Human gene patents: the possible impacts on genetic services healthcare

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ABSTRACT

- The patent system has been seen as a critical factor driving innovation in clinical medicine, particularly in medical devices and diagnostic assays.
- The licence terms and business model proposed by Myriad Genetics Inc. for testing the hereditary breast cancer susceptibility genes *BRCA1* and *BRCA2* could stifle innovation (particularly if other companies adopt similar business models), and are likely to limit the ability to provide high quality public genetic testing services in Australia.
- Under the Myriad model, testing for the *BRCA1* gene would be undertaken by an organisation removed from the integrated public healthcare system. Based on overseas experience, Australia can expect a 2–3-fold increase in the cost of this testing, which will provide only partial information on the hereditary breast cancer status of the patient.
- Commercial exploitation of gene patents needs to be regulated to balance the patent holders' right to profit from their inventions (necessary to drive further innovation) and the public policy objective of high quality, equitable healthcare.

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MANY DISEASE-CAUSING GENES have been discovered and patented. More than 9360 letters patent have been filed, covering about 127 000 human gene and partial gene sequences.[1] The discovery of new disease genes has been rapidly assimilated into clinical practice through refining in-house assays developed in clinical research laboratories. Many of these procedures are now validated analytical methods used for predictive and diagnostic genetic tests. Publicly funded hospitals and institutions provide these genetic tests through an integrated clinical framework that ensures they are offered equitably to families or individuals with strong evidence of a hereditary disease.

Commercial involvement and patenting is well established in healthcare. The patent system is a government intervention into the commercial free-market designed to prevent market failure, foster innovation and provide a period of monopoly protection for inventors. For many years, this intervention has been seen as a critical factor driving innovation in clinical medicine, particularly in the fields of medical devices and diagnostic assays. Without patent protection, public benefit arising from such developments would be much less. However, increasing commercial pressure is leading patent holders to develop new strategies and business models for the commercial exploitation of their inventions. These new strategies and business models are designed to take maximum advantage of the very broad claims often included in patents relating to human genes and functional genetic sequences. They threaten the optimal provision of genetic healthcare and the integrated clinical services through which they are currently provided.[2-4] A model of particular concern to the healthcare industry, and which may provide a test case for the exploitation of other disease gene patents, is that developed by Myriad Genetics Inc. and its commercial partner in Australia, Genetic Technologies.

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Case study: the hereditary breast cancer gene patents

Myriad has been granted patents in many countries, including Australia, over *BRCA1* and has filed claims over *BRCA2*, two genes that are associated with an increased susceptibility to familial breast and ovarian cancers. The Myriad business model is to license the test exclusively to a limited number of commercial genetic laboratories within specific geographic regions. However, these laboratories may only be licensed to perform limited testing of the *BRCA* genes, with complete sequence analysis performed only by Myriad in Salt Lake City (Utah, USA).[2,5]

This exclusive licensing practice for testing the *BRCA1* gene effectively creates a diagnostic monopoly on familial breast cancer testing. It blocks complete gene testing for a disease that can arise from a number of genes, and prevents gene testing laboratories offering an integrated laboratory and counselling clinical service. Furthermore, it restricts future research in this area. Although patent law does not usually prevent genuine research from being undertaken, even if patented inventions are used for that purpose,[6,7] the Myriad business model can control access to and use of genetic material, thus restricting further research and stifling innovation.[6,8,9] The use of patent rights in this way is directly contrary to the fundamental policy objectives underlying the patent system.[7]

Conflicting public policy objectives

The patent system aims to prevent market failure with regard to new and useful inventions by awarding to patentees a legally enforceable, limited-term monopoly over their publicly disclosed inventions.[10] In so doing, the patent system not only prevents the unauthorised "free riding" that is a cause of market failure, it also encourages innovation in two distinct ways. First, by protecting patentees from imitation for a strictly limited period, patents force potential competitors to improve on and "invent around" existing patents. Second, by making publicly available the details of all patented inventions, the patents system provides researchers and potential competitors with an extensive database of relevant information from which to pursue further innovation and improvements.

