

Our treacherous genes

The perils of an information explosion • by Tony McGleenan

The first draft of the Human Genome Project has been completed. While it has initiated a completely new era of biological research, it has also amplified public concerns about the possibilities of genetic discrimination, uninsurability and breaches of confidentiality. The dispute about ownership of genetic information, between the Human Genome Organization and its counterpart in industry, clearly illustrates the contentious nature of genetic research. The sequence of the more than three billion base pairs published at the end of the US\$3 billion project does not unveil particular details about any one individual. But the technological advances that have enabled this project to be completed far ahead of its schedule have provided new diagnostic and predictive techniques for potential diseases. It is at this, perhaps less dramatic, level that progress in genetic information technology poses particular legal, ethical and social challenges.

Technological advances that have provided new diagnostic techniques pose particular legal, ethical and social challenges

Policies that seek to offer protection for those who suffer from, or have risk factors for, genetically caused diseases are frequently based on the model of monogenic illness. But this simplistic approach ignores the complexity of most diseases, which are in fact non-inherited and multifactorial. Indeed, the major killers in the developed countries—diabetes, coronary heart diseases and cancer—are caused by a combination of inherited and environmental factors in most cases. As a recent Swedish study demonstrated, inherited

factors make only a minor contribution to the susceptibility for most types of cancers (Lichtenstein *et al.*, 2000). Viral and bacterial infections like AIDS, hepatitis or tuberculosis rely even less on genetic components, if at all. It is therefore important that sensitive decisions based on scientific results are used to draft the guidelines for acquisition and use of genetic information. Care must be taken to curb pernicious and unwarranted uses of genetic information without unduly restricting the clinical and research value of this technology.

The use of genetic information in actuarial decision-making is not entirely objective but an arbitrary product of the current state of research

The value of genetic information for life and health insurers is a particular cause for concern. Insurance companies insist that they must have access to all relevant information to prevent the phenomenon of adverse selection, whereby individuals fail to disclose the results of a negative genetic test but subsequently purchase abnormally large quantities of insurance. A series of such insurance claims could potentially ruin an insurance company. The industry argues that increased use of genetic tests means that, in order to avoid adverse selection and thus commercial ruin, they must seek disclosure of any existing diagnostic information. However, these arguments should be subjected to careful scrutiny. The use of genetic information in actuarial decision-making is not an entirely objective practice. Only some predispositions or illnesses can be diagnosed. Thus, the tests available, the indi-

viduals subjected to them and, ultimately, the information available to insurers is only an arbitrary product of the current state of research into genetic illnesses (McGleenan *et al.*, 1999). Furthermore, the arguments presented by the insurance industry about the dangers of adverse selection, while strong, are not compelling. Studies have shown that the life insurance industry could absorb the additional costs of a policy of *not* seeking the results of genetic tests (MacDonald, 1997). Where insurance is an essential prerequisite for social goods such as healthcare or housing, legislation may become necessary to prevent the insurance industry from seeking disclosure of genetic information. Such measures could prevent serious social inequities and ensure the continued development of genetic diagnostic technology.

