ETHICS WATCH

Patentability and higher life forms

Most of the recent controversy over the patenting of genes has focused on the barriers that patents place in the way of research and medical care1. But the issue of whether patents should be granted at all on genetic inventions is still pertinent. The Canadian Supreme Court recently denied a patent on a transgenic mouse, and the European Patent Office and several countries would not grant patents on cloning embryos or people.

The Canadian decision that a mouse that had been genetically engineered to express an oncogene was not patentable was surprising for several reasons. Europe, Japan and the United States had all previously granted patents on genetically engineered mice, although they had the power to deny patents on the grounds of "*ordre public* and morality" — a power which Canadian law does not grant. However, the Canadian court concluded — in a 5–4 decision — that genetically engineered "higher life forms" are not patentable because they cannot be reduced to material objects, and, therefore, are not the new "manufactures" or "compositions of matter" required by Canadian patent law[2]. In addition, the court's distinction between "higher" and "lower" life forms might not be workable, and requires a belief in a vitalistic life-force that has long been absent from contemporary biology.

A more difficult question concerns whether patents should be granted on processes for cloning or modifying the germline of human beings, for human–animal chimaeras and for human stem-cell technologies. Although the European Union specifically prohibits such patents[3], the situation in the United States remains unclear. United States anti-patenting activists have applied for a patent on methods of making human–mouse chimaeras to publicize this issue and to block the ability to make such chimaeras if the patent is granted[4].

Objections to such patents might have more of a symbolic than a substantive basis. A patent on cloning embryos or genetically modifying a human would give a right to exclude someone from making or using that invention, but would give no right to sell or control individuals born as a result. Also, such inventions would not always lead to harm — germline genetic-engineering or stem-cell modification might be essential for some people to have healthy children, just as access to patented drugs is necessary for those suffering from some diseases to survive. Patent holders have an interest in profiting from their inventions, and, therefore, are likely to license their use. Patent uses that harm other individuals can be regulated or prohibited without changing the terms for awarding patents.

Yet, patents are sufficiently commercial that they are easily associated with ideas of human commodification and control. With genetic and biotechnological developments sparking fears of misuse, legal questions about patentability have become the focus of a battle over genetic technology. Whether, and how, new inventions should be used raises complex policy issues that are best considered by legislative or regulatory bodies, not by the patent offices charged with determining whether biotech innovations are patentable.

John A. Robertson, University of Texas School of Law
email: jrobertson@mail.law.utexas.edu

REFERENCES [1]Andrews, L. B. Genes and patent policy: rethinking intellectual property rights. Nature Rev. Genet. **3**, 803–808 (2002) | [2]Harvard College v. Canada (Commissioner of Patents) SCC 76. File No. 28155 (2002) | [3]Council Directive 98/44/EC on the legal protection of biotechnological inventions O.J. (L 213) 13 (1998) | [4]Check, E. Biotech critic tries to sew up research on chimaeras. Nature 421, 4 (2003)

Diptych: 'Yin/Yang lilac', by Jacques Deshaies (2002) (detail).

EVOLUTION

One beats two

It makes sense to have spares of those things you might need to change at a moment's notice (such as tyres, light bulbs and fuses) but the evolutionary advantages of having two sets of chromosomes — diploidy — are less obvious. Now the experimental work in yeast of Zeyl and colleagues has shown that the prevalence of diploidy cannot be put down to a greater rate of adaptation compared to haploids.

It has been suggested that the more frequent production of adaptive mutations — double the alleles means double the opportunity for adaptive mutations to arise — might explain why seed plants and multicellular animals are predominantly diploid. Zeyl *et al.* tested this hypothesis by comparing five haploid and five diploid populations of *Saccharomyces cerevisiae*. As these populations were propagated through 2,000 generations in a liquid medium with limited nutrients — which forces cells to compete for these resources — mutants with higher rates of growth and survival arose and increased in frequency.

Measuring the fitness of the experimental populations relative to the unselected diploid ancestor every 200–300 generations showed that haploids adapted significantly faster than diploids to the new environment. This was good experimental evidence supporting the idea that in large diploid populations the additional opportunities for adaptive mutations to arise are outweighed by the increased time required for their fixation, because of their lower selective advantage in heterozygotes compared with haploids.

Repeating the experiment in small populations showed that the haploid advantage was lost (that is, the rates of adaptation were indistinguishable between haploids and diploids), confirming that in small populations the rate at which adaptive mutations arise is more of a limiting factor than it is in large populations.

The work of Zeyl *et al.* shows that diploidy does not necessarily lead to a greater rate of adaptation, so we cannot base a general explanation of its prevalence on this idea. The authors suggest that similar future theoretical and empirical studies should consider the consequences of different possible correlations between selection and dominance. In future, understanding how the dominance of adaptive mutations varies with respect to the fitness advantage they confer might well be crucial if we are to understand why diploidy is so popular.

Nick Campbell

References and links

ORIGINAL RESEARCH PAPER Zeyl, C. *et al.* An evolutionary advantage of haploidy in large yeast populations. *Science* **299**, 555–558 (2003)
WEB SITE
Clifford Zeyl's lab: http://www.wfu.edu/~zeylcw/zeylcw.htm