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Gene Patents: A Broken Incentives System

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Abstract

The proliferation of patents on human genes has raised important ethical questions centered on the conflict of patient rights and intellectual property rights. With the Supreme Court's June 2013 decision that altered the patent eligibility of genetic material, it is important to reexamine the ethical implications of gene patents as a concept. Such patents suggest an ownership of genetic material that may hinder access to healthcare and inhibit medical progress. The application of the current patent system to genetic material thus violates patients' rights without fulfilling the system's goal of promoting innovation, suggesting a need for a revised incentives infrastructure.

Keywords

Gene patents; Myriad; Ethics

Myriad Genetics & Gene Patents

The rapid progress of gene sequencing technology since the 1970s has facilitated important advances in medical knowledge, diagnostics, and treatment, but it has also raised ethical questions regarding the role of such technology in the practice of medicine (Gold & Carbone 2010). Gene patents are at the center of one such dilemma. Since the first patent for a human gene was granted in 1980 (Gold & Carbone 2010), 3000–5000 genes have been patented in the US (Cook-Deegan 2008), making it increasingly important to resolve the conflict that the patents create between patient rights and intellectual property rights. In particular, over the past decade, the patents on BRCA1 and BRCA2 held by Myriad Genetics, Inc., and its subsidiary, Myriad Genetic Laboratories, Inc., (“Myriad”) have sparked substantial controversy. While Myriad was not the first or only entity to file a gene patent, its licensing practices and the lawsuits surrounding its patents quickly placed it in the international spotlight.

Myriad started its search for the chromosomal location of the BRCA1 gene in the early 1990s (Gold & Carbone 2010). Soon after the company published its first paper on BRCA1 in 1994, it filed for patents to cover the gene and 47 sequence variants (Gold & Carbone 2010). Two years later, Myriad filed similar patents for BRCA2, claiming the right to prevent others from using the sequence information it had gathered for screening, diagnosis, or the development of therapeutics (Gold & Carbone 2010). Subsequent lawsuits have

resulted in amendments to the patents, several of which reduced the scope of Myriad's patents to cover the specific gene mutations named in the patents and the diagnostics for detecting those variants, rather than BRCA variants in general (Gold & Carbone 2010). While the US courts generally had upheld the legal patentability of human genes over the years (Lever 2001), the US Supreme Court's most recent opinion drew a distinction between gene patents covering artificially synthesized complementary DNA and those for the isolation of specific genes. The Court decided that only the former is eligible for patent since the latter constitutes a discovery, not an invention (Association for Molecular Pathology [AMP] v. Myriad 2013). Rather than debating the details behind the chemistry of DNA isolation and manipulation, however, it may be more useful to consider the ethical implications of gene patents as a general concept. From this viewpoint, the Myriad case highlights the need for a more ethical incentives system than the current patent system because although incentives for research and development are important to medical progress, gene patents violate the rights of patients to access potentially life-saving information and treatment.

Ownership Rights

Under the assumption that patents are a type of intellectual property and that ownership of intellectual property is similar to ownership of physical property, gene patents raise several questions of ownership assignment. First, as naturally occurring sequences of DNA, genes arguably belong in the public domain rather than in the ownership of individuals or companies (Lever 2001). Stars, for example, are not patentable because they are discoveries rather than inventions that can be claimed by a single individual (Macer 2002). The same reasoning would argue that genes should also be ineligible for patent.

Even more fundamentally, however, genes can be considered a natural part of the human and thus morally wrong to treat as property (Ratcliffe 2011). In fact, the Universal Declaration on the Human Genome and Human Rights, adopted by the UN General Assembly in 1998, states that "The human genome in its natural state shall not give rise to financial gain" (UNESCO 1997, p. 43). While it is possible to argue whether isolated DNA is the same as in vivo DNA "in its natural state" (UNESCO 1997, p. 43) the debate would ignore the original goal of the Declaration—to protect human rights and the use of the human genome (Macer 2002). Because part of the rationale for patenting genes is that gene sequences contain useful information, these patents arguably view genes as a "physical embodiment of biological information" (AMP v. USPTO 2010, p. 185) rather than purely a chemical entity. As such, they are part of the composition of humans, and assigning ownership to a specific individual or entity would violate human rights.

Finally, returning to the assumption of gene patents as a type of intellectual property, it is important to consider that intellectual property rights are not necessarily natural rights. According to John Locke, the right of ownership is a fundamental human right. Ownership rights, however, are defined differently in different countries, may clash with other natural rights like the right to life, and may even deprive others of the right to ownership (Schroeder & Singer 2011). These arguments suggest that ownership rights are not natural rights, and

natural rights like the right to life should supersede intellectual property ownership, including gene patenting.

