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Cashing in on your Genes



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Isolated gene sequences are being patented by companies meaning that only they can make, use or sell anything to do with that gene. So how does this affect possible life-saving research?

GENES – WE are full of them. Each of us has around 20,000 protein-encoding sequences of information packed into our DNA that get switched on and off as we go through life.

We now know that some of the gene variants we inherit could increase our risk of disease, while others may change their information later on and cause trouble. Meanwhile pathogens like viruses and bacteria have their own arsenals of genetic tricks to make their living from us. And overall, knowing about particular genes that can cause, treat or cure disease can form the basis of a human therapy.

But what happens when someone takes out a patent on a disease-related gene? There is an ongoing case in the US against Myriad (see panel), a company that provides tests for mutations in breast and ovarian cancer susceptibility genes.

Their patents around the Brca1 and Brca2 genes are under question, and it's not the first time that the issue of patenting a gene or protein has squirmed into the public gaze.

“The idea of patenting biological subject matter has been fairly controversial over the years,” says Barry Purdy, a European patent attorney and a partner at intellectual property firm PurdyLucey.

“[European law] was drafted in 1972 but really didn’t say anything about patenting biological subject matter, really it was silent on it because it was before molecular biology started getting really up and running. So as people were discovering new proteins and genes it was unclear whether patents could be granted and, if they were granted, whether they would be valid.”

It took a while to clear up the confusion, he says. “The European parliament started discussing a directive on biotechnology in 1988 but it was so controversial it was another 10 years before it was passed into European law. There were a lot of dissenting voices.”

Eventually the law was put in place, and it confirmed you could patent biological subject matter such as a gene or protein if you were the first person to isolate it from its natural environment, or if you could produce it by means of a technical process, explains Purdy.

“If you take a gene for angiogenin, which is a human growth factor, that gene and protein has been around for hundreds of thousands of years in humans, so it’s not new,” he says.

“But the researchers in Harvard who discovered it were the first to sequence the gene and take it out and isolate it, to produce it by means of a technical process. So they were able to get a patent on that gene. They have the right for 20 years to prevent anyone from making, using or selling that protein or the gene that encodes that protein so they have ultimate protection.”

In practice, does that make it tricky to carry out research on a gene such as angiogenin, which could hold clues to new therapies?

“There is a research exemption in the patent law – so if you are doing pure research on a particular gene or protein, really patent holders wouldn’t go out of their way to inhibit that,” says Purdy.

However when it comes to commercialising outputs of that research, if someone else holds a patent it could throw up a barrier, he says. “It doesn’t mean you can’t commercialise it but it might limit who you can commercialise it with.”

So from a research and innovation perspective, is gene patenting useful or not? Luke O’Neill, professor of biochemistry at Trinity College Dublin and co-founder of spin-out Opsona Therapeutics, has been down the road with a few patents and he thinks the crux lies in whether the gene or resulting protein in question has a commercial application.

“I have three patents in progress based on a gene discovered in my lab,” he says. “These include the gene itself and what are called ‘use patents’ – how the gene might be used as a drug target in a range of diseases or for a diagnostic.”

Gene patents offer a way for universities to make money through licences and, as in O’Neill’s case, can help forge relationships with commercial partners, as he found out first hand.

“Having patent applications indicated that I had experience and know-how, which gave me credibility in the setting up of Opsona and also in licensing to what was Wyeth (now Pfizer). So my current view is that it’s okay to patent a gene but only if there is a prospect for commercial development.”

An important point is that it’s not always just about the gene itself, he notes. “It is becoming apparent that the value in the gene isn’t worth protecting. What is worth protecting is the invention of the drug that targets the gene or gene product, or the diagnostic test.”

He does not believe that gene patents stifle innovation. “Big pharma will often ignore them and other academics aren’t bothered by them.

“Patenting also allows academics to publish and discuss their findings openly and the main reason academics patent discoveries is often to allow them to do just that,” he says.

A more substantial barrier than gene patents is the wider issue of secrecy in pharma, biotech and academia, according to O’Neill, as it may be holding back early-stage discovery research.

“If we knew the mistakes that were made or the approaches taken in a given project, it has to help progress, both from pooling ideas and to avoid unnecessary delays and duplications.”

Myriad Issues

EARLIER THIS year a US district court judge put the cat squarely among the pigeons in a case that has once again brought the thorny question of gene patents to the fore.

