

# **Biotechnological inventions: patenting of genes and life forms, and the impact of patenting on upstream science**

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The expansion of intellectual property law during the last 30 years has been breathtaking. There are clear beneficiaries, but the value for society as a whole is less certain. Indeed, many consider that exploration and innovation are threatened by the continued advance of IP, and that a culture of exclusive-rights patenting is an important contributor to the global health gap. We should not move towards harmonisation without examining these issues with care.

## **Patenting of life forms**

To begin with the most obviously contentious subject, should life forms be patentable? Logically, the answer is straightforward if the criteria as they now stand are followed accurately. A life form as it occurs in nature is not patentable because there is no inventive step. A captured life form is also not patentable, because the concept of caging is not novel (though a new and ingenious design of cage might be). A modified life form is patentable, but only as far as the actual modification is concerned. This view is intermediate between current patent practice, which has allowed excessively broad claims on the strength of a limited modification (cotton, for example), and the vitalist position that nothing to do with life should be patentable. Neither of these extremes make sense. To think about this wide gap of opinion, it helps to project forward to the time (probably sometime during this century) when new life forms will be synthesised from scratch. Such life forms will surely be inventions, and therefore patentable. We shall understand them fully, so the mystical element will be gone (incidentally, that's not to say there should be no sense of wonder at such an accomplishment). Before that point it will be commonplace to modify life forms so extensively that their origins are unclear.

These projections warn us that appeals to morality to prohibit patenting of life forms will not in the end be sustainable<sup>1</sup>. But that is not to say that the issue is trivial, just that it cannot be dealt with at the level of patent claims. Conflicts arise because under the current exclusive-rights system possession of a patent confers too much power. We therefore need to institute stricter controls on use. Until that has been done, it is better to retain an illogical but precautionary position on claims.

## **Patenting of genes**

Early submissions assumed that genes are novel chemical entities, subject to composition of matter patents. Unquestionably, a novel gene that had been synthesised from scratch, and served a useful purpose, could legitimately be considered in this way. In the future, such molecules will be commonplace, but at the moment patented genes do not meet this criterion. Rather, they are discoveries, and the inventive step consists in their ingenious isolation from nature. This view has been enshrined in the European Directive<sup>2</sup>, yet now makes little sense because the

isolation of genes has been obvious for many years. With the sequencing and open release of whole genomes that has taken place over the last decade, there is little room left for this argument. Landmark events in this shift of practice were the Bermuda agreement on human sequence release in 1996 and the finishing of the human genome sequence in 2003. Many other genomes have also been sequenced, and the resulting accumulation of prior art has altered the way that gene patenting can be viewed. There has been a corresponding shift to claims through functionality, but to protect a whole gene requires a stacking of speculative clauses that goes far beyond demonstrable utility. The resulting patents are unjustifiably broad<sup>3</sup>.

In 2001 USPTO raised the bar to require "specific, substantial and credible utility", but still a recent survey found 20% of human genes had some level of patent protection<sup>4</sup>. To be strict, functionality of any kind is discovery not invention, and so logically gene patenting should not be allowed at all: it can only be justified as a working compromise. Indeed, recent statistics show some shifting towards process patents, which is no bad thing. I remember being assured 15 years ago that strong gene patents would be essential to ensure that companies' efforts spread out, rather than focussing on a few easy targets. Ironically, the pharmaceutical scene is now awash with lookalike drugs, an outcome that has nothing to do with patents and everything to do with markets.

An important aspect of gene patenting is that the utility of genes and genomes lies purely in their information content. The information can just as well be held in a computer or written in a book; composition of matter is irrelevant, because the conversion of the information from one form to another is unsurprising. The same cannot yet be said of proteins, because we cannot predict the properties of a protein from the sequence of its parent gene; this situation will gradually change, with practice driven by free release of protein structures just as it was with genome sequence<sup>5</sup>.

## **Impact of patenting on upstream science**

There are many anecdotal accounts of research being abandoned because of the danger of patent infringement (patent blocks), and of difficulties in arranging licenses because of multiple overlapping patents (patent thickets). Many studies have been, and are being, conducted in order to estimate the extent of the problems. The conclusions are mixed, with some of the differences being attributable to varying remits<sup>6</sup> and limited sampling, and the problems are greater than they appear at first sight.