Access to Care

In medical ethics, the principle of justice argues that every person should have equal access to the best available care, especially when lack of care compromises a person's natural right to life. Whether genetic testing should be performed in all cases where it is clinically indicated and whether companies should be able to directly market tests to consumers are related but separate ethical issues. Here, the question is that of accessibility to diagnostic testing if there is sufficient clinical benefit and a person desires to have the test. Patents are legal entities designed to reward inventors for the time and resources that they invest by granting them exclusive rights to the invention for a specific period of time, often twenty years (Gold & Carbone 2010). A major problem with gene patents, however, is their potential to limit patient access to appropriate diagnostics.

Individuals with a BRCA1/2 mutation carry a cumulative lifetime risk of 40–80% for breast cancer and 16–40% for ovarian cancer, compared to 12.7 and 1.4% in the general population (Gold & Carbone 2010). Screening is beneficial because prophylactic treatment and increased surveillance are available for those who test positive. With Myriad's patent on the BRCA1/2 genes along with its exclusive licensing practices, tests for BRCA1/2 genes were priced between \$395 and \$2400 when they were released in 1996 (Gold & Carbone 2010). Without competition, the company had no incentive to lower the prices. High diagnostic costs preclude certain patients from access to testing, but it can also decrease the number or quality of services offered by the hospital because hospital-based laboratories absorb much of the cost of outsourced diagnostics when insurance does not completely cover the costs (Merz & Cho 2005).

Perhaps patents do not inherently hinder patient access to care and generous licensing practices can mitigate the problem. In cystic fibrosis genetic testing, for example, gene patents were licensed more widely than the BRCA genes, and studies have shown that the existence of a gene patent does not seem to have impeded patient access to testing for cystic fibrosis mutations (Chandrasekharan, Heaney, James, Conover, & Cook-Deegan 2010). No difference in access has also been noted in colon cancer, which was similarly less exclusively licensed, and the pricing for genetic tests for colon cancer is comparable to that of the BRCA1/2 tests (Cook-Deegan et al. 2010). On the other hand, when the gene associated with hereditary hemochromatosis was patented, there was a 26% decrease in the number of laboratories testing for it, suggesting that gene patents are not without consequence (Cho 2010). In fact, companies like the Genetics and IVF Institute and the University of Pennsylvania's Genetic Diagnostic Laboratory were performing BRCA1/2 tests at the time when Myriad first marketed its tests, and Myriad sent cease and desist letters to both companies asserting their patent rights (Gold & Carbone 2010; AMP v. Myriad 2013). Since there is a potential conflict of interest between a company's financial interests and patients' access to care, it seems unethical to base the access to diagnostics and therapy on an individual company's practices regarding patent stringency and licensing.

Research & Development

In addition to limiting immediate access to healthcare, gene patents may hinder research and development of next-generation diagnostics and therapeutics, compromising future patient care. Prior to the Supreme Court decision in June 2013 that isolated DNA is ineligible for patent (AMP v. Myriad 2013), it was technically illegal for researchers to study a patented gene and develop new diagnostics or therapeutics, since most genetic research requires DNA isolation (Gold & Carbone 2010). Next-generation whole-genome sequencing for diagnostic purposes, for example, could have violated multiple patents. The June 2013 court decision, however, states that cDNA, a version of the gene comprising only the regions coding for protein, is eligible for patent, despite the fact that cDNA is derived from naturally-occurring mRNA sequences (AMP v. Myriad 2013). Since cDNA is widely used for biological research, this stipulation is still a significant one. Thus, although the question of whether specific technologies violate patent protection is primarily a legal issue of patent definition (Price 2012), ethical issues arise because uncertainty about whether patent rights will be pursued against researchers may dissuade some from pursuing research in the field, slowing the advent of new diagnostics and therapies into the clinic (Gold & Carbone 2010).

Historically, academic research has been a gray area, and most scientists circumvent patents on research tools by “simply ignoring them” (Gold & Carbone 2010, p. S44). Myriad, for example, claims to fully support research with no intention to pursue lawsuits. They also provide testing to NIH researchers and NIH-funded investigators at a discount or at-cost, and the existence of over 6000 journal articles on PubMed about the BRCA genes suggests that research has not been completely halted by the Myriad patent (Gold & Carbone 2010). The fact of the matter is, however, that patents still create limitations. The majority of genetics laboratories have had at least one gene patent asserted against them, even though patent holders like Myriad often are willing to grant some sort of license or discounted pricing for research use (Merz & Cho 2005). Furthermore, research is not limited to government-funded projects, and limits on industry-based research can significantly slow progress in a field.

