

## **Patenting Genes: A Fast and Furious Primer**

Genetic research has transformed our understanding of our place in the world. We know that we inherit much from our ancestors, but until recently we focused upon cultural lineages. We now know the mechanism of our genetic inheritance and this encompasses truly amazing facts about our connections to all living creatures. We are identifying the specific fibers of this web of connections and our genes are the pathway for this information, posing and solving multi-tiered genealogical riddles. We now know that we share genes with remote and unlikely cohabitants. Yet genes and the information that they hold are entangled in a property dispute. Patents have been issued for genes, which is to say that property rights have been conferred upon individuals who are thereby empowered to exclude others from the use of the genes that they own. It is a deeply puzzling development, as though genes were someone's clever invention or a business's private formula. This paper will briefly describe how genes were brought within a property rights regime and summarize some of the problems that are arising because of that approach. This paper will also address some other concerns that are being raised about genetic research and its impending applications.

### **Whose Genes?**

You go to a health care facility. You are treated within the range of your expectations and released. Later you discover that you are special in an unforeseen way because your DNA, a sample of which was extracted during your treatment, has valuable

qualities. Moreover, you discover that somebody has patented your DNA, or at least whatever it is that they patented started as your DNA. You didn't know that you would be the source of the DNA patent, you didn't agree to be that source and now you are forbidden from using your own DNA in violation of the patent. That's right, you cannot exploit the resource that is your own DNA without a license from the patent holder. It would appear that you don't fully own all of your parts. Somebody else has laid claim to your DNA and apparently that claim will be upheld in court. How did this strange scenario arise? How did you lose control of your DNA?

To answer these questions, let's briefly review the history of patents and the purposes that patent protections are intended to serve. We will see that initially patent protections were refused to natural processes. That view was modified relatively recently, a change that opened the door to multiple human gene patent filings. That flurry of filings cannot persist because the human genome is finite. An important qualification is that variations in the gene sequences are extensive. Still, there are four times as many gene patent applications pending as there are genes in the human genome. With the multiple filings, there are multiple stakeholders and their stakes will likely overlap, at least apparently, at least until contentious litigation sorts it all out. And at the end of the day, recognized stakeholders will hold patents to genes and gene sequences and they will charge fees for the use of those patents.

## A Brief History

Patents are provided for in the U.S Constitution. Article I, Sec. 8 provides that Congress shall have Power “To promote the Progress of Science and Useful Arts by securing for limited Times to Authors and Inventors the exclusive Right to their Writings and Discoveries.”<sup>1</sup> The Patent Act of 1793, in language written by Thomas Jefferson, declared that patents could be obtained for “any new and useful art, machine, manufacture, or composition of matter, or any new or useful improvement thereof.” In 1952 Congress replaced “art” with “process.”<sup>2</sup> Otherwise, this phrasing remains the core of the patent code. “Anything under the sun made by man” can be patented so long as it is new, non-obvious and useful. A further caveat: the utility should be definite and known at the time of invention.

What are patents? They are temporary monopolies granted by the federal government to encourage the disclosure of how inventions work so that others can make use of those inventions. The purpose is to reward inventors for their efforts, to encourage public disclosure of their inventions, to provide for the commercialization of those inventions, and to promote further innovation. An invention is provided limited term protection so that the benefits of the invention can accrue to a large number of people.

Inventions are eligible for patents. The laws of nature and naturally occurring things are not patentable. The “product of nature” doctrine excludes objects discovered in the natural world. Processes for extracting those objects can be patented, but not the

objects themselves. For example, a newly discovered plant or bird or mineral cannot be patented. Horticulturists undermined this doctrine early in the 20<sup>th</sup> Century. They wanted intellectual property protection for the plant varieties that they, applying Mendel's laws of heredity, had produced. Plant breeders were devising varieties resistant to disease or rich in nutritional or medicinal qualities. Without protection, these varieties were vulnerable to piracy and the plant breeders alleged that the incentive to pursue further research would flag. They finessed the "product of nature" doctrine by arguing that a variety resulting from cultivation was the creation of human agency and therefore was patentable. Cultivated plants were not products of nature, but of human action. The arguments of the plant breeders prevailed. A Plant Patent Act was enacted in 1930,<sup>3</sup> though it limited patent protection to plants that could be reproduced asexually, i.e., by buddings, graftings, root clippings or divided bulbs.

