THE LOCKED CODE

Despite numerous attempts to prevent it, patenting of genes is still legal. **Geoff Watts** explains the problems

A bill introduced earlier this year in the US House of Representatives had one indisputable virtue: brevity. Congressmen Xavier Becerra and Dave Weldon's proposed Genomic Research and Diagnostic Accessibility Act would have added a new section to the US legal code. The bill ran thus: "Notwithstanding any other provision of law, no patent may be obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies."¹ That was it.

Had the bill been passed it would have resolved a long running dispute over the legitimacy of patenting genes. But it was not to be. The bill ran out of time, gene patenting remains legal, and the argument goes on. Given that the patent system is long established and generally agreed to be socially desirable, why should its application to genes have proved so contentious?

For many reasons—not the least of which is a widespread reluctance to view DNA as just another chemical. The information encoded within our genes has helped to make us what we are, influences our health and longevity, and may even offer insights into our close relatives. Hence we have declarations of the kind issued by Unesco, which talks of the genome as our "common human heritage."²

The problem with conferring a special status on DNA is that the underpinning emotions can swamp any attempt at reasoned discussion. One notable example is an opinion piece by Michael Crichton, the author of *Jurassic Park*, in the *New York Times* earlier this year.³ "You can't patent snow, eagles or gravity, and you shouldn't be able to patent genes either," he insisted. "Yet by now one fifth of the genes in your body are privately owned." The implication—that Genentec or some other biotechnology company will soon be knocking at the door demanding payback—

is of course nonsense. But this is the climate in which dialogue on the many real and multilayered concerns raised by gene patenting is too often conducted. So how best to unpick this helically twisted mess?

Patent decisions

At first sight, the conventions governing patentability seem to rule out genes. As products of nature—a term that obviously encompasses any molecule of human DNA—genes are not supposed to be subject to patent law. However, bodies ranging from the courts to the European Union⁴ have decided that a natural product that has been isolated, purified, or otherwise altered is patentable.

This raises the issue of invention as opposed to discovery. Patents are intended to cover only the former—although, surprisingly, the relevant US statute does use the word discovery: "Whoever invents or discovers any new or useful process, machine, manufacture or composition of matter . . . may obtain a patent." Although the wording does muddy the waters somewhat, patents have not in practice been granted to applicants who have put no inventive effort into whatever they're laying claim to—you never could have patented water simply by bottling it.

The further you delve into gene patenting, the more technical the issues become. When patent offices examine new applications, they use several criteria including novelty, inventiveness, and usefulness.

A review published by the Nuffield Council on Bioethics succinctly summarised the position on novelty and inventiveness: "Patent offices take the view that extracting genetic information encoded by a DNA sequence is not just a matter of gaining scientific knowledge about a natural phenomenon [because] it involves the use of cloning techniques to create an artificial molecule."⁵ In this sense

What would have justified the issue of a patent in the 1990s might not in the 2000s

the process can be described as both novel and inventive. At least that was the position until a few years ago. But technology has moved on and circumstances have changed: most notably the publication of the human genome sequence. What would have justified the issue of a patent in the 1990s might not in the 2000s.

A further complication is the relatively relaxed stance of the US Patent Office. Applications that would not satisfy the European Patent Office have found favour in its US counterpart. The same is true for another core patenting criterion: usefulness or utility. In the 1990s the US office was inundated with applications for genes or gene fragments for which the demonstration of utility was, to say the least, vague. Claims amounted to little more than saying, "This is a gene. As such it must be important, and we'll test for it."

In January 2001, following public consultation, the US office decided to raise the bar. It now requires gene patent claims to have a "specific and substantial and credible utility."⁶ Officials interpret credible as meaning that the utility of the invention must have been shown to be theoretically possible—even though it need not have been shown in practice. The authors of the Nuffield report, however, think this standard is still too low. "The current state of genetics and biochemistry does not make it difficult to suggest functions for DNA

ESP/DOCK/SPH

sequences that are 'theoretically possible,' in the sense that they are not ruled out by what is already known; but this should not suffice for the award of a patent."⁵

Do patents matter?

