FROM BIRTH TO DEATH AND BENCH TO CLINIC

THE HASTINGS CENTER BIOETHICS BRIEFING BOOK

for Journalists, Policymakers, and Campaigns

CHAPTER 15

Gene Patents

Robert Cook-Deegan, "Gene Patents," in *From Birth to Death and Bench to Clinic: The Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns*, ed. Mary Crowley (Garrison, NY: The Hastings Center, 2008), 69-72.

gene patents

by Robert Cook-Deegan

Framing the Issue

About about 3,000 to 5,000 patents on human genes have been granted in the United States. At first blush it seems odd to patent a gene, which is why the practice has been controversial since it began nearly three decades ago.

The public debate about patenting genes is partly about discomfiture with patenting all natural products and partly about practical concerns with the consequences—balancing the need for commercial incentives to develop treatments and screening tests with the virtues of open science (see chapter 20, "Intellectual Property and Biomedicine"). The same controversies surrounding biomedical patents in general are amplified when the patent is on a building block of life.

The idea that genes can be owned is unethical to those who see the human genome as our common heritage. One particular concern is that patents make the cost of genetic tests and genetic therapies unacceptably high by stifling competition, a concern expressed perhaps most famously in the worldwide uproar over patenting the BRCA1 and BRCA2 genes associated with cancer. Another fear is that gene patents may inhibit biomedical innovation by blocking scientists' access to genes and genetic materials that are essential to research.

Gene Patenting: Science and History

A gene patent is intellectual property, which gives the patent holder the right to exclude others from making, using, selling, or importing an invention for a period of time, usually 20 years. Although gene patents often base their claims at least partly on whole genes, they also cover many kinds of inventions involving the components of genes and genetic technologies (see box, "Gene Patenting Glossary"), including:

- Associations between a DNA variant and a disease, condition, or function
- The DNA sequence that makes a particular protein, regulates a gene, or is useful for studying genetic variations
- RNA sequences that turn genes on or off, or control other functions
- Cell lines, methods of treatment, and diagnostics
- Transgenic animal models of disease and genes used to make them

The first patent on a recombinant DNA method was granted

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HIGHLIGHTS

- There are 3,000–5,000 U.S. patents on human genes and 47,000 on inventions involving genetic material.
- Gene patenting is unethical to those who see the human genome as our common heritage.
- One concern is that patents might make the cost of genetic tests and genetic therapies unacceptably high.
- Another concern is that gene patents may inhibit biomedical innovation by blocking scientists' access to genes and genetic materials essential to research.
- Though gene patenting is widely accepted throughout the world, many countries limit the scope of gene patents as a way to minimize the negative impact on health care costs and on the free flow of information in research.
- A patent reform bill passed the House of Representatives and is pending in the Senate; there is also a bipartisan bill to ban gene patenting.

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Gene Patenting Glossary

Gene – A basic building block of heredity consisting of a segment of DNA; it encodes a product, usually a protein but sometimes an RNA.

DNA (deoxyribonucleic acid) – A double-stranded molecule within each cell that encodes hereditary information; also the template for RNA molecules that turn genes on and off.

RNA (ribonucleic acid) – A molecule within each cell that determines protein synthesis and transmits hereditary information.

Recombinant DNA – Artificial DNA made by splicing DNA strands from different organisms. It is used for many purposes, such as replicating DNA for research, producing important proteins, and devising gene therapies.

in December 1980, just six months after the United States Supreme Court ruled in *Diamond v. Chakrabarty* that a life form could be patented. The patent, shared by Stanford University and the University of California, laid the groundwork for using cells to produce useful proteins and turning them into valuable drugs. Well before the Supreme Court decision, in 1977, the University of California had applied for patents on genes for insulin and growth hormone; the patent for insulin was granted in 1982 and the one for growth hormone in 1987. Gene patents were an extension of the legal doctrines that permitted patents on hormones, vaccines, and other "natural products" that had been turned into useful forms. Patent offices around to world had no great difficulty concluding that genes could be patented in isolated and purified form. An estimated 47,000 patents claiming something about DNA or RNA have been granted in the United States.

Marketplace for Patented Genes

Gene patents generally claim one or more of these five purposes:

- Drugs from therapeutic proteins or gene transfer into cells
- Genetic tests for diagnosis or screening
- Research tools
- Nonmedical uses for identification, forensics, and ancestry-tracing
- Controlling which genes are turned on or off in a cell or tissue

A single patent may fit in more than one category. A patent may claim a DNA sequence that is both a research tool and a method to make a protein, for example, or one that is both a research tool and a diagnostic test.