### The Current View

The U.S. Supreme Court briefly weighed in on these issues in 1948 in Funk Brothers Seed Co. v. Kalo Inoculant.<sup>4</sup> The court held that no patent should issue for a bacterial mixture because patents cannot issue for the discovery of a phenomena of nature. "They are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusive to none."<sup>5</sup> The Court revisited these issues in 1980, in Diamond v. Chakrabarty<sup>6</sup> and radically reshaped the patent landscape. The Patent and Trademark Office (PTO) had denied Chakrabarty, a General Electric chemist, a patent for a bacterium bio-engineered to consume oil slicks

because the bacterium was a living organism. The Court, acutely aware of the rapidly accelerating commercialization of research results in molecular biology, overruled the PTO. The Court ruled that whether the invention is alive or not is irrelevant. The determinative consideration instead is whether the invention is a product of human ingenuity. Chakrabarty's bacterium were non-naturally occurring objects dependent for their existence upon his ingenuity. Therefore, they were patentable.

Harvard University subsequently patented its onco-mouse, which had been genetically engineered to be susceptible to cancer.<sup>7</sup> Harvard sought protection not merely for the method of producing these mice, but also for the mice as a product of that method lest others, using different methods, reproduce that product. Harvard did not limit its application to transgenic mice. Rather, it sought and was granted a patent for any transgenic mammal, excluding human beings, which contained in its genes an activated oncogene that had been introduced at its embryonic stage.

Chakrabarty and its aftermath lead the PTO to modify its position on the patentability of genes and gene sequences. Isolated and purified DNA molecules can be patented even though they have the same sequence as a naturally occurring gene. They are eligible because the isolated and purified DNA did not occur in that isolated and purified form in nature. Human intervention is the causal explanation for the difference. Synthetic DNA preparations are similarly eligible for patents because their purified states are different from the naturally occurring compound.

The distinctions identified in the plant breeders' arguments were thought then to have limited scope because the plant breeders could not describe in detail the actual mechanics of their invention. Contemporary microbiologist can provide detailed descriptions of their methods and products and they are spreading their ingenuity into the furthest reaches of the human genome and the non-human natural world and they are filing patents for whatever they can usefully isolate with their ingenuity.

Commentators have pointed out that the isolated and purified genes for which patents are being issued were not changed, redesigned or improved to make them useful. Indeed, their utility depends upon functional equivalence with the naturally occurring substance. Furthermore, though the replicated DNA sequence, isolated and purified, does not exist in nature without human intervention, the patent for that replicated sequence will be used to exclude others from developing the naturally occurring gene that was replicated. Patent protection encompasses more than the replicated DNA sequence. Effective ownership of the naturally occurring gene is also conferred upon the party who replicates it.

#### A Confusion of Profits

What are the benefits and demerits of this frenetic effort to patent genes and gene sequences? Clearly, providing intellectual property protection has encouraged investment and research. Gene patents are value generators; they enable the packaging of bio-technology for profitable production and use. We are in the midst of a Gold Rush to

identify potentially beneficial (and profitable) genetic treatments and enhancements. The aim is to own, control and monetize these treatments and enhancements. However, because there is little coordination of these efforts, conflicts and complications can arise.

One complication is known as a “submarine patent.” This is a broadly encompassing, early filing which surfaces when another inventor’s work gives it value at a later time. An untested inclusive claim can inhibit downstream development and research. The PTO recently issued guidelines to address this complication, raising the utility bar to prevent gene patents from claiming “throw-away” utilities, e.g., the cover of a shampoo additive use, as a means to blocking later, better focused applications. Moreover, genes code for multiple proteins. A patent for a particular gene names a series of nucleotide sequences (called exons) that code for a particular protein. Sets of exons are separately patentable which allows for multiple utility claims for individual genes.

Another complication is referred to as “the problem of the anti-commons.” Rather than too many individuals sharing access to a single resource and wasting that resource, there are many fragments of intellectual property in potential future products and this fragmentation discourages the development of those products. Multiple owners each have a right to exclude others from a scarce resource and thus no one has effective use of the resource. This problem is acute for diseases and condition associated with multiple genes; fragmented licensing burdens the development of treatment options.

These two complications fit in a larger theme, which is the decline of public knowledge fed by enlarged patent and copyright protections. Patent holders do insist upon the collection of their fees. Intellectual property is an increasingly large part of GNP. For some companies, licensing fees exceed operating income. There are long-term down trends in government research and development funding and various previously quasi-governmental entities, such as Bell Labs, are now private. University research is increasingly tied to corporate sponsorship and that sponsorship entails private ownership claims for the product of the research.