The potentially adverse consequences of patenting became clear in the tangled and now notorious case of the American company Myriad Genetics and its hold over BRCA1, a gene affecting susceptibility to breast cancer. The European Patent Office granted Myriad patents on the diagnostic use of the gene. In 2002 several organisations, including the French Institut Curie, lodged objections on various technical grounds including "inadequacies in the gene sequence" and on lack of inventiveness. In January 2005 the patent office upheld the objections, prompting the institute and its collaborators to issue a celebratory press release: "It is a victory for respect of the law on monopolistic abuses that result in unwarranted appropriation of key know-how likely to lead to health care improvements."⁷

One reason for the triumphant tone was that Myriad had been unwilling to license its patent to others. It had insisted that all DNA samples be sent for analysis to the company's own laboratories in the United States and wanted to charge more than \$2500 (£1250; €1800) for each test.

Further complicating the patenting issue is that entire genes are not the only bits of DNA in question. Patents have also been filed for expressed sequence tags. These are small lengths of DNA with a nucleotide sequence identical to that found at one end of a gene. As such they're invaluable for locating particular genes in a complete genome. Because expressed sequence tags are parts of whole genes, patents may overlap.

This also applies to single nucleotide polymorphisms or SNPs. These are small genetic variants: differences in single base pairs that occur in roughly one in every 1000 nucleotides. Some are linked to a person's risk of specific illnesses and, importantly for drug companies, affect the body's response to certain chemicals.

As it happens, agreement has been reached over SNPs. This followed the creation of the SNP Consortium,⁸ an international group originally comprising several drug companies and the Wellcome Trust. In an attempt to prevent patent wrangles the consortium set out to identify and map all the SNPs in the human genome and then make this information freely available.

On gene patenting in general, however, the debate continues. The arguments in favour are: allowing inventors to recoup their investment; avoiding duplication of effort; encouraging further research, etc. The arguments

against are predominately about the scope and number of patents, and the consequential risks that routine discoveries will be unjustifiably rewarded, or that the practical application of knowledge will be prohibitively expensive or otherwise restricted.

The principle spelt out in the failed US congressional bill would, for good or ill, have cut through all this argument—in America, at least. But because the dispute has remained unresolved for so long, and many patents already exist, we are now in a position to begin asking if gene patenting is turning out to be good or bad in actual practice. By studying patents filed between 1980 and 2003, the University of Sussex's PATGEN project has tried to do just this.⁹ Although its report points out that definitive answers are not yet possible, its measured conclusion seems to hint that patenting genes does not merit too much concern: "With the number of patent applications in decline, more stringent examination procedures and the likely restriction of the scope of patents by case law . . . the negative impact of DNA patenting may turn out to be more limited than some had feared."⁹

In all likelihood the future of intellectual property claims in genomic research will be neither all public nor all private but a shifting combination of the two.

Natural selection, commendably pragmatic, has always imposed a "pick and mix" regime on the evolution of the genome. A similar approach may be equally appropriate in decisions about patenting it.

Geoff Watts is a freelance journalist geoff@scileg.freemove.co.uk

Competing interests: None declared.

- 1 Genomic Research and Accessibility Act. Washington, DC: Library of Congress, 2007. http://thomas.loc.gov/home/gpoxmlc110/h977_ih.xml.
- 2 Unesco. *Universal declaration on the human genome and human rights*. Paris: Unesco, 1997.
- 3 Crichton M. Patenting life. *New York Times* 2007 Feb 13.
- 4 European Parliament and Council. *Directive 98/44/EC on the legal protection of biotechnological inventions*. 1998.
- 5 Nuffield Council on Bioethics. *The ethics of patenting DNA*. London: 2002.
- 6 US Patent Office. *Utility examination guidelines*. www.uspto.gov/web/offices/com/sol/notices/utltxmguide.pdf.
- 7 Institut Curie. *Another victory for opponent of patents held by Myriad Genetics*. Press release 31 Jan 2005. www.curie.fr/upload/presse/myriadpatents310105.pdf.
- 8 Wellcome Trust. *The SNP consortium and international hapmap project*. www.wellcome.ac.uk/doc_WTD003500.html.
- 9 University of Sussex Science and Technology Policy Research. *The patenting of human DNA: global trends in public and private sector activity*. Brighton: SPRU, 2006.