In March Judge Robert W Sweet upheld a legal challenge by the American Civil Liberties Union against patents held by Myriad Genetics on the breast and ovarian susceptibility genes Brca1 and Brca2.

The company – which markets diagnostics to test people for mutations in the genes that could substantially hike up their cancer risk – is appealing the decision relating to its seven gene patents, and the case rumbles on as the latest in a long line of clashes between Myriad and the clinical and scientific communities.

A general sticking point has been the granting of patents on genes removed from their natural environment, even though the information it contains is the same as the DNA in a living organism.

Sweet’s ruling addressed the question in the Myriad case by saying “the patents at issue directed to ‘isolated DNA’ containing sequences found in nature are unsustainable as a matter of law” and they were deemed unpatentable.

If the appeal is upheld, the case could have far-reaching implications for the patents already granted on around 20 per cent of human genes.

And in the Myriad case in particular, the challenge is a step in the right direction towards more open competition in the market for genetic testing, according to the scientist who discovered the *Brcal* gene, Mary-Claire King, now American Cancer Research Professor at the University of Washington Seattle.

“[Patents] constrain the competition on the best and most efficient ways of doing the test, and in this case in practical terms what it has meant is that the most modern technology has not been applied,” she tells us.

The case also highlights the difference in gene patenting landscapes between the US and Europe, notes patent attorney Barry Purdy, particularly around the scope of Myriad’s US patents, which covered mutations in *BrcA* genes that hadn’t even yet been discovered.

“Some of the patent claims they had were granted broadly. But when the equivalent patents were granted in Europe they were opposed by a number of third parties and the claims were restricted severely,” he says.

He believes gene patenting serves a purpose to protect investment in bringing innovations to market, but he would welcome more support for the type of complex diagnosis that Myriad was offering.

“I wouldn’t agree that the patent system needs to be changed in terms of diagnostics but I think the policy makers need to think about genetic lab based diagnostic tests,” he says. “There does appear to be an issue with those tests, that possibly because of the way these patents were granted the technology is not being made available for people in the best possible way.”

So what are the ethics?

EVERY SO often a new technology comes along that blows open an entire new way of doing things. The advent of molecular genetics, and in particular the sequencing of DNA, was one of those “disruptive” technologies and it has taken our ability to understand and use biological molecules to a new level.

But resulting discoveries haven’t always had a soft landing in the wider world and genetic technologies have often generated fear as well as awe.

From genetically-modified organisms to gene therapies and gene-based diagnosis of disease, the ability to work out – and work with – DNA has spawned rafts of ethical issues.

So where does gene patenting stand? At the broad level, patenting is there to encourage and protect discoveries, says Prof Bert Gordijn, who directs the Institute of Ethics at Dublin City University. “If you look at justification of the patent system as a whole, it promotes

innovation and that's positive for the public good. And secondly a patent is a fair reward for a useful invention," he says. But patenting of DNA in particular has stuck in the craw of many. "Some people believe that genes, and in particular human genes, have a special status – that they are common heritage, they belong to all of us and they ought not to be patented," says Gordijn, a former member of the research advisory board at the European Patent Organisation (EPO).

As well as such philosophical arguments, more technical objections have also been raised about the validity of taking out a patent on a gene. "Some say genes are not eligible for patenting, that they don't comply with legal criteria. Is there inventiveness? If you just isolate DNA sequences to use them in a diagnostic test, does that involve a step that's really inventive and non-obvious to a skilled worker? And if you just isolate a sequence of genes is it enough to claim novelty?" The consequences of taking out a gene patent may also pose ethical concerns if it increases the price of a therapy or diagnostic and so restricts patient access to them, he adds.

European regulations protect against unethical practices like human cloning, but if a patent is evaluated and considered valid, then a complaint against it is considered only after the patent is granted, and this is driving the ethical discussions down a judicial route, says Gordijn.

"At the EPO the examiners are saying we are just technical guys . . . we are not specialists in ethics and so the ethical discussions are postponed until the patent is granted and then it is appealed," he says.

From a medical perspective, patents on genes can protect the commercial use of their information in genetic-based products and diagnostic tests. But those products can themselves raise several issues, notes David Smith, associate professor of healthcare ethics at the Royal College of Surgeons in Ireland.

Genetic testing for different diseases or the risk of developing them invites a host of ethical questions including who owns the genetic test information, confidentiality and whether family members should have access to the results if it has an impact on them, issues of consent for testing children and whether people have the right to receive or refuse the results of the test, he says.