A particularly comprehensive survey, combined with review material, has recently been published by the National Research Committee of the US<sup>7</sup>. The response rate was low, at 33%, but appeared representative. The conclusion is that there is some inhibition of research by third party patents, but in most fields only a minority of researchers declare significant impediment. The exception is in the area of gene-based diagnostic tests, where a majority had experienced interference. Two other findings are very significant. One is that the motivation of not-for-profit researchers by patenting (7%) is slight, compared with motivation by scientific importance (97%) personal interest (95%) and availability of funding (80%). The second is that the majority of researchers appear to be unaware of any threat from third party patents,

even when they have been given warnings by their institutions. The committee warns that as patent administrators become more active in exploiting their assets, and as the complexity of research increases (involving many different genes in one experiment, for example), blocks to research will become more frequent.

The attitude of these researchers calls to mind a couple of personal experiences. One was in the early days of automated sequencing. The supplier of our machines tried to keep the emerging data encrypted, so that we would be tied to their software throughout analysis. This was unacceptable, because it inhibited our own automation of sample tracking and data correction that was essential for developing high throughput processing. After fruitless argument, we gave up on negotiation and decrypted the output file from the machine. I have since been told that this would now be illegal (at least in the US), but remember: we did not steal the software, we merely recovered our own data. The point is that this is how scientists operate, and the surveys concluding that all is well are not necessarily a vindication of the system: they often mean that people are getting around or ignoring the obstacles put in their way by patents. Tightening the system will be destructive of science.

The second experience, shared like the first with other non-profit sequencing groups, resulted from the acquisition of Kary Mullis' PCR patent by Roche, who interpreted the patent as giving them rights over all thermostable polymerases. We were all using these enzymes on a large scale in our sequencing reactions (not for PCR), and Roche's prices became a prohibitive expense for us. So we started preparing our own enzyme, hoping that we would be protected by research exemption. We soon learned that was not true, as legal letters began to arrive first in the US and then the UK. The situation was eventually resolved by a challenge to Roche from another company, bringing down the price to a fair level, and incidentally showing that Roche never did have the rights but were bluffing. This illustrates one of the great problems with patents: granting is cheap, but opposition is costly and beyond the means of non-profit organisations. The exact limits of the research exemption still need clarification.

Overall the conclusion from the NRC is that patents already have a small negative effect on upstream research, and that this is likely to increase. To offset this trend, it recommends a number of measures to maintain the vigour of public research.

Another useful review, from the Danish Board of Technology<sup>1</sup>, is interesting in showing how little regard most firms in that country have for patents. The exceptions are biotech and drug companies - confirmation that biology is suffering from a Klondike effect, with an abundance of speculative claims. One recommendation of the DBT is the establishment of a remuneration based patent system alongside the present exclusive-rights based system.

I must not be disingenuous in ignoring those academic scientists who have done well under the present system and consider that more patents are a good idea. There has recently been something of a campaign in the UK broadsheets to advertise the success of these entrepreneurs. I am happy for them, happy for me in that their profits are contributing to my pension scheme, and happy for us all if it means that their knowledge is rapidly translated into benefits for society. But some of their comments make questionable reading. For example, one said that those working for him need "to be willing to put their neck on the line and be passionate. I would kill for this

company". He adds that this attitude contrasts with most academic scientists, yet that is not my experience at all: passion for one's field is exactly what you find in academia. But what particularly interests me is his reference to his company. An unmitigated drive to bring one's product to market is of dubious benefit in a health system. His attitude, writ large, leads to dominance of marketing over dispassionate evaluation of medicines and to the sort of adversarial relationship that the pharmaceutical industry has with its regulators. As a patient, I find it disturbing.

Of course individual reward is only a minor benefit of upstream patenting, compared with the need to secure venture capital to finance downstream R&D. This is how the system operates at present, and we all work within it. It's important to remind ourselves, however, that for healthcare this system is proving alarmingly inadequate. No more than 10% of the world's disease burden is being taken care of, and even in the richest countries people suffering from rare conditions are not well served. Whilst patents are not solely to blame for the situation, over-reliance on them is counterproductive. Efforts are being made, through public private partnerships and international treaties, to find solutions. It would be invidious if strengthening of patent rules turned out to undermine these vital developments.

