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Patenting human genetic material: refocusing the debate

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Abstract

The biotechnology industry has become firmly established over the past twenty years and gene patents have played an important part in this phenomenon. However, concerns have been raised over the patentability of human genetic material, through public protests and international statements, but to little effect. Here we discuss some of these concerns, the patent authorities' response to them, and ways in which to address these issues and to move the debate forward using current legal structures.

Recent news events make it obvious that there is still much controversy concerning the granting of patents over human genetic material. Politicians have played on both the hype and apprehensions surrounding this issue. The March 2000 statement by Bill Clinton and Tony Blair on the need for public access to human genetic information, and the June 2000 declaration by Elisabeth Guigou, the French Justice Minister, that human genetic patents violate French ethical norms, point to the politically charged nature of the patenting debate. Despite over a decade of vigorous academic and public discussion, the issue of whether we ought to allow patents on human genetic material seems, on the surface, to be unresolved. Commentators, ranging from the technology critic Jeremy Rifkin¹ to the American College of Medical Genetics², have cautioned against what they perceive to be an overly liberal application of patent law in the context of human genetic material. Even international bodies have expressed concern. For example, UNESCO's 1997 Universal Declaration on the Human Genome and Human Rights states that "[the] human genome in its natural state shall not give rise to financial gains". Some have even gone so far as to characterize the patenting of human genes as a form of "biopiracy"³.

For better or worse, this debate over whether human gene patents are appropriate has had little effect on those agencies that grant patents. Patent offices around the world have issued patents on human genetic 'inventions' without any unique or significant policy barriers since the beginning of the human genome project^{4,5} (BOX 1). With the possible exception of France, the momentum of legal precedent, amplified by international enthusiasm for the biotechnology industry, has overtaken the debate over patentability. The broad concerns about the ethical appropriateness of human gene patents — such as about dignity, the sanctity of human life and the commoditization of human tissue — have failed to influence patent policy in any meaningful way. As long as patent applicants satisfy the technical requirements of their

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region's patent office, a patent will be issued. Even in France, where there is continuing debate at the highest governmental levels over the patentability of human genetic information⁶, no gene patent granted by the European Patent Office (EPO) has been invalidated.

Despite the reality that the debate over human genetic patents has been overtaken by practice, we should not completely abandon the discussion over possible changes to the patent system. Some of the concerns about current patent policies have merit. Indeed, there are many reasons why the debate may even intensify in the years to come. For example, an increasing perception that human tissue has financial value⁷, the granting of controversial patents⁸, increased litigation over intellectual property rights in biotechnology, the spreading of public anxiety associated with biotechnology⁹, and the growing ties between industry and academia¹⁰ are all emerging issues that will contribute to the debate on gene patents. As such, a consideration of why there has been, at best, only incremental change in an area so central to biotechnology policy seems essential.

The goals of this paper are: first, to highlight some of the reasons why the broad concerns about the patentability of genetic material have had such a limited effect on actual patent policy; and second, to review several specific, practical concerns associated with human gene patents that might be addressed within current legal frameworks. It must be noted that there is already a great deal of literature that analyses the moral, policy and legal justification both for and against property and patent rights in human tissue^{11,12}. A critique of this important work is beyond the scope of this paper. Moreover, we believe that the largely unfettered march of patent law in this area is indication enough that, so far, this commentary has failed to generate much change. Whether you are an advocate or a critic of human gene patents, a refocusing of the debate seems worthwhile¹³. By moving the debate from the broad assertion that human genetic material cannot be patented to a more focused discussion of the specific and demonstrated benefits and concerns about human gene patents, we may be able to have a more constructive debate.

What is a patent?

To begin, let us consider some basic patent principles. Although there is some variation between countries, there are several broad principles that are common to all patent systems. A patent is a limited-term monopoly—in most cases lasting 20 years—to prohibit others from making, using, selling or importing an invention. An invention is a thing, a way of making a thing, or a way of doing something that is new, non-obvious and useful (or has industrial application), and does not exist in nature in the same form. 'New' means that the invention has never before been described in the relevant literature; 'non-obvious' means that the invention contains a spark—perhaps a small one—of creativity; and a 'useful or industrial application' means that the invention has some use in the real world, usually a commercial use.

