Staking claims in the biotechnology Klondike

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My first brush with intellectual property came through defending free data release from the human genome project. I was amazed at the tacit acceptance by some that this information could and should be privatized. The product was not an invention: a genome sequence is a clear-cut case of public domain material.

People need a robust system for handling intellectual property, but patents have ambivalent effects. Patent protection stimulates some forms of creativity, and there are many winners. However, by stifling other forms of creativity, and by eroding the public domain, property rights create losers too. Patents are only one form of incentive, and most great scientific discoveries were made not for future claims to intellectual property rights, but for the fun and joy of exploration. The pressures to enclose the public domain are rife, reaching even into WHO — as we have seen in its policy over bird flu sequences, recently contested by Ilaria Capua.[W1]

The value of patents is often argued through parallels between the growth of patenting and increasing prosperity. But proof of causality is missing. One can equally point to parallelisms between obesity and prosperity or between global warming and prosperity. However, nobody suggests that obesity or global warming are causes of prosperity, they are unwanted by-products. Undoubtedly, robust patents have an important part to play, but we should be cautious in giving them too much credit for industrial success. I was at one time persuaded that strong patents would stimulate a wide variety of pharmaceutical innovation across the genome, but the field is now awash with look-alike drugs focused on a small number of targets. Evidently markets, not patents, drive drug development. The success of the biotechnology industry in the United States should be seen in the context of this country having a very effective public domain system. It also has strong patent law, but drug discoveries are often rooted in the public domain. In general, the developing countries that have shown the fastest economic growth are those that retained relatively protected markets until they reached a position of strength. The same was the case for Europe and the USA a century ago. We must ensure that harmonization of international patent law does not become a way for developed countries to pull up the ladder.

An obviously contentious subject is the patenting of life forms. The answer is straightforward if current criteria are used properly. 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, although 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. There is currently a big gap between those who want to patent entire micro-organisms, and people who feel that life should not be patented under any circumstances. Current patent practice has allowed excessively broad claims on the strength of a limited modification; cotton, for example. Neither of these extremes makes sense. To think about this wide gap of opinion, it helps to project forward to the time, probably during this century, when new life forms will be synthesized from scratch. Such life forms will be inventions, and therefore patentable. We shall understand them fully, so the mystical element will be gone, but even before that point it will be commonplace to modify life forms so extensively that their origins are unclear.

Patenting of genes has been defended on the grounds that genes are novel chemical entities, subject to composition of matter patents. Unquestionably, a novel gene that had been synthesized 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,[W2] yet now makes little sense because the isolation of genes has been obvious for many years.

In 2001 the United States Patent and Trademark Office raised the bar to require "specific, substantial and credible utility", but a recent survey found that 20% of human genes had some level of patent protection.[3] To be strict, functionality of any kind is discovery — not invention — so gene patenting should not be allowed at all: it can only be justified as a working compromise.

An important aspect of gene patenting is that the utility of genes and genomes lies purely in their information content. It makes more sense to think of genes as software rather than chemical entities. 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 can not yet be said of proteins, because we can not 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.[W4]

There are many anecdotal accounts of research being abandoned because of the danger of patent infringement (patent blocks), and of difficulties in arranging licences because of multiple overlapping patents (patent thickets). Studies should eventually show us the real extent of this problem,[W5,6–7] but most researchers are reportedly unaware of any threat from third-party patents, even

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when they have been warned of such by their institutions.

This attitude reminds me of how, in the early days of automated sequencing, the supplier of our machines wanted to keep the emerging data encrypted, so that we would be obliged to use their software for analysis of our data. This inhibited our 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, even though we did not steal the software but merely recovered our own data.

When Roche acquired Kary Mullis' patent for polymerase chain reaction (PCR), they interpreted their exclusive rights to this technique as applying to all thermostable polymerases. At the time, we were all using these enzymes on a large scale in our sequencing reactions, and Roche's prices became prohibitively expensive for us. So we started preparing our own enzyme, hoping that we would be protected by research exemption. We soon started receiving legal advice to the contrary. The situation was eventually resolved when another company challenged Roche on the breadth of the patent, and won the right to market its own enzyme. One of the great problems is that granting patents is relatively cheap, but opposing them is very costly and beyond the means of non-profit organizations. The exact limits of the research exemption still need clarification.

Individual reward is only a minor benefit of upstream patenting, compared with the need to fund downstream research and development. This is how the system operates at present, and we all work within it. However, it is important to remind ourselves that for health care this system is proving alarmingly inadequate. No more than 10% of the world's disease burden is being taken care of, and people suffer needlessly even in the richest countries. Patents are not solely to blame for this situation, but 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 such vital developments.

Science, along with other sorts of creative activity, depends heavily on the material and processes of the public domain. It is too simplistic to define the contents of the public domain as everything which is not patented. 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.

Attempts are being made to provide some options in the middle ground between the extremes of patenting and free release, for example by patent pooling and by intermediate forms of licensing. The General Public License (GPL) of the Free Software Foundation is an established bridge over this gap.[W8] In software, the GPL is as important as patenting and there seems no reason why it should not have similar international status. CAMBIA's Biological Innovation for an Open Society (BIOS) licences are adapted for patented technologies in the life sciences.[W9] They provide a commons in which improvements in biological tools can be shared. CAMBIA itself originated as an escape from proprietary monopolization of tools for plant transformation. Another example is Creative Commons, and its spin-off, Science Commons, which are helping to change the world of science publishing and material transfer agreements.[W10] Both BIOS and Science Commons can be regarded as particular cases of patent pooling, but their proactive approach and clear licensing templates are driving innovation in this area.

Twenty years ago it seemed possible that common sense would prevail, and that a better balance between public and private domains would emerge spontaneously. This is not happening, and it seems that we need to both strengthen the public domain and make more use of intermediate licensing methods. Exclusive rights patents confer too much power on the holder, and a system of remuneration-based patents, as proposed by the Danish Board of Technology,[11] may be a valuable alternative. Finally, we should pursue international commitment to better handling of intellectual property in biomedical research and development.[W12] ■

Competing interests: Sir John Sulston is a former Director of the Wellcome Trust Sanger Institute and a current member of the Human Genetics Commission, which advises the Government of the United Kingdom of Great Britain and Northern Ireland on matters pertaining to the human genetics. Views expressed in this article, which has been adapted from his presentations to the WIPO Open Forum on the Draft Substantive Patent Law Treaty, are those of the author, and not necessarily those of the Commission, the Institute, WIPO, WHO, or their respective Member States.

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