Areas of Controversy

Most of the ethical as well as legal disputes over gene patenting have to do with patents for therapeutic proteins, genetic tests, and research. Each of these areas has its own set of concerns.

Therapeutic proteins. Patents on inventions that enable production of a protein to treat a disease are among the most valuable because of their potential to lead to blockbuster drugs. They are also the targets of most of the litigation concerning gene patents.

Many biotechnology companies, including Genentech and Amgen, sprung up in the heady days of the late 1970s and early 1980s to exploit the new technologies of recombinant DNA and cell fusion. Insulin was the first recombinant product, approved for marketing in 1982. Rat insulin was initially cloned at the University of California, San Francisco, and Genentech licensed cloned human insulin to Eli Lilly. Other top-selling drugs followed, including tissue plasminogen activator for stroke, growth hormone for small children deficient in the hormone, and erythropoietin for anemia—the latter two drugs finding substantial illegal use in sports doping (see chapter 33, "Sports Enhancement"). Most of these substances were the subjects of costly, protracted legal battles over patent rights.

Diagnostics. Genetic mutations can confer an inherited increased risk of cancer and other diseases. Patents are held on individual genes, their mutations, and on the tests developed to screen for the mutations. These patents have incited among the loudest and most widespread outcries against gene patenting. The controversy includes concern that monopolies on genetic tests make their prices unacceptably high and that these monopolies may reduce incentives to correct flaws in the tests or to adopt new technologies.

The most widely known gene patent controversy is the scientific and public furor that erupted over patenting BRCA1 and BRCA2, genes that affect the risk of cancer. Mutations in BRCA1 and BRCA2 account for an estimated 5–10% of breast cancer cases, as well as significantly elevated risk for ovarian and other cancers.

Myriad Genetics, a company in Utah, secured

the patents to the genes, their mutations, and the screenings tests. In an attempt to enforce its patent rights, Myriad sent letters to laboratories throughout the world asserting that testing had to be done through Myriad's laboratory or laboratories that it licensed. These letters, many sent in 2001, triggered outrage by researchers, doctors, breast cancer advocates, and governments.

In Canada, the health ministry of Ontario publicly refused to honor the terms of Myriad's Canadian licensee, and so far no patent infringement lawsuit has been filed. In effect, the Canadian patents are being ignored. In Europe, a group of nonprofit institutions challenged Myriad's patents, which resulted in a considerable narrowing of one BRCA1 patent, while action on the other BRCA1 patents remains pending. A BRCA2 patent was then granted to the Cancer Research Campaign, a cancer research charity in the United Kingdom, which has stated its intent to enable unrestricted access to and use of the gene. There are also broad BRCA patents in Australia and New Zealand. The licensee in that region is allowing nonexclusive licensing, but recent indication is that the Australian patent may be enforced.

Myriad still exercises a dominant patent position in the United States, where it is the main provider of testing for BRCA1 and BRCA2 mutations. Myriad's monopoly in this country is controversial. On the other hand, it is hard to attribute problems directly to patents. Genetic tests for colon cancer have no one dominant patent holder, and yet they are comparable in cost and present similar technical challenges in the form of false negatives and positives.

Research. One of the greatest fears about gene patents is that they could inhibit scientific progress. Making genes in the laboratory is essential for many kinds of research, and restrictions on the use of patented genes would be difficult to work around. In a 2002 case, *Madey v. Duke*, the Court of Appeals for the Federal Circuit made clear that academic institutions could be held liable for patent infringement even in nonprofit research.

In practice, however, no research institution has been sued for studying a gene or using it in academic research. This is partly because the patent holders stand to benefit from research that reveals how their patented genes work, and partly because of the difficulty in proving damages from mere use in research. But there has been litigation involving companies that supply transgenic animals, which incorporate patented genes and are themselves subject to patents, and companies using research tools aimed at creating commercial products and services. One gray zone is the use of materials or processes with gene patents in clinical research, such as genetic testing in the context of a clinical trial. Laboratories offering patented genetic tests for research studies have been asked to "cease and desist" unless they refer materials to or get a license from the patent holder.

In addition to the concern that patent holders could block access to essential research material, some critics have raised the specter that patents could impede innovation by creating an "anticommons" effect, in which scientists avoid avenues of research that would require long and expensive negotiations with multiple patent holders. Allowing too many patents for incremental inventions increases the risk of the anticommons effect. However, surveys of scientists in academia and industry have not shown a powerful anticommons effect or blocking effect in research.