As such, the international patent system offers substantial public benefits. But, as a recent Canadian study shows, it is often a second-best instrument, at least in part because of opportunistic behaviour, such as the use of blocking patents and restrictive licensing terms, on the part of patentees.[11] The Canadian study also shows that the welfare gains associated with the patent system can be increased if the system incorporates effective research exemptions and related freedom-to-operate provisions.

The policy objective underlying the Australian public healthcare system is equitable access to healthcare for all Australians. There is concern that Myriad's licence terms for *BRCA1* and *BRCA2* testing may threaten the ability of healthcare authorities in Australia to deliver high quality genetic testing. There are several ways in which Myriad's terms can have this effect:

- By limiting testing to certain commercial laboratories, the licence terms disrupt the closely linked publicly funded testing, clinical and counselling services.
- Publicly funded genetic testing services will still be required to provide other non-patented and thus not commercially attractive gene tests, compromising their viability and expertise.
- The licence terms have been projected to result in a two- to threefold increase in genetic testing costs,[2,7,12] affecting the budgets of public genetics services.
- Performing all full-sequence testing at one overseas commercial laboratory bypasses national jurisdiction and procedures for ensuring quality control and peer review.
- The licence terms exclude the development and use of complementary or alternative technologies for testing for *BRCA* mutations which currently may not be identified by the patented technology.[3,12]

Thus, the Myriad patents and business model have major implications for other genetic diseases with commercial significance. If other companies follow the Myriad precedent, then negotiating licences and implementing gene tests within the scope of those licences will pose an overwhelming logistical impediment to the maintenance of integrated, publicly funded, functional laboratory and clinical services.

Government responses

In countries such as Canada, Belgium, the Netherlands and France, governments and research agencies are calling for national guidelines and regulation of gene testing through legislation as an imperative.[4,7,11] These countries also recognise that freedom to undertake further research on disease genes is critical for developing new disease tests and therapies and improving healthcare. This research will not take place unless there is opportunity for new discoveries to be commercially explored — a very difficult proposition in the light of the broad claims being granted in some disease gene patents.[3,9]

In Australia, guidelines produced by the National Health and Medical Research Council and the Human Genetics Society of Australasia recommend that diagnostic and predictive genetic testing should be available to those with genuine, proven need, on a basis that promotes optimal patient care. Testing should be performed according to best practice guidelines, which include:

- use of laboratories with links to clinical genetics services and other referrers;
- informed consent procedures and pre-test counselling;
- appropriate testing standards and quality systems requiring peer-reviewed laboratory accreditation;
- expert interpretation of results; and
- continuing support and post-test counselling.

In response to growing community and government concerns, the Australian Health Ministers Advisory Council recently established a Working Group to report generally on gene patents, and the Australian Law Reform Commission was instructed to conduct an inquiry into gene patenting and intellectual property. Through these committees, the Australian governments are seeking to develop strategies to strengthen the basic tenets of the patent system and to clarify how patents can best act for public good. For the problem is not in patenting of disease genes; rather it lies in how patents are permitted to be commercially exercised or exploited. This insight suggests a possible solution.

Allow patenting but regulate commercial exploitation

In our opinion, new diagnostic or predictive genetic tests should be subject to evaluation and endorsement by an expert body before their introduction into clinical practice. The expert body should consider test accuracy, clinical utility and appropriateness, and cost and cost-effectiveness. The expert body should also be empowered to consider, and impose, terms requiring that tests be broadly licensed with licensing agreements that should not unreasonably limit access.

A whole-of-government approach should be adopted to fund and regulate genetic testing, with a view to establishing national genetic testing guidelines and using existing statutory frameworks to regulate genetic testing.

Government funding for testing, through Medicare Benefits Schedule payments, should be restricted initially to Australian publicly funded facilities, to ensure stringent budgetary control, particularly during the development of

regulatory and funding frameworks. This would ensure a robust Australian genetic testing infrastructure and the continuation of relevant capabilities in the public system. This is particularly important in encouraging further innovation so that new knowledge will benefit Australians and Australian biotechnology and healthcare.

Competing interests

None identified.

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