What rights does a patent provide for its holder? Someone with a patent over a new mousetrap, for example, can prevent rivals from manufacturing that mousetrap, selling the mousetrap, or otherwise using that mousetrap in any manner. Similarly, the patent holder of a new method to measure heart rates can prevent others from measuring heart rates using that method. The patent does not, by itself, give the patent holder the right to measure heart rates. To do so, the patent holder may have to comply with local legislation that applies to the measurement of heart rates. For example, regulation may require that any new heart-rate measurement method pass certain safety tests before being marketed.

One of the principal goals of patent law is to allow an inventor to make money out of an invention. A patent holder can do so in two main ways. First, to the extent that no law prevents it, a patent holder can make and sell the invention to the public. Second, the patent holder can give someone else the right to do so. This is called a licence. A licence may be exclusive, sole

or non-exclusive. An exclusive licence is one that permits only the person receiving the licence to make use of the invention. In a sole licence, only the patent holder and the person receiving the licence can use the invention. In a non-exclusive licence, the patent holder and anyone else that the patent holder chooses can use the invention. So, where an invention is subject to an exclusive or sole licence, few people have the right to use the invention. In the case of a non-exclusive licence, many people could have the right to use the invention. If this happens, the invention is said to have been broadly licensed.

Each country grants its own patents. Each country's patents are valid only within that country. So, a United States patent has no application in Canada or in Germany and may contain different specific rights than patents in those countries. A set of international agreements establish some general standards that apply to patents. These include: the length of the monopoly, the requirements of novelty, non-obviousness and utility, the requirement that the inventor fully describe the invention, and the basic rights that attach to a patent. Nevertheless, because each country defines its own patent laws, differences do exist. Even in the European Union, where the EPO grants patents in each of the participating countries, the use and strength of the patents granted by the EPO depends on national law. For example, if the EPO grants a patent over a DNA sequence in Europe, the ability to use those patents in Germany and in France, for example, may differ. The European Union is, at present, contemplating the possibility of creating a Europe-wide patent that would not depend on national law.

Public debate's lack of impact

There are undoubtedly strong economic and policy arguments to support the granting of human genetic patents (for example, as an impetus for private investment in costly research). Indeed, for those in the biotechnology industry, patent protection is viewed as an essential element of the commercialization process¹⁴. Nevertheless, one would have thought that the intensity of the public debate over gene patenting would have had a more profound effect on patent policy. But, as discussed above, this is not the case. It is worth considering why this may be.

Probably the biggest factor is that, in most countries, intellectual property law is not structured to handle social policy considerations. The patent offices in the United States, Canada and Japan, for instance, are not empowered to consider ethical and policy issues. The recent decision by Canada's Federal Court of Appeal, allowing the patent on the 'onco-mouse', stands as a good example of the lack of policy discretion granted to patent offices¹⁵. In this case, the patent applicant was seeking a patent on a genetically modified mouse that can be used for cancer research. Originally, the patent office decided that higher life forms — such as the onco-mouse — are not patentable in Canada. On appeal, however, the Court held that the elected legislature should decide the policy issue of patentability rather than the patent office or the courts. European countries follow the European Patent Convention, which provides that "inventions shall not be considered patentable where their commercial exploitation would be contrary to 'ordre public' (public policy) or morality". But even with this provision, public policy considerations have had little effect in the context of patenting human genes. For example, the challenges mounted against the patenting of higher life forms on grounds of public policy, including the applications for patents on the onco-mouse and genetically engineered soya, failed to stop patents on these inventions¹⁶.

