Owning mankind: an assessment of biological patents

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Medical innovation is a complex force at the convergence of business, big pharma, governments and patient need. This intricacy reaches its apex in genomic innovation. As the study of our very selves, human genomics concerns the biological nature of each individual. The application of genomics affects all of us – and thus we have an active interest in its research and proliferation.

Gene patents are a key tool that governments use to encourage innovation genomics. A biological, genetic or genomic patent is a patent on an invention in the field of biology. Such a patent allows the patent holder to exclude others from making, using, selling, or importing the protected invention for a set period of time. The extent of biological patents varies among jurisdictions, and may include biological technology and products, genetically modified organisms and genetic material. This exchange is supposed to spur innovation both before and after the patent is conferred. (Sharples, Andrew, 2011)

A tension exists between personalized medicine's need for access to scientific advances, and the patent system's reward of exclusive use or non-use to innovators. With fairness and access fundamental aspects of medical research, the right to exclude enshrined in patents can be seen to violate this fundamental principle. This tension must be resolved for patents to fulfill their function as contributors to the common welfare of patients.

It is through this lens of ubiquitous importance that this paper will examine the impact of genomic patents. The discussion around patents in the public conscious is split between two discussions. The first concerns the ethics of

patenting genetic material, and the second on whether biological patents help or hinder innovation. This paper will focus on the latter issue: the utility of patents in the realm of genetics and genomics. Though the ethical considerations are of importance they are irrelevant if it transpires that patents hinder innovation. For in that instance, even if patents were ethical they serve no functional use in society if they do not aid in the evolution of medicine.

It is clear that despite the theoretical basis for patents, the reality is that patents undercut patients and worsen their access to medical care. This happens on a number of fronts: access, follow-up innovation, research and development. This paper will examine each of these areas and analyse the manner in which genomic patents undermine their very reason for existing, and in turn fail the millions of individuals who need the information that patents allow companies to lock away.

Brief history of genomic patenting

Gene patenting differs across jurisdiction. This paper will focus mainly upon genetic patenting in the United States and in particular the experience of Myriad, a company that owns the patent rights to the BRCA 1 and BRCA 2 gene.

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). Based on survey results, it has been estimated that nearly 20% of all human genes are covered by US patents. In late 2005, this figure corresponded to 4382 of the 23,688 genes in the human gene database of the National Center for Biotechnology Information.

Among the early DNA patents, several technologies were particularly conspicuous: recombinant DNA cloning, DNA and RNA sequencing, synthesis of DNA and RNA molecules, polymerase chain reaction (PCR), cell fusion techniques for making monoclonal antibodies, and computational tools to analyze data from molecular genetic analysis. Some of the most valuable DNA patents were in regards to DNA molecules that specified the amino acid sequence of proteins with known therapeutic value. (Cook-Deegan, and Heaney, 2010)

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. By 2005, the BRCA1 gene was subject to 14 different patents owned by 12 different entities. The United States Patent and Trademark Office (USPTO) records identified 69 US patents citing BRCA1 in the claims and 38 US patents citing BRCA2 in the claims. Utah-based Myriad Genetics holds at least seven patents directed to the BRCA1 gene or the BRCA1 protein. *(*Solomon and Sieczkiewicz, 2007)

While the US courts generally have upheld the legal patentability of human genes over the years (Lever 2001), the US Supreme Court's most recent decision in Association for Molecular Pathology v. Myriad Genetics drew a distinction between gene patents covering artificially synthesized complementary DNA and those for the isolation of specific genes. The court unanimously ruled that, "A

naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," invalidating Myriad's patents on the BRCA1 and BRCA2 genes. However, the Court also held synthesized DNA sequences, not occurring in nature, are eligible for a patent since the latter constitutes a discovery, not an invention.

Why do we patent?

Supporters of genomic patents claim that patents encourage investment and innovation in genomics. Many claim that the property rights upon which patents are founded are a human right. This is grounded in the notion of natural rights, namely that people have a right to the fruits of their labours, whether that is physical or in the case of genomic patents, intellectual.

