to apply the technology to medical diagnostics. But Weaver fears that the company could become ensnared in a thicket of thousands of patents. "Who knows how much it would cost in legal fees just to sort through that?" he says.

Weaver and others in his line of business are looking to the US Supreme Court to prune that thicket. On 15 April, the court will hear arguments in a long-running lawsuit intended to answer one question: are human genes actually patentable? Yet the implications of the court's decision — expected by the end of June — may be narrower for business and medicine than many people hope and think. The case is limited to patents that cover the sequence of a gene, rather than methods used to analyse it (see 'A plethora of patents'). "Symbolically, this case is a pretty big deal," says Robert Cook-Deegan, a policy researcher at Duke University in Durham, North Carolina. "But the practical consequences of it are limited."

The case, *Association for Molecular Pathology* v. *Myriad Genetics*, tackles the validity of patents owned by Myriad Genetics, a medical diagnostics company based in Salt Lake City, Utah, on isolated DNA that encompasses the human genes *BRCA1* and *BRCA2*. Certain forms of these genes increase the risk of breast, ovarian and other cancers. Myriad says that its patents are necessary to protect its investment in research. But physicians and patients charge that the intellectual-property restrictions have limited development of — and access to — medical tests based on the genes. In 2009, the American Civil Liberties Union and the Public Patent Foundation, both based in New York, sued Myriad. The case has been rumbling through the courts ever since.

To many in biotechnology, it has ramifications beyond specific genes. The case highlights concerns that a network of individual gene patents could threaten the future of personalized medicine and whole-genome sequencing by blocking companies and clinicians from reporting a patient's genetic risk factors for different diseases. "It's as if somebody had a patent on the X-ray images of the pelvic region of a human being," says Weaver. "You could administer the test, but you wouldn't be able to inform the patient about that region. It's crazy."

By some estimates, the number of patents on human DNA is indeed extensive. In 2005, researchers reported that 20% of human genes had been patented[1]. Two weeks ago, another team raised that estimate to at least 41% (ref. 2). But some dispute these numbers and their implications. Christopher Holman, a law professor at the University of Missouri-Kansas City, read through 533 of the 4,270 patents referenced in the 2005 study, and found that more than one-quarter were unlikely to limit genetic testing[3]. "The literature is full of this kind of problem," he says.

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His analysis was backed up by Nicholson Price, an academic fellow at Harvard Law School in Cambridge, Massachusetts, who found that few, if any, DNA patents would be infringed by companies or clinics sequencing whole genomes of individuals for medical insight[4]. Many, for example, apply only to the selective isolation of specific stretches of DNA, says Price, whereas whole-genome sequencing is an untargeted sweep of the entire genome.

Myriad's contested patents are part of a dying breed, says David Resnick, a patent attorney at the law firm Nixon Peabody in Boston, Massachusetts. They were filed in 1995, before much of the human genome was sequenced and put into the public domain. Many other US gene patents issued before the human genome was sequenced are no longer enforced, because the companies that hold them have stopped paying maintenance fees. "This case is a conversation we should have had 20 years ago," says Resnick. "It's moot now."

Cook-Deegan thinks that whole-genome approaches may still be threatened if courts interpret patent claims broadly. Christopher Mason, a genomics researcher at Weill Cornell Medical College in New York, says that companies and clinics should not have to bear the risk of a court case. "If you're so sure those patents won't be a problem," he says, "when I get sued, you'll pay my court fees."

The irony is that even if Myriad's patents are ruled invalid, tests for mutations in the *BRCA1* and *BRCA2* genes may not become more widely available. Myriad's portfolio also includes patents on methods of analysing *BRCA* genes for links to cancer — and these are outside the scope of the current case. "If the Supreme Court says, 'No, genes aren't patentable', what's going to change about that test?" asks Resnick. "Not one person is going to be able to get it that couldn't before." ■

1. Jensen, K. & Murray, F. *Science* **310,** 239–240 (2005).
2. Rosenfeld, J. & Mason, C. E. *Genome Med.* **5,** 27 (2013).
3. Homan, C. M. *Soc. Sci. Res. Network* http://dx.doi.org/10.2139/ssrn.1894715 (2011).
4. Price, W. N. *Cardozo Law Rev.* **33,** 1601–1631 (2012).

THE WIDER VIEW

A plethora of patents

The phrase 'gene patent' is as ambiguous as it is emotionally charged. The US Supreme Court is set to evaluate whether genes that occur in nature can be claimed as innovations, but in so doing, it will focus on a narrow category of gene patent.

The patents in contention stake claims on isolated DNA sequences that make up *BRCA* genes. A federal court ruled in 2011 that isolating DNA changes it significantly from its natural state, rendering it fair game for a patent. (Legal scholars expect considerable time in arguments this month to be devoted to analysing what 'isolated' means.)

But gene patents come in other flavours. Some are filed on engineered DNA sequences, others on gene variants linked to traits such as increased cancer risk. Yet others are filed on methods to determine whether a gene variant is present — blocking competitors from performing genetic tests. These are generally more vulnerable to court challenge than are patents that directly claim DNA sequences, and are easier to work around through new methodology. **H.L.**