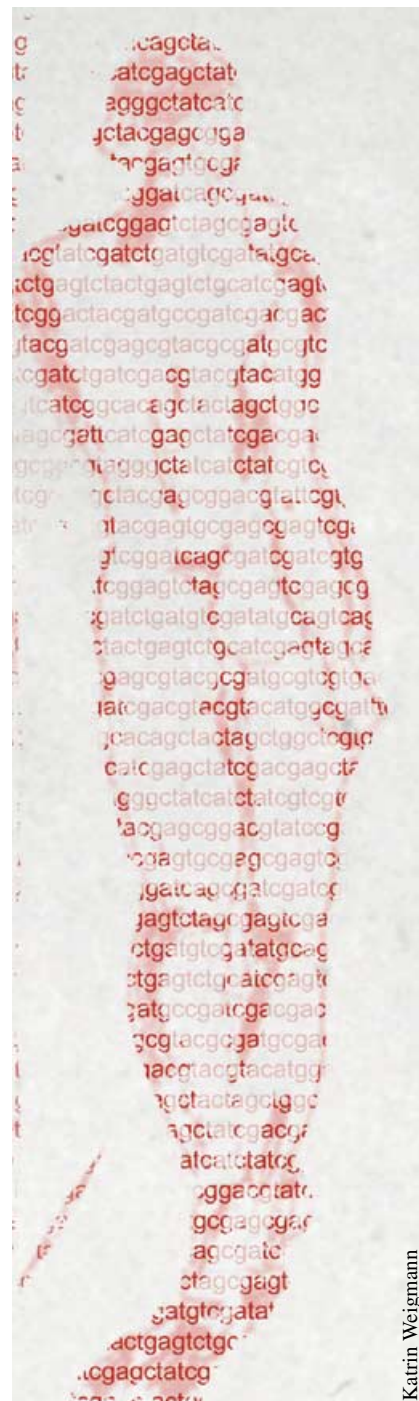
The proliferation of genetic information also poses challenges for the patients' right of confidentiality. Inevitably, some individuals will seek to keep the results of their genetic diagnosis private; yet such rights will often be in direct conflict with the interests of family members. They may claim, with some justification, a right to know the nature of familial genetic information. Alternatively, in cases of catastrophic inherited illnesses such as Huntington's disease, family members may seek to establish a right *not* to know the diagnosis of a sibling or relative. (Chadwick *et al.*, 1997). A recent article in *The New York Times* described the tough choices for family members when prenatal and mid-life genetic tests for a number of diseases become commonplace (Lewin, 2000). A case can be made for treating genetic information sensitively because it is personal information, rather than because it is uniquely private. However, affording individuals an absolute right to maintain secrecy could have

potentially disastrous consequences for relatives or scientific research.

The potential for abuse of genetic information has led to sustained calls for the introduction of legal protection of genetic privacy. The 'European Convention on Biomedicine', recently endorsed by 39 countries, attempts to introduce some protection for the genetic information of individuals. Article 13 of the Convention states that "any form of discrimination against a person on grounds of his or her genetic heritage is prohibited." In the USA, more than forty individual states have enacted genetic privacy legislation. But 'Genetic Privacy and Nondiscrimination Acts' introduced in the Senate in 1997 and in the House of Representatives last year, which would regulate these matters on a federal level, are still being discussed in the various subcommittees. Both drafts seek to protect individuals from being discriminated against by health insurers and employers. But, whereas the European Convention grants comprehensive protection against discrimination, the American bills will allow exemptions: "An employer may request or require or use the genetic information of an employee for [...] determining a genotype that is otherwise directly related to the work and is consistent with business necessity" (bill S. 422 in the Senate). As 'business necessity' is not further defined in either bill, abuse of this exception by employers might be possible.

However, laws designed to protect genetic privacy are often inadequate and inappropriate responses to public concerns. Their major weakness is that they address only the secondary consequences of abuse rather than tackling the primary issues that make citizens fear disclosure of genetic information. In the USA, genetic privacy laws have emerged as a response to social injustices, which come from the privatization of the health insurance industry. Private health insurers try to deny coverage to individuals who have an increased susceptibility to certain diseases. Thus, genetic privacy laws provide an indirect and ineffective means of addressing the problems that arise from continued political failure to provide a system of affordable universal healthcare.

Pressure seems to be growing in European states for the implementation of similar genetic privacy laws. But such laws will offer protection to only a relatively



limited class of ill, or potentially ill, individuals whose diagnosis has been effected through a molecular genetic test. These norms will not offer any protection to either those whose diagnosis has been made by non-predictive genetic means such as family history, or those whose illness has been identified by non-genetic methods. Only individuals who suffer

from a form of illness detected by a commercial molecular test will benefit from the protection of genetic privacy laws.

Genetic privacy laws may also have a potentially detrimental impact upon scientific research. The most commonly used model for genetic privacy protection affords individuals property rights for their own genetic material. But such rights are likely to severely inflate the cost of research. Genotyping has become essential for pharmaceutical corporations to develop new drug products. Genetic privacy laws may result either in a reduction of this research or, perhaps more likely, increase the expenses for drug development due to additional legal costs. These costs will ultimately be passed on to the patient through more expensive treatments. Furthermore, the creation of privacy rights in genetic information runs counter to the fact that public health research involves a sophisticated form of molecular epidemiology. Indeed, some academic researchers in the USA fear that genetic privacy protection will dry out clinical research because individuals view their genetic information as a toxic heritage that ought to be concealed from third parties at all costs.