The goal of patent officials is to apply the technical rules of patent law to permit the greatest number of patents. As such, the criteria that determine whether a patent application should be denied are generally narrowly interpreted. It has been argued that, "the EPO applies the maxim that 'exclusions from patentability are to be construed narrowly'"¹⁷. In addition, many of the exclusion criteria and cautionary declarations concerning these patents, such as the UNESCO statement against financial gain from genes in their 'natural form', have little real meaning (for

example, patent law has never allowed the patenting of something in its ‘natural form’). This means that such measures are unlikely to change the way patent offices do business.

Box 1 | Genetic patents

Patent offices have, for years, granted patents over genetic material, whether human or otherwise. Once genetic material — whether a gene, a DNA sequence, cDNA, EST (expressed sequence tag) or SNP (single nucleotide polymorphism) — has been isolated and meets the tests of novelty, non-obviousness, and utility or industrial application, it is patentable. In legal terms, genetic sequences as they exist within the body are not patentable because they are classed as being either products of nature (as in the United States) or discoveries rather than inventions (as they are considered to be in Europe). The inventor, therefore, must describe the isolation of the sequence and a use for it.

Claims can be drafted to the isolated genetic material itself. For example, a person could claim a patent right over isolated genetic sequences (for example, United States patent no. 6,083,688 — Platelet glycoprotein V gene and uses) or isolated genetic sequences, such as SNPs or ESTs (for example, United States patent no. 6,083,721 — Isolated nucleic acid molecules encoding PARG, a GTPase activating protein which interacts with PTPL1), or for a cDNA (United States patent no. 6,083,719 — Cytidine deaminase cDNA as a positive selectable marker for gene transfer, gene therapy and protein synthesis).

Methods of using the genetic sequence may also be patented. For example, a person can claim the use of a genetic sequence as part of a living organism that would otherwise not possess that genetic sequence (such as the patent above — United States patent no. 6,083,719).

One continuing debate that concerns the patenting of genetic information relates to the utility requirement. Although it is true that almost any identified genetic sequence has some use, patent law requires that this use be more than abstract. This usually means that the inventor must describe the function of the gene and that this function must be more than simply of scientific interest. But how much knowledge the inventor must possess of the specific function of the genetic sequence within the body has not yet been firmly established within patent law. The new proposed utility guidelines in the United States require that the utility be real, substantial and credible.

Another important reason why patent law has marched forward in the face of public anxiety is that genetics and biotechnology are an increasingly important component of Western economies. This has led to the paradoxical situation where one arm of a government formally recognizes ethical and policy concerns about gene patents, whereas another arm enthusiastically promotes biotechnology. In this climate, any policy that has the potential to affect the growth of this emerging industry will be met with a degree of suspicion. The sharp decline in biotechnology stocks that followed the mistaken perception that the Clinton and Blair announcement would lead to new patent rules (for example, the share price of Incyte Pharmaceuticals fell by 27% following the announcement) shows the industry’s sensitivity to this issue¹⁸. Indeed, it has been suggested in the United States that “if you can’t patent it, don’t invest in it”¹⁹.

It must also be recognized that United States patent jurisprudence has had a profound effect on international patent law. Since the key United States Supreme Court case of *Diamond versus Chakrabarty* in 1980, where an oil-eating bacterium was found to be patentable, it seems that there is little that cannot be viewed as being patentable subject matter, providing that the ‘invention’ has an element of human ingenuity. The United States has been active in encouraging other countries to comply with its patent norms. For example, international trade

agreements specify that human genetic patents can only be excluded if the sale of human genes were to jeopardize public safety, public health or the environment.

Identifying the practical concerns

So far, public concerns about how morally appropriate it is to allow patents on human genetic material have dominated much of the debate. Commentators have, however, also noted various other concerns that, if overlooked, could lead to specific social harms. From adversely affecting the research environment to hampering the distribution of useful technologies, these concerns seem more tangible than the claims that patents infringe human dignity or may lead to the commoditization of the human experience²⁰. Although these moral and ethical issues remain critical to the overall debate, a consideration of the more practical (and, in some cases, measurable) concerns may prove to be a more fruitful path towards constructive patent reform. Below, we discuss a few such examples.