Patenting is based on the theory that in the status quo competitive markets under-incentivise innovation due to the high social good of ideas. Patents give inventors the ability to exercise intellectual property rights over their ideas. In turn this enables them to capture a higher share of the social returns to their research investments. This is particularly crucial in medicine broadly where research and development is highly costly. By awarding inventors a temporary right to exclude others from marketing their invention, patents aim to allow inventors to uniquely benefit from the invention for a brief period of time, as a way to re-coup their research and development costs. This in turn provides dynamic incentives for investments in new technologies. Optimal patent policy design has traditionally been framed as a trade-off between this benefit of providing incentives for the development of new technologies and the cost of

deadweight loss from higher prices during the life of the patent. (Bhaven and Williams, 2015)

In exchange for the legal protection afforded by a patent, patent owners are required to disclose the details of their invention. Some argue that patents may further promote innovation by forcing inventors to find new ways to solve a problem (Merz & Cho 2005). Exclusivity may also allow diagnostic companies like Myriad to compile comprehensive databases or to generate funds for future drug discovery and clinical trials. (Gold & Carbone 2010).

The realities of patenting

Research and Development

Patents view discoveries as discrete entities – a view that is particularly problematic in genomic research. In genetics progress tends to build upon previous breakthroughs and involve multiple different innovations. At the outset researchers often have very little idea about which patents they may violate. This means that researchers are either prohibited from beginning, or continue researching despite the possibility of violating patents. Historically, academic research has been a gray area, and most scientists circumvent patents on research tools by "simply ignoring them." (Gold & Carbone 2010) If that is the case then patents are redundant in the first instance as they fail to protect the idea they purport to. Further as more genes are patented, intellectual property becomes fragmented, preventing research institutions from collecting all the

pieces necessary for practical application. Conceptualising genes as finite objects of nature mean they cannot be worked around if patented. In either case patents are failing to fulfil their function, and on both grounds ought to be reassessed.

Institutions with patents push back against this view, and claim to balance both issues. Myriad maintains that it fully supports research with no intention to pursue lawsuits. The company points to its provision discounted or at-cost testing to NIH researchers and NIH-funded investigators. Further, 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). Despite this, it is clear 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) Murray and Stern found a mild inhibitory effect of patenting on subsequent publications in Nature and Biotechnology . Another analysis of a subset of the same date looked at 2,647 patented sequences, and their effects on future citations in the scientific literature after a patent was granted. In comparisons between cancer and noncancer genes, disease- associated compared to non-disease-associated genes, and, Huang and Murray found a 5% to 17% decrease in such citations. (Huang and Murray, 2009). This points to the conclusion that a gene's immediate utility and relevance led to more negative impacts on subsequent published citations.

Patents may in fact fail to promote research and development as they do not target the underlying reason that research happens in the first place. Patents do not necessarily always reward effort. As such there must be another impetus for research. Lever and Chandrasekharan suggest that altruism or scientific interests often motivate researchers more than patents. (Lever 2001; Chandrasekharan 2010) Indeed in the case of the quest to find the BRCA gene researchers at Le Centre de recherché du CHUL in Quebec and the Cancer Institute in Tokyo had been involved in the search for the sequence, but Myriad claimed the sole patent rights. Similarly the search for BRCA2 saw 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. Though altruism may be an insufficient explanation for all of scientific research, it is clear that the present asymmetric system of reward devalues the collaborative effort that is often required to sequence a gene.

Lastly, though perhaps initially patents can be viewed as having a positive effect on the rate of innovation, it may be that in the long run the patent process itself may dissuade many research institutions from attempting to gain a patent in the first place. After the Supreme Courts decision in June 2013 that that isolated DNA is ineligible for patent (AMP v. Myriad 2013) it became 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)

The ambiguity around whether specific technologies are covered under patents is primarily a legal issue regarding patent definition. (Price 2012) However with little ability to know whether patents will be infringed, research institutions may be dissuaded from pursuing research in a given field, leading to a chilling effect on the advent of new diagnostics and therapies. (Gold & Carbone 2010).

Access

When we consider the utility of patents it is crucial to remember that the purpose of genomic patents it to benefit human health. In this light patient access becomes a fundamental aspect of patents that must be assessed. For some patents the implications are limited to diagnostic care and future diagnostics and therapeutics. However for other gene patents it could mean the direct inability of patients to access life-saving therapeutic treatment. The risk seems particularly acute with respect to the diagnostic and therapeutic tools arising from genetic testing that hold specific value for a subset of the population. Already this tension between patient access and patent holder rights has clashed in the legal sphere, with the judicial systems introduction of ethical exceptions that overcome a patent holder's right to exclude. The capabilities of patent holders to deny life-saving treatments means that patents do not serve their basic purpose of providing access to those that need it.