Individuals view their genetic information as a toxic heritage that ought to be concealed from third parties at all costs

The protection of genetic information is a subject of great concern because misuse of such information has many social implications. But the introduction of genetic privacy laws addresses only the secondary consequences rather than the primary social problems. Policymakers need to examine carefully the reasons why the acquisition and use of genetic information is such a source of public anxiety. There are clear tensions between the need to protect individual rights and the desire to advance the common good through developments in genetic technology. Only when these tensions are adequately addressed can the full clinical and scientific potential of genetic technology be realized.

Chadwick, R., Levitt, M. and Shickle, D. (1997) *The Right to Know and the Right not to Know*. Avebury Press, Aldershot, UK.

Lewin, T. (July 21, 2000) Genetic testing brings tough new choice in families. *The New York Times*.

Lichtenstein, P., Holm, N.V., Verkasalo, P.K., Iliadou, A., Kaprio, J., Koskenvuo, M., Pukkala, E., Skytthe, A. and Hemminki, K. (2000) Environmental and heritable factors in the causation of cancer—analysis of cohorts of twins from Sweden, Denmark, and Finland. *N. Engl. J. Med.*, **343**, 78–85.

MacDonald, A.S. (1997) How will improved forecasts of individual lifetimes affect underwriting? *Philos. Trans. R. Soc. Lond. B Biol. Sci.*, **352**, 1067–1075.

McGleenan, T., Wiesing, U. and Ewald, F. (1999) *Genetics and Insurance*. Springer Verlag, New York, NY.

The author is senior lecturer at the School of Law of Queen's University in Belfast.
E-mail: t.mcgleenan@qub.ac.uk

DOI: 10.1093/embo-reports/kvd061



Rewarding true innovation

Experimental use exemption and the trends in gene patenting • by Luca Falciola

In 1980, the US Supreme Court decision in *Diamond v. Chakrabarty* not only helped considerably the development of the biotech industry, but also affected practices in the intellectual property area. After the rejection of the US Patent Office's claim that living organisms *per se* cannot be patented, companies now were able to seek a wider protection for products created using DNA recombinant technologies, while patent offices were given the opportunity to expand their activities into this area.

The speed at which genetic information is accumulated by far exceeds the speed at which patent offices can examine applications thoroughly

During the 1980s, recombinant proteins were mostly developed for the treatment of pathologies such as diabetes, anemia, growth disorders and infertility. The properties of these molecules were well characterized *in vivo*, so patent offices were able to apply the well established principles of patent law—utility, inventiveness, novelty and unity—in a satisfactory way.

But in the last decade, technological advances in sequencing and bioinformatics have allowed biotech companies to identify, massively and at low cost, novel

gene sequences for which they are seeking patent protection (Figure 1; Table I). The speed at which genetic information is now accumulated and submitted to patent offices by far exceeds the speed at which genes can be even roughly characterized, and that at which patent offices can examine applications thoroughly to decide on their patentability (Figures 2 and 3).

Due to this trend, a hard-to-calculate, but enormous and increasing bulk of genetic information has become *de facto* a research tool (Ducor, 1999). As had been made clear in articles and discussions in journals like *Nature* and *Science*, many scientists regard this as a major deterrent to research, and hold the patent system responsible for this distortion of law practice. However, before labeling the whole patent system as faulty, the actual impact of this patenting frenzy on the activities of research laboratories should be evaluated, taking into account some of the concepts of patent law, as well as some consequences of the current situation.

Apart from the basic requirements for obtaining a patent, the patent system also assigns a fundamental importance to the concept of experimental use exemption to patent infringement (Ducor, 1999). This institution stems directly from the original goal of the patent system to promote innovation by granting, in exchange for public disclosure of the invention, a time-limited exclusivity for commercial exploitation.

Patent infringement takes place if a product or a method covered by a patent is produced, used, imported or sold without permission or license from the patentee. A researcher working on a patented matter to improve it cannot be sued for patent infringement as the experimental use exemption applies to his work.

A researcher working on a patented matter to improve it or for non-commercial research cannot be sued for patent infringement

Patent literature makes available to the public a large body of knowledge in terms of DNA/protein sequences, biological materials deposited in public collections such as the American Type Culture Collection, and experimental results, which is not always, or only later, disclosed in other form. This information is published in a format compliant with Patent Offices procedures of analysis, which are different from those of the scientific peer-reviewing system, but scientists can find and make use of relevant first-hand data for the purpose of their research.

Some attention should be taken in considering the possibility that some research activities may not fall under the experimental use exemption. In non-corporate