These complications have real world consequences. Medical research and patient care are both affected. Licensing fees obviously influence patient care; cost is an inevitable variable in the health care equation and patent holders are concerned to generate revenue from their patents. Some tests are not administered because the associated licensing fees exceed the available resources, i.e., patients are deprived of appropriate health care. This is not a new problem, but an intensive variation on a persisting problem of weighing costs against anticipated benefits. A corporate officer, answerable to stockholders for dividends and stock values, is setting the price of licensing fees. Research and development costs for that corporation can be substantial. Indeed, the costs of unsuccessful or ongoing research are paid with revenue from successful patents. Patents are financial assets and thus stock analysts and amortization tables dictate licensing fees. These fee problems may be amenable to solutions that are consistent with the current patent law regime. Compulsory licensing, or the prohibition of exclusive

licensing, or requiring non-exclusive licensing for publicly funded research, or liability exclusions for experimental or clinical use may defuse some current strains in the system.

Despite mounting concerns about licensing costs, we should anticipate that legislatures and courts will be slow to configure sweeping changes to gene patent law. Current gene patent doctrine has engendered property right expectations among gene patent holders. Detrimental reliance upon recognized property rights often persuades legislatures and courts against changes that significantly diminish (or disappoint) those property rights. However they may arise, once conferred, property rights exert an inertial force upon later legal developments. There is an irony to this reluctance to disturb the status quo because it seems that genes are analyzable both as material molecules and as information systems. It is the former analysis that supported the reasoning of Chakrabarty, but it is likely the latter analysis, though it is less amenable to traditional patent categories, that better predicts the future trajectory of genetic research.<sup>8</sup>

Bioinformatics is the merger of microbiology and computer engineering and it will empower inexpensive, individualized genetic testing. A further caution: whether they are claims founded on material or information, it is unclear that gene patents satisfy the core patent criterion of non-obviousness.<sup>9</sup>

### Ecological Reservations

Broader questions than these, less deferential to the current patent regime, have been raised. What is the status of transgenic animals? Animal rights groups contend that

the patents on living organisms degrade animals. Are there limits to what genes can be introduced into test animals? Do we care how abnormal or grotesque the resultant animals may be? Does a willingness to impose these burdens on animals reveal or shape our sensitivities about other matters? Environmental groups worry about escaped transgenic animals and plants. What impact will these modified life forms have upon the wilderness, whether reproducing among themselves or interbreeding with wild flora and fauna? Will these modified life forms out-compete native life forms as various other exotics, such as Kudzu and tamarisk, have overwhelmed native plant species. Monocultures are susceptible to precipitous declines when confronted with effective competitive forces. Will escaped transgenic animals and plants diminish the genetic variation that has proven an effective natural defense against the vulnerabilities of particular genes? Can and should transgenic life forms be engineered so that they cannot reproduce themselves?

What impacts will these developments have on individual farmers and the farming sector of the economy? Will they further exacerbate the marginalization of small farmers and accelerate the growth of corporate farming practices? Less independent agents than subcontractors, farmers do not have the means to resist instruction from the large corporations that collect and transport their products to use particular seed stocks. It isn't clear that large corporations, answerable to stockholders on a quarterly basis, have an appropriate perspective on the value of natural processes. Nor is it clear that corporate management, aside from the potential errors of a short-term profit horizon, capably respond to distinctive local variability in terrain and climate (and history). Further, how

should we respond to the distrust of genetically modified foods that is surprisingly deep rooted and resilient in many countries of the world, including developing countries where the benefits of genetically modified foods seem most obvious and needed?

### Treatments or Enhancements?

Among those who are comfortable with the prospects of a genetically enhanced future, there is the problem of the distinction between treatment and enhancement. We may be likely to agree that genetic treatments are appropriately paid for with common resources, e.g., health insurance programs or government subsidies. We are considerably less likely to agree to expend common resources for enhancements. A genetic disposition to a terrible disease that can be treated with early genetic interventions likely makes a persuasive claim upon our shared resources. An eye color preference is considerably less persuasive. Is the appropriate solution then private payment for genetic enhancements? First, it may not always be clear where the line between treatment and enhancement lies. For example, how much deviation from a norm is required to substantiate a treatment claim? More importantly, do we want to endorse a society in which enhancements are available only to those who can afford them? Eye color seems a relatively innocuous example. How about height or baldness or fast twitch muscles? Does it matter that these qualities correlate with material success in a particular society, or that they promote reproductive fitness? How about powers of concentration or energy or longevity? Are these qualities appropriated meted out according to who has the means to afford them?

Will parents regard their enhanced children as investments who owe a return on those enhancements? Do parents (or the society that subsidizes the treatment) have justifiable expectations that enhanced children utilize their genetic advantages? Are these questions relevant across international boundaries? Should we genetically intervene to treat acne in teenagers in this country when we could intervene to treat far more serious conditions in other countries? If genetic interventions prove to have pronounced beneficial impacts, should they remain the province of individual patent holders or should they instead be held as public trusts, serving the common heritage of humankind?