## **Integration and harmonisation**

Are patents a necessary driver in an economic system? Remarkably, there is little or no direct evidence for benefit, and some contrary indications. True, there has been a good flow of innovation and a rise in prosperity in the industrialised countries. True, this correlates with increasing levels of patenting. But where is the evidence for causality? Are patents, like global warming, a side-product of prosperity that will become destructive if not reigned in? Continual additions to IP law without research into their efficacy are misguided<sup>1,8</sup>.

On the other hand, science, along with other sorts of creative activity, depends heavily on the public domain. The contents of the public domain are often dismissed as everything which is not patented, but that is too simplistic. Contribution to the public domain is an active step involving scientific publication, and other forms of data release, under tight rules of quality control. Knowledge in the public domain is available to be used by all, and provides the fertile medium in which future discoveries will be made. Conflict is arising because the public domain is being invaded by the advance of patenting. We are seeing the early effects of this change, and future effects may be severe unless we pay attention to correcting the imbalance. Hence the NRC's top recommendation to "foster free exchange of data, information and materials"<sup>7</sup>.

Twenty years ago it seemed possible that common sense would prevail, and that a better balance would emerge spontaneously. This is not happening, and it seems that we need to actively strengthen and structure the public domain. There are two complementary ways to go. First, the public domain needs to be formalised and given a high status, otherwise it will continue to be eroded to the disadvantage of all. My discoveries and inventions are not diminished by their free release; rather they are given greater long term value, and should be recognised as such by policymakers. Second, the gap between free release and patents is too wide. Many attempts are being made to bridge that gap, for example by patent pooling and by intermediate

forms of licensing such as BIOS<sup>9</sup> and Science Commons<sup>10</sup>. In the end patents are just tools, to be used in one way or another, and we need to learn how to integrate them with other tools for progress and prosperity.

It's important that WIPO is at the centre of this integrative task. Two years ago some of us wrote a letter calling for a discussion about open access in this forum<sup>11</sup>, which was strongly opposed by vested interests pressuring WIPO to confine itself to a narrower remit. But WIPO means intellectual property organisation, not patent organisation; indeed its original mandate was even broader - to stimulate "creative intellectual activity". If the integration does not take place here, then where else? What other forum is there? This is of great relevance today, to the theme of this meeting, for harmonisation is only a virtue if it results in something good for all. Otherwise we are better off with diversity.

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<sup>1</sup> Danish Board of Technology (2005) Recommendations for a Patent System of the Future. <http://www.tekno.dk/subpage.php3?article=1132&toppic=kategori11&language=uk&category=11>

<sup>2</sup> European Commission (1998). Directive on the Legal Protection of Biotechnological Inventions 98/44/EC, 6 July 1998. [http://www.europarl.eu.int/comparl/tempcom/genetics/links/directive\\_44\\_en.pdf](http://www.europarl.eu.int/comparl/tempcom/genetics/links/directive_44_en.pdf)

<sup>3</sup> Matthijs, G. (2004) Patenting genes *Brit. Med. J.* **329** 1358-1360

<sup>4</sup> Jensen, K. and F. Murray (2005) Intellectual Property Landscape of the Human Genome *Science* **310** 239-240

<sup>5</sup> <http://www.wellcome.ac.uk/en/genome/thegenome/hg03n002.html>  
<http://nihroadmap.nih.gov/structuralbiology/>

<sup>6</sup> Intellectual Property Institute (2004): Patents for Genetic Sequences: the competitiveness of current UK Law and Practice. A study on behalf of the Department of Trade and Industries. [http://www.dti.gov.uk/5397\\_DTi\\_Patent\\_Study.pdf](http://www.dti.gov.uk/5397_DTi_Patent_Study.pdf)

<sup>7</sup> Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health  
Committee on Intellectual Property Rights in Genomic and Protein Research and Innovation, National Research Council (2006)  
<http://www.nap.edu/catalog/11487.html>

<sup>8</sup> The Adelphi Charter, Royal Society of Arts (2005)  
<http://www.adelphicharter.org/>

<sup>9</sup> CAMBIA (2004) The CAMBIA BIOS Initiative: Biological Innovation for Open Society. CAMBIA, Australia, [www.cambia.org](http://www.cambia.org)

<sup>10</sup> <http://sciencecommons.org/>

<sup>11</sup> <http://www.cptech.org/ip/wipo/kamil-idris-7july2003.pdf>  
Butler, D. (2003) Drive for patent-free innovation gathers pace *Nature* **424** 118