Patents are designed to provide incentives for innovation and for the development of products from which the public can benefit. The logic behind patents is straightforward. If we pay people to invent, produce and distribute products (by granting them limited monopolies), they will do so. Unfortunately, this logic does not always work. Sometimes, patents may actually deter innovation and the development or availability of products or clinical services^{21,22}.

The limited monopoly granted to patent holders, for example, allows them to prevent others from independently investigating and offering new products, such as genetic tests and associated technologies. Some claim that this occurred when a patent over a sequence from the *BRCA1* gene was granted — a gene that is associated with hereditary breast and ovarian cancer²³. Such situations are sufficiently serious to have caused professional organizations to issue position statements about the patenting and licensing of disease-related genes and clinical procedures^{2,24}. For instance, the American College of Medical Genetics has called for broad licensing policies to ensure that access to tests is not inappropriately hindered². Preliminary evidence gives some credence to the concern. A pilot study of directors and other personnel from clinical laboratories doing DNA-based genetic tests found that 25% of these people reported that their labs had been prevented from continuing to offer or conduct a clinical test that they had developed and validated. In addition, 48% reported that they had decided not to develop or conduct at least one test because of a known patent²⁵.

Because patents are perceived to be such an important part of the commercialization process, they have also been implicated in the concerns associated with how genetic products, such as gene tests, are used and marketed²⁶. In general, when only one organization is able to provide a particular clinical service, it becomes more difficult to evaluate the service or compare its quality with competitor products. Moreover, patents also have the potential to increase the costs associated with the provision of genetic technologies. For example, the price of the test for the *APOE* gene for Alzheimer disease almost doubled after a commercial laboratory acquired an exclusive licence for the patent.

Gene patents may also prevent the conduct of research. Although many assume that basic research is exempt from patent infringement, there is no general statutory exemption for experimental use in the United States (although there is a specific one to permit clinical trials). Although United States courts recognize a patent exemption for ‘philosophical’ study, the scope of this exemption is, at best, confusing and, at worst, extremely narrow, leading many commentators to call for an amendment of the patent law itself^{27–29}. Again, preliminary data indicate that this concern is not misplaced. One study found that 14 out of 27 holders of patents on genetic tests said they would require a researcher to apply for a licence to study the penetrance and prevalence of the genetic mutation covered by their patent³⁰. The situation is

clearer for researchers in Europe. Under the European Patent Convention, both commercial and non-commercial research is permitted on the subject matter of a patent.

Some commentators have also suggested that the growing emphasis on patents has helped to create an atmosphere of secrecy among researchers² (particularly among “investigators in the field of genetics”³¹) and has skewed university research towards a commercial orientation^{29,32,33}. For example, one study of United States life-science faculties found that involvement with industry (which inevitably includes patent considerations) increased the chance that a researcher believed his or her “choice of research topics had been influenced by the likelihood that the results would have commercial application”³⁴.

Specific responses

The following discussion of policy concerns regarding patents on human genetic material is not intended to be exhaustive. Instead, we wish to illustrate here that practical and tangible policy concerns exist that can be separated out from the general debate over the appropriateness of human gene patents. Unlike some of the broader concerns over the commercialization of and definitions of humanity, policy makers can begin to address these concerns through direct and discrete legislative, judicial and regulatory responses. Whether it can be considered to be justifiable or not, a radical alteration in patent law — such as prohibiting the patenting of human genetic material — is unlikely to be tenable, because there are too many forces pushing the patent agenda forward. Moreover, it is far from clear that a wholesale abandonment of gene patents would be desirable. However, we may be able to craft specific responses to specific concerns. Because such an approach would target specific problems, rather than trying to disallow an entire class of patents, it may be a more manageable approach to patent reform. In this section, we discuss a few strategies that could be considered as ways to move this debate forward.

