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The dangers of diagnostic monopolies

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Gene patents are meant to encourage innovation, but in DNA diagnostics, they have stirred controversy. Amid worries and worst-case scenarios, there are few empirical studies to help form an accurate picture of how patents affect clinical genetic testing in the United States. We assembled eight case studies addressing the effects of patents and licensing on access to genetic tests for ten conditions. The studies were prepared for a task force of the Secretary's Advisory Committee on Genetics, Health and Society and are available as inputs to a draft report¹ for the US Secretary of Health and Human Services. They paint a complex picture of the patent landscape.

Despite the fears, patents have not caused irreparable harm in genetic diagnostics, but neither have they proven greatly advantageous. Although our findings detect no pervasive effects that consistently help or hinder clinical access to genetic testing, there are some problems that could be addressed to the benefit of patients, researchers, health professionals and companies alike.

Pricing and availability

Most concerns centre on monopoly situations, in which exclusive licensing results in a single dominant provider. But prices of patented and exclusively licensed tests are not dramatically or consistently higher than those of tests without a monopoly — a contrast with the strong price effects of drug patents. For example, unit prices for BRCA testing (for breast cancer susceptibility) — provided solely in the United States by Myriad Genetics in Salt Lake City, Utah — are comparable with similar tests for colon cancer susceptibility available from many labs under non-exclusive licences. We also do not find consistent price effects of patents in other case studies. Other factors affect pricing, such as efficiencies of scale from high-volume testing and the way health plans use administrative codes to pay for tests.

Prices would matter less if everyone in the United States were insured for genetic diagnostic tests. Health-plan coverage and reimbursement are problems even when many labs offer a test. But with only one provider, the absence of alternatives can exacerbate the problem. Some health plans do not have a contract with the sole provider, for example. Nevertheless, after ten years of testing, Myriad now reports payment arrangements that substantially cover costs for more than 90% of tests, so problems in coverage and payment cannot solely be attributable to monopolies. One justification for gene patents is that they speed up the development of tests. But the patent incentive is usually not necessary. Barriers to test development are fairly low compared with in the 1990s, when the genetic bases for most of the conditions we studied were elucidated. Academic labs typically offer testing soon after publication of an association, when demand exists. After exclusive licences are issued, however, the licensee enforces patents to 'clear' the market of competitors.

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Monopoly effects on test quality are equivocal. For example, in 2006, Myriad's methods of BRCA testing were shown to miss some DNA deletions and rearrangements². Yet such problems cannot be ascribed only to the monopoly. Problems are apparent in genetic testing for other conditions offered by labs with non-exclusive rights. Test quality is a general problem but monopolies can exacerbate it.

Sole providers can also, for better or worse, establish standards of care. Licences for patents related to risk prediction for Huntington's disease and Alzheimer's disease enforced clinical standards set by the professional community³. If compliance with standards is desirable, patents can achieve it. But is a standard of care set by a single provider desirable? In other countries, testing labs take various approaches before ordering full-sequence BRCA testing as licensed by Myriad. Yet in the United States, Myriad sets the standard because it alone can do testing. If testing alternatives are valuable, exclusive licences limit their availability.

Exclusive licences are difficult for other companies to develop around. Most genetic disorders are heterogeneous — different genes and mutations lead to clinically similar syndromes. An exclusive licence to one or a few common genes or mutations can drive testing to one provider, regardless of whether licensed patents cover all varieties of the disease. This 'penumbra effect' seems to have driven testing for predisposition to Alzheimer's disease, spinocerebellar ataxia and hereditary hearing loss to Athena Diagnostics in Worcester, Massachusetts, and long-QT syndrome testing (for inherited cardiac arrhythmia) to PGxHealth in New Haven, Connecticut. The effect gives the sole provider a leg-up in incorporating new variants into its assay. It also alters patent incentives for others. If a gene or pathogenic variant is discovered but not patented, a sole test provider can incorporate it into its testing, paying nothing to the discoverer. If the discoverer wants a piece of the action or to break the monopoly, he or she must patent it.

Once exclusive rights to common genes or mutations exist, the only realistic option is to license new variants exclusively, either to the existing sole provider (augmenting the monopoly) or to a rival company. Indeed, the potential for mutually blocking patent rights seems to be developing: PGxHealth has been the sole long-QT test laboratory for several years, based on exclusive rights to several patents. But the University of Utah in Salt Lake City recently awarded exclusive rights for other long-QT-related patents to Bio-Reference Laboratories in Elmwood Park, New Jersey. It remains to be seen how this situation will affect patient access.

An instrumental right

Some companies that have used patents to build their businesses claim that their services are of equal or better quality than university and reference laboratory services. But, in our case studies, clinicians, patient groups and even other companies argue that patents should be non-exclusively licensed for diagnostic purposes. Who should provide proof as to whether patents and exclusive licences are promoting or interfering with progress?