The other side of the argument is that the patent system in fact promotes research and development. In exchange for the legal protection afforded by a patent, patent owners are required to disclose the details of their invention, and patents may promote innovation by forcing inventors to find new ways to solve a problem (Merz & Cho 2005). Furthermore, exclusivity may allow diagnostic companies like Myriad to compile comprehensive databases or to generate funds for future drug discovery and clinical trials. In fact, the latter was part of Myriad’s business model, and as of 2010, its diagnostics business had not yet made a profit on its own (Gold & Carbone 2010).

While the information sharing required by patents is important to medical progress, the problem with this argument is that patents do not necessarily reward effort and are often not the driving factor for research in a given field. In fact, research shows that altruism or scientific interests often motivate researchers more than patents (Lever 2001; Chandrasekharan 2010). With the search for the BRCA genes, for example, researchers at le Centre de recherche du CHUL in Quebec and the Cancer Institute in Tokyo had been involved in the search for the sequence of BRCA1, but Myriad claimed the sole patent

rights. The BRCA2 patent followed a similar story with over 40 researchers at multiple institutions around the world contributing to the research that led to the eventual sequencing and development of diagnostics (Gold & Carbone 2010). The sequencing of the BRCA1/2 genes was thus the culmination of many years of work by teams of researchers at multiple institutions, although the majority of the patents were granted to Myriad.

Furthermore, the patent holder is not obligated to share data that it aggregates. This is a particular concern in Myriad's case—when Myriad first started research on the BRCA genes, it received both public and private funding for the identification of the genes (Gold & Carbone 2010). Since public resources were used for this research, it is arguable that the data generated and perhaps even the diagnostic products created should be available for public use. In fact, many gene patents are the product of government and nonprofit-funded research rather than patent profits from other products (Chandrasekharan 2010). Finally, while data aggregation and exclusivity may be beneficial for research because it reduces redundancy, it also risks decreasing the number of approaches with which researchers approach a question, slowing the progress of research in a field in general.

In Myriad's case, potential limits on research and development are an ethical concern because it affects the quality and availability of patient care. Patients who do not have access to testing or whose test results are falsely negative may not have the opportunity for prophylactic screening and treatment. New diagnostics, including whole genome sequencing, could decrease the chances of this situation (Price 2012). Even for the patients who receive diagnostic care, research into new therapeutics could change outcomes. Prophylactic mastectomy or oophorectomy are available for women carrying the mutation and have shown modest benefit, but the procedures carry high risks and are without definitive benefit, since cancer risk cannot be eliminated completely (Bermejo-Perez, Marquez-Calderon, & Llanos-Mendez 2007). For those with BRCA1/2-mutated cancers, targeted treatments like PARP inhibitors are now available but still require significant research (Rios & Puhalla 2011). The BRCA patents thus affect the quality of care available to both current and future patients.

Utility of Gene Patents

In considering the ethics of gene patents, it is important to remember that a basic goal of the patent system is to encourage innovation, and the goal of biomedical innovation is to benefit human health. Thus, while it is important to protect inventors' rights, it is also crucial to protect patients' access to diagnostics and treatment. Although patents do not by definition prevent patients from accessing care, patents that assign ownership of genes to individuals or companies create possible barriers to access. It is important to consider the implications of such barriers—for Myriad, the barriers are primarily for diagnostic care and future diagnostics and therapeutics, but for other gene patents, the barriers could be direct access to life-saving therapeutic treatment.

Despite the problems with the patent system, completely annulling it is not the perfect solution because it has a role in promoting innovation. More feasible solutions include more narrowly defined patents (Soini, Ayme, & Matthijs 2008; Macer 2002), patent review

processes involving ethicists (Macer 2002), or perhaps a new incentives system for research and development altogether. A new incentives system is an attractive solution that could simultaneously solve the problem of gene ownership as well as ensuring access to care and promotion of research and development. The major challenge would be in its formulation and the infrastructural changes necessary to make it feasible. Even with such challenges, it is clear that the current patent system creates major ethical dilemmas when applied to human genes. The question then is whether a more ethical patent-type system is possible, and whether it would apply to only human genes or also to genes that encode small molecule drugs, to natural compounds, to all diagnostics and therapeutics, or perhaps to all patentable products.

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Biography

Yun-Han Huang, B.S., is a second year MD-PhD student at the Weill Cornell/Rockefeller/Sloan-Kettering Tri-Institutional Program. In her undergraduate research, she studied poly(ADP-ribose) and DNA damage signaling pathways in the labs of Dr. Paul Chang (MIT) and Dr. Janet Hall (Institut Curie), and she continues to be interested in cancer research.

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