In Myriad's case, potential limits on access means that 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 arising. (Price 2012) However therapeutics, based on the BRCA 1 and BRCA 2 gene could radically change outcomes. (Bermejo-Perez) Currently the University of Utah has the right to collect substantial royalties on the tests that tens of thousands of women in Europe undergo every year. In the United States, Myriad now charges more than $3000 for a full analysis of both BRCA1 and BRCA2 and $460 for a single mutation test. 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. (Research and Innovation, Board on Science, Technology, and Economic Policy, Committee on Science, Technology, and Law, Policy, and Global Affairs, National Research Council, 2005).

The problems with BRCA in particular become even more acute when one considers that Myriad initially received both private and public funding. (Gold & Carbone 2010). Public funding seeks to aid medical research for the public good within a framework in which it is inherently accepted that medical access is a right. That public resources were used implies that the data generated and perhaps even the diagnostic products created should be available for public use. Many gene patents are the product of government and nonprofit-funded research rather than patent profits from other products, meaning that in

actuality companies that are not entirely private funded have some obligation to ensure access. (Chandrasekharan 2010)

Genetic patents complicate genetic testing more broadly. In the process of genetic testing exclusive rights to just one blocking claim for any gene associated with a given condition can discourage market entry by other. In the testing process the gene or allele to be identified cannot be known in advance, thus which patents might be infringed cannot be entirely predicted. A single clinical syndrome may require testing for the multiple different genes and specific mutations that play a role in its expression. (Heaney, 2010) With genetic patents these different genes and mutations may be covered by a variety of patents. A laboratory offering testing services for that condition cannot know in advance which mutation will be found, and often not even which gene. In order to comply with patent law, clinics are limited to testing specifically for the genes that they hold patents for.

In reality this culminates in genetic monopolies swiftly being concentrated in a small group of firms. If any firm holds exclusive rights to any method or sequence then the lone exclusive licensee can in effect secure the entire market as the only laboratory that can test for all variants. (Deegan, 2010) Thus a single blocking patent on a normal gene or any common disease-associated variant can be sufficient, if exclusively licensed to just one provider, to limit testing by other laboratories for that clinical condition.

Follow up Innovation

At best empirical evidence demonstrates that patents have a net neutral effect. At worst patents dampen innovation. In an extensive empirical overview Sampat

and Williams found that patents do not hinder follow-on innovation in the context of human genes. Conversely patents do not spur follow-on innovation in the context of human genes. In the instance that patents neither help nor hinder genomic research then they must be judged on their utility in other ways, such as research and access.

However evidence suggests that follow-up innovation is uniquely negatively impacted in the case of genomic patents, in a manner in which other industries are not. To some degree genomic patents presume that the patent holder can develop all possible follow-on inventions themselves, thereby achieving the socially important follow-on inventions. (Furman and Stern, 2011) Multiple studies suggest that patents limit access to research materials and consequently inhibit the creation of new research lines. (Aghion et al., 2008) Other sources suggest that limiting access to research materials may discourage basic research as well as the creation of new research lines. Extensive patent related conflicts have a similar chilling effect to follow up innovation that can be observed in research and development. The pharmaceutical firm Bristol Myers reports abandoning research on more than fifty cancer-related proteins due to conflicts with gene patent holders (Pollack, 2001).

Conclusion

The recent rapidity of scientific innovation and technological advancements has given us the tools to access, isolate, and analyse the human body in ways previously unthinkable. This biotechnological revolution promises a future of

rich scientific discovery. As the realities of personalized medicine begin to crystallise it is clear that the patent system is impeding the potential for new diagnostics and treatments.

If patents are to play a continuing role in genomic research then the system must be overhauled. Potentially replacing the system with a process that involves ethicists and has more narrowly defined parametres may go some way towards addressing the numerous issues patents pose. However the system as it stands fails to enhance and benefit the patients for whom it claims to. Instead the system removes crucial scientific knowledge from general usage and prevents the innovation needed to harness the power of new genomic information.

If patents do not maximise health outcomes for those who are a part of the structure, then on both practical and principled grounds they cannot be a part of the system. The benefits of medical innovation must be disseminated across society for its true intentions to take effect. Only when patents can enhance this process should their presence be endorsed.

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