We propose that patient rights should trump patent rights if a company engages in practices that undermine the purpose of patents in the first place. The burden of proof should lie with the companies enforcing patent rights.

Patenting is a right, but an instrumental one. The US Constitution states that patents are granted to promote public good through advancing science and technology. The stakes are high when human health is involved. Governments should take action when harm is apparent or foreseeable, especially when technologies spring from public funding. The government has powers that have not been used: to decide coverage and reimbursement for tests, to regulate and to ensure that patent rights promote health and safety under the 1980 Bayh – Dole Act.

Academic institutions play an important part in clinical genetic testing. They own most of the patents relevant to Mendelian disease testing⁴, and 60% of clinical genetic testing laboratories are within universities⁵. Academic institutions thus both own most genetic-diagnostic patents and operate many of the laboratories against which such patents are enforced. This paradox derives from technology licensing and clinical laboratory services that are run by different parts of universities and have different missions. These need to be aligned. A non-binding statement endorsed by the Association of University Technology Managers in 2007 says “licenses should not hinder clinical research, professional education and training, use by public health authorities, independent validation of test results or quality verification and/or control”.⁶

As we attempted to reconstruct custody chains for the relevant intellectual property, university technology licensing offices were often among the missing links, failing to provide information despite repeated inquiries. If we are to demand transparency from private genetic testing laboratories, academic institutions that license technologies arising from federal grants should be at least as willing to provide information. Research institutions that use public dollars to create licensed inventions are publicly accountable for the disposition of the resulting intellectual property.

Looking to the future, robust genomic technologies promise to transform genetic testing. The price of full-genome sequencing will drop, and speed and accuracy will improve. Soon, sequencing a person’s entire genome will cost less than current tests for one or a few genes. Yet thousands of patents claim human DNA sequences⁷ and so some patent claims will be infringed by full-genome sequencing. This legacy of patented sequences could cause considerable mischief, depending on how intellectual property is managed. As genetic testing is transformed by new technologies, patenting and licensing practices and government oversight should focus on the net social benefit for patients as well as on freedom to innovate.

References

1. Secretary’s Advisory Committee on Genetics, Health, and Society . Public Consultation Draft Report on Gene Patents and Licensing Practices and their Impact on Patient Access to Genetic Tests. 2009. Available at http://oba.od.nih.gov/SACGHS/sacghs_public_comments.html
2. Walsh T, et al. J Am Med Assoc 2006;295:1379–1388.
3. Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health. Natl Acad Press. 2005
4. Henry MR, Cho MK, Weaver MA, Merz JF. J Law Med Ethics 2003;31:442–449. [PubMed: 14626552]
5. Cho MK, et al. J Mol Diagn 2003;5:3–8. [PubMed: 12552073]
6. In the Public Interest: Nine Points to Consider in Licensing University Technology. (Assoc. Univ. Technol. Managers, 2007). Available at <http://www-leland.stanford.edu/group/OTL/industry/resources/whitepaper-10.pdf>
7. Jensen K, Murray F. Science 2005;310:239–240. [PubMed: 16224006]

Recommendations in case of monopoly

We find six obstructive practices and policies that we think should negate gene patent enforcement for diagnostic-testing companies with exclusive rights. Patient rights should trump patent rights if a company's policies do not permit:

- Basic clinical research, including genetic testing in clinical trials or health-services research
- Performing a test in a form that it does not offer (such as prenatal or preimplantation diagnosis)
- Testing in a territory where the company does not offer a test but has exclusive rights
- Getting second opinions or verification testing
- Testing those not covered by its payment agreements with insurers and health plans
- Research and development to make testing more comprehensive, more accurate or less expensive

As unique guardians of key information, sole-provider laboratories have a responsibility to

- Share data about allele frequency, number of tests, aggregate results and other facts relevant to public health
- Contribute to public databases that catalogue variants and contribute to their interpretation
- Perform proficiency testing and otherwise ensure quality of testing
- Disclose intellectual-property ownership and licensing provisions related to genetic diagnostics

Figure 1.

Table 1

Genetic testing licensing in the United States

Condition	Test provider(s)	Patent(s) owner	Licensing
Tay-Sachs disease	Various	National Institutes of Health (NIH)	Not licensed
Inherited risk of colorectal cancer	Myriad and others	University	Non-exclusive
Inherited risk of breast/ovarian cancer	Myriad Genetics	University, Myriad, NIH	Myriad(exclusive)
Canavan disease	Various	Miami Children's Hospital	Private settlement
Cystic fibrosis	Various	University and hospital	Non-exclusive
Alzheimer's disease	Athena Diagnostics	University	Athena (exclusive)
Spinocerebellar ataxia	Athena	University and Athena	Athena (exclusive)
Hemochromatosis	Various	BioRad	Non-exclusive
Hearing loss	Athena and others	University and hospital	Athena (exclusive)
Long-QT syndrome	PGxHealth	University	Possible mutual block