Though fears that gene patents could stifle research have not been borne out, for the most part, commentators are now raising questions about how the many existing gene patents might be used in the future, particularly with the advent of high-speed, low-cost DNA sequencing and other technologies. These technologies, originally confined to research, are increasingly being used for ancestry-tracing, "personal genomics" offered directly to consumers, and other commercial purposes. If lucrative markets emerge, the incentives to exercise intellectual property rights in gene patents will also rise, and that could influence what kind of—and how much—commercial research and development takes place.

Policy Options

Michael Crichton's 2006 novel, *Next*, contains an author's note that begins, "Stop patenting genes." In a February 13, 2007, *New York Times* op-ed, Dr. Crichton said, "Gene patents are now used to halt research, prevent medical testing and keep vital information from you and your doctor." Dr. Crichton teamed up with Lori Andrews, a prominent law professor and expert on biotechnologies from the Chicago-Kent College of Law, and found resonance with Representatives Xavier Becerra and Dave Weldon, who introduced HR 977, a bipartisan bill in the 110th Congress to halt future patenting of

RESOURCES

Web sites

- www.ama-assn.org – the American Medical Association. Includes a professional resources page on gene patenting with background and links.
- www.gpoaccess.gov/fr/ – the Federal Register. Includes the United States Patent and Trademark Office's 2001 guidelines on gene patenting.

Recent news

- "Patently Flawed" (editorial), *Boston Globe*, July 23, 2007.
- Michael Crichton, "Patenting Life," *New York Times*, February 13, 2007.

Further reading

- Timothy Caulfield, Tania Bubela, and C J. Murdoch, "Myriad in the Mass Media: The Covering of a Gene Patent Controversy," *Genetics in Medicine*, December 2007.
- Stephen A. Merrill and Anne-Marie Mazza, eds., *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* (Washington, D.C.: National Research Council, 2006).
- Tom Walsh et al., "Spectrum of Mutations in BRCA1, BRCA2, CHEK2, and TP53 in Families at High Risk of Breast Cancer," *Journal of the American Medical Association*, March 2006.
- Mary-Claire King et al., "Tamoxifen and Breast Cancer Incidence among Women with Inherited Mutations in BRCA1 and BRCA2: National Surgical Adjuvant Breast and Bowel Project (NSABP-P1) Breast Cancer Prevention Trial," *Journal of the American Medical Association*, November 2001.
- Michael A. Heller and Rebecca S. Eisenberg, "Can Patents Deter Innovation? The Anticommons in Biomedical Research," *Science*, May 1, 1998.

See relevant legislation in appendix.

DNA sequences. Crichton's assertions about the adverse impacts of gene patents are in dispute, and the Becerra-Weldon bill has become the stimulus for ongoing debate.

A 2005 National Research Council report included gene patents in a discussion of ways that Congress, the executive branch, and the courts could ensure rapid progress in life sciences and their application. It recommended, for example, an exemption from infringement liability when verifying genetic testing results. Some of the recommendations have since been addressed by decisions of the U.S. Supreme Court and by a patent reform bill in Congress.

The patent reform bill passed the House in September 2007 and is pending in the Senate. Two provisions are particularly relevant to gene patents. One provision would introduce a procedure for challenging a patent after it is issued similar to the opposition process that narrowed the BRCA1 patent claims in Europe. Another provision would shift the U.S. standard for inventorship from a "first to invent" to a "first inventor to file." This change would reduce protracted legal disputes like the dispute over the patent for the cystic fibrosis gene, which took almost 10 years to resolve. France and Belgium have national laws that exempt diagnostic and research uses of gene patents from infringement liability, and have also created statutory authority for government to force patent-owners to license patents if not doing so would threaten public health. Legal scholars have proposed such policy options for U.S. law.

Scholars have written about gene patents for almost 20 years. Innovations have continued, and this is reassuring. But progress in science and its application does not prove that the patent system as applied to DNA methods and genes is optimal. The conclusions are timid, but useful:

- Gene patents have proven useful in developing some therapeutic proteins.
- Neither the harms nor the benefits of DNA patents for clinical genetic testing is clear.
- Fears that gene patents might impede scientific research have not been borne out, at least to date.

A gene patent is the exclusive rights to a specific sequence of DNA (a gene) given by a government to the individual, organization, or corporation who claims to have first identified the gene.Â Gene patents have often resulted in companies having sole ownership of genetic testing for patented genes. On June 13, 2013, in the case of the Association for Molecular Pathology v. Myriad Genetics, Inc., the Supreme Court of the United States ruled that human genes cannot be patented in the U.S. because DNA is a "product of nature."