

The problems of patents on diagnostic testing kits

Diagnostic kits are biotechnological tools that provide information about a patient's health by analyzing biological variables related to a particular biological state or outcome. Diagnostics exist for healthy conditions like pregnancy, transient diseases like viral infection, and chronic diseases like cancers and genetic disorders. Kits utilize a wide variety of biochemical, cytogenetic, and/or molecular methods to analyze samples of nucleic acids, chromosomes, proteins, metabolites, and other small molecules¹.

Driven by improvements in genomics and the promise of personalized medicine, genetic diagnostic tests are increasing in number, improving in quality, and generating a fair amount of excitement:

Genetic testing originally was a tool for evaluating a person's risk of developing or passing on single-gene disorders, enabling early detection of inherited diseases or conditions. However, advancing knowledge of the human genome—coupled with rapidly evolving technologies—is providing new opportunities to assess common, multifactorial disorders such as heart disease, diabetes, asthma, and mental illness, which likely involve multiple genes and environmental factors. Moreover, genetic testing increasingly is being developed for use in personalized medicine, for example, for targeted treatment selection, identification and quantification of treatment risks, monitoring of treatment effectiveness and prognosis, and personalized disease management. Thus, the number of tests being developed and used in clinical practice will increase over time².

The types of patents most strongly associated with genetic tests based on DNA samples are "composition of matter/manufacture claims to isolated nucleic acid molecules (typically for molecules that are useful as probes against genetic markers); manufacture claims to genetic test kits; process claims to diagnosis through genetic testing; and manufacture claims to gene chips and microarrays¹." Patents on isolated nucleic acid molecules and on diagnostic processes are referred to as "diagnostic methods."

Controversial Case Studies

To understand how patents and diagnostic tests interact, we'll review two controversial diagnostic method patents and use them as a concrete, if somewhat extreme, basis for exploring the problems of patents on diagnostic testing kits.

Myriad Genetics was granted diagnostic method patents (both composition and method patents) on particular alleles of the BRCA1 and BRCA2 genes that indicate risk for breast and ovarian cancer in 1990. Myriad had previously conducted significant research to determine the clinical validity of predictions based on the two alleles. Their patents covered both sequencing a patient's BRCA genes and comparing the results with the risky alleles. Currently Myriad is still the sole provider of BRCA1 and BRCA2 cancer diagnostics based on complete sequencing of the genes, despite less expensive BRCA testing becoming available through public laboratories in the mid 1990's. This alternate testing is based on a 2-step diagnostic that involves using analysis of the BRCA proteins as a guide for limited sequencing of the BRCA genes³. It will be interesting to see how Myriad attempts to protect its sequencing patents in the face of falling genome sequencing costs.

A more controversial diagnostic method patent was awarded to three medical school professors from the University of Colorado and eventually licensed to Metabolite Laboratories. The patent covered measuring the total concentration of homocysteine in a patient's bloodstream and correlating high levels with vitamin B-12 deficiency. This patent is controversial because Metabolite asserts licensing rights for the "process" of correlating high homocysteine levels with vitamin deficiency. Although other inventors might find alternate methods of measuring homocysteine levels, there is only one way of doing the correlation, providing Metabolite with a strong monopoly on the patent⁴.

Metabolite licensed the diagnostic to LabCorp, whom later switched to a different vendor's kit to measure homocysteine levels while continuing to promote the correlation method protected by Metabolite's patent to customers. Metabolite took them to

¹ U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services. (http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf)

² What's the Point in Patenting Genes? (<http://beta.technologyreview.com/biomedicine/22704/page1/>)

³ History of a gene patent: tracing the development and application of commercial BRCA testing. (<http://www.ncbi.nlm.nih.gov/pubmed/14748275>)

⁴ Laboratory Corporation of America Holdings v. Metabolite Laboratories, Inc. and Competitive Technologies, Inc. (<http://topics.law.cornell.edu/supct/cert/04-607>)

court. LabCorp appealed, and the case progressed to the Supreme Court. However, the Court encountered a technicality and didn't rule one way or the other.

These two cases present a startling aspect of diagnostic method patents: the strongest parts of the patent are not the composition claims, but the process claims. While another inventor might be able to "engineer around" a particular material or manufacturing process, in principle a broad interpretation process claim could be impossible to uniquely reinvent.

Based on these two oversimplified case studies, I have several concerns about patents and diagnostics:

Concern 1 Diagnostic method patents with unique process claims may be impossible for other inventors to engineer around and consequently would amplify the effective monopoly granted to the patent holder. The patent holder would have absolute monopoly over the price, supply, and use of the diagnostic. If they elected to exclusively license the patent, patients and scientists might suffer because they wouldn't be able to seek a second opinion on the results of the diagnostic, or perform the diagnostic in alternate forms not offered by the patent holder (i.e. neonatal), or in territories where the patent was respected but the diagnostic was not sold.

Despite these concerns, previous studies of diagnostic kits in monopoly situations have not found that they are consistently more expensive or worse in quality than non-exclusively licensed kits^{1,2}.

Concern 2 Ubiquitous genome sequencing will undermine the composition claims of diagnostic method patents, leaving only the unique process claims. When an individual has their genome sequenced, they may be incidentally infringing on certain composition claims of diagnostic methods based on sequencing particular genes. Even if not, it is imaginable that once the sequence data is in hand, it would be much easier to infringe on a process claim or patent, since the transaction cost would just involve analyzing the particular sequence data in the manner specified in the patent. Hence the falling costs of genomic sequencing technology, the ubiquity of computers, and the public disclosure of analytical methods in the patent application could combine to make infringement easier to do and harder to detect. This might be a source of pressure for owners of analytical processes patents to explore alternative strategies for monetizing their inventions, at the very least with broad, cheap licensing, or more radically with commons-based frameworks.

Concern 3 Many gene markers suspected of clinical relevance may be patented based on preliminary work but never clinically investigated in trials. When patents have prevented other interested parties from running the trials themselves due to inordinate licensing costs, there have been calls for the construction of a commons for gene markers, organized by the government, that researchers would be free to investigate and collaborate on, similar to the Human Genome Project. This could be a good candidate for further research⁵.

Lastly, as our ability to sample biological systems becomes more powerful and less expensive, and our understanding of these systems becomes more complete, there will be growing opportunities to develop "multiplex" kits that measure the state of hundreds or thousands of different samples of the system, beyond just nucleic acids. Due to the chemical heterogeneity of metabolomes, it is unlikely an iterative metabolomic "sequencing" reaction analogous to the nucleic acid sequencing process will be developed. In the worst case, unique probes will be needed to detect each metabolite. If each is encumbered with its own IP, the transaction cost of licensing them for a high-throughput measurement device might make commercialization impossible. Therefore, metabolomics researchers and developers may have strong incentives to participate in a metabolomics sensor commons.

Further research questions

- How common and how strong are process patents for most diagnostics (not just the crazy extremes)?
- Are there any existing multiplex diagnostics? How are the individual probes or tests licensed? Is there an opportunity for promoting a commons approach?
- What are the basic stats of the Diagnostic Kit subsector: market cap, top 10 most profitable kits, typical lifecycle and development cost.

⁵ *What's the Point in Patenting Genes?* (<http://beta.technologyreview.com/biomedicine/22704/page1/>)