One of the simplest and most obvious ways to mitigate the concerns about the impact of patents on research and the development of genetic products would be to apply current patenting rules more stringently. For example, should we allow patents over any genetic sequence or only for those that the inventor has identified a known, clear and substantive function for? Many groups have argued that only the latter merits the reward of a patent^{22,35}. If patents are allowed on upstream discoveries, such as expressed sequence tags (ESTs), it might discourage the development of useful downstream inventions, such as genetic tests. Such an approach would also reduce the number of patents granted to those that have been well and narrowly described, thereby diminishing the “overlap and fragmentation of patent claims” that can negatively affect the dissemination of genetic technologies²². According to some commentators, such an approach is in agreement with existing patent legislation³⁶. For example, it has been noted that “the courts have applied these standards much more loosely than is required by the statute”. And, because no new legal framework is required, this is a relatively easy strategy for many countries to adopt. Indeed, this is a strategy that is already being considered, as shown by the United Patent Office’s recent interim guidelines that call for a stricter application of the utility requirement³⁷.

There are several other policies that could address the problems that patents raise in relation to research and the dissemination of technology. For example, the experimental-use exemption in the United States and Canada could be clarified to allow research to occur on the subject of a patent without fear of patent-infringement litigation. In addition, broader licensing policies that apply to certain subclasses of gene patents (for example, patents on clinically valuable genetic tests) could be considered. This reform would help to ensure that access to useful technologies is not hindered and that costs are not elevated by a monopolization of clinical services. Indeed, some United States physician groups have taken the position that patents on

genetic-testing procedures should be broadly licensed, for a reasonable fee, to any lab meeting technical and quality standards^{2,24}.

As we briefly noted above, patent law has also been implicated in issues associated with the commercialization process. Although patent law may not be the best forum in which to address ethical and policy concerns associated with the commercialization of genetic information (for example, federal regulation agencies, such as the United States Food and Drug Administration, seem well placed to meet many of the concerns)³⁸, patents are critical for the commercialization process. Given this, we ought to explore ways of harnessing the powerful economic incentives attached to patents as a means of mitigating the ethical concerns associated with the use of patented genetic inventions, such as the premature or inappropriate implementation of genetic technologies^{26,29,38–41}. For example, patent holders could be held to be liable for the unethical or negligent use of genetic inventions. Although such an approach would undoubtedly be controversial, it is not beyond the stretch of current negligence law⁴². Because the patent holder can use licensing agreements to control access to a given genetic invention, it is arguable that a patent holder could be expected to ensure that a licensee of that invention be required to meet emerging legal and ethical norms associated with the use of the technology, such as the requirement to provide fully informed consent or genetic counselling where appropriate.

Finally, two further strategies seem essential. First, and perhaps most importantly, more research is needed on the actual benefits and harms of human gene patents. Much of the public debate seems to be based on broad assumptions that patents either encourage innovation and product development or that they are bad for society generally. As much as possible, reform initiatives should be based on credible evidence. Second, it is important to encourage an open, continuing and informed dialogue between concerned members of the public, patent law experts, researchers, ethicists and the biotechnology industry.

Consequences and progress

Although many of the concerns highlighted in this article are the natural consequence of the use of patents in a market economy, policy makers need to reflect on whether these are the consequences they wish to encourage. Patents exist within a complex social and economic environment that includes various social values, research practices and business pressures. We are mindful that, in some situations, modifying patent law may reduce one problem (such as permitting more competition), while magnifying others (such as reducing incentives to conduct research and development). Nevertheless, although care must be taken, this debate needs to progress to ensure that patenting practices, as applied to genetic material, fulfil the ultimate objective of encouraging the development of genetic technologies into products for the public's good.

Update – note added in proof

The recent announcement that scientists will share a patent over a disease-related gene⁴³ with a patient advocacy group, who provided the researchers with blood and tissue samples⁴⁴, is a positive sign that researchers take seriously their moral responsibility to donors. Such steps are in agreement with recent policy statements issued by HUGO⁴⁵. Binding legal measures would help to ensure that researchers and companies who comply with this type of ethical norm do not face unfair competition from those who do not.

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Greenpeace activists protesting against patents on genetic material outside the European Patent Office, Munich, Germany. Image courtesy of Associated Press, © Associated Press.