These questions about affordability and accessibility are not raised in a vacuum. We have already made important distributional decisions about access to medical care and are largely unmoved by disparities across communities within our country or across international borders. Should these precedents shape our judgments about how we shall address impending access to genetic enhancements? If an extremely inexpensive intervention redeemed a life otherwise miserable and woeful, would we refuse to intervene because the intervention would establish an awkward precedent, i.e., if a small expense produces a dramatic result, at what expense point do we desist from intervention? Are we satisfied with a simple market strategy? Indeed, references to a market strategy default are misleading because various kinds of market structures actually operate within specific market economies, many of which structures involve government or professional guidance and constraints.

These questions about access will be complicated by the globalization of the biotechnology economy. Other cultures have different views about the value of property and ingenuity. Protecting profits for a corporate entity in a distant place is often outweighed by the needs of fellow nationals here and now. It seems an inevitable extrapolation from current practices that the most lucrative treatments and enhancements will be copied in developing countries. Enforcing patents in those developing countries will be an on-going project and it will likely affect pricing and production policies in developing countries.

### Choosing A Future

Let me close with a few observations about our growing separation from the natural world from which we arose. What is the appropriate attitude to adopt regards the natural world and how do we fit ourselves within that world. Humans have struggled against the limits of the natural world throughout our history, but our success rates have spiraled exponentially in the last century. We are on the verge of unloosing ourselves in unprecedented ways from our biology. Religious leaders have focused much attention on the hubris latent in genetic research. These concerns invoke conceptions of human integrity and dignity as constraints upon the ambitions of genetic research. The frequently profound deliberations of the abortion debate are relevant here, but they focus upon the origin of human life as a function of conception or viability. Genetic interventions strain the logic of these deliberations because they mostly do not intend to

curtail a (potential) human life. They do, nonetheless, press hard on our received views of the human condition.

A troubling question is whether these advances in genetic technology tend to reduce natural things to mere material and promote a commodification of human body parts? Do we lose a perspective on the holistic character of the natural world when we reduce it to the genetic components of its various parts? This kind of question cannot allege simple causal vectors. Rather, they suggest that multiple causes cumulatively and synergistically increase our separation from the non-human world. Genetic intervention is the latest giant step in downhill stampede. We are encouraged to view ourselves as the masters of our destiny; everything else is fodder for our ambitions. Indeed, the momentum of our enhanced control and manipulation of the non-human propels us beyond an appreciation of a connection with that non-human world.<sup>10</sup> That momentum may drive us away from our histories. We are starting to direct the course of our evolution, making self-conscious choices about what we are as a species, and we may be anxious to disassociate from our former selves. Choosing our evolutionary direction is a truly remarkable enterprise and it may be that the challenge is avoidable. It may also be that we are largely backing into that future, stumbling on a course chosen for its commercial opportunities and its cultural aggrandizements. The challenge begs the most fundamental questions about how a group should reach decisions about important issues. If identifying legitimate and reliable decision-making procedures didn't raise enough problems, there is the further complication of difficult and elusive subject matter. The science is sophisticated and most of those whose lives will be improved thereby have, at

best, an elementary grasp of the subject. We hasten into a genetically enhanced future whose mechanisms and impacts are understood only in the broadest terms.

## Conclusion

It is fairly clear that gene patents have provided incentives for investments in genetic research. It is less clear that gene patents, as presently configured, are an appropriate means for sharing the benefits of that research. It is also clear that the pace of genetic research and its likely impacts upon us has accelerated to the very limits of our ability to grasp its significance. We are developing the practical means to direct our course as a species in ways that would baffle the science fiction of only a few decades ago and we struggle to phrase these issues as matters that merit our solemn and resolute attention.

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<sup>1</sup> Patent Act of 1793, Ch. 11, 1 Stat.319, 319 (1795).

<sup>2</sup> Act of July 19, 1952, Ch. 950, 66 Stat. 792, 797 (1952), 35 USC101 (2000).

<sup>3</sup> 46 Stat, 376 (1930), codified as amended, 35 USC 161-164 (2000).

<sup>4</sup> 333 U.S. 127 (1948).

<sup>5</sup> *Ibid.*, pg. 130.

<sup>6</sup> 447 U.S. 303 (1980).

<sup>7</sup> U.S. Patent Number 4,736,866 (issued April 12, 1988).

<sup>8</sup> Rebecca S. Eisenberg, "How Can You Patent Genes?" *The American Journal of Bioethics*, Vol. 2, No. 3, pg. 3-11.

<sup>9</sup> Lori B. Andrews, "Genes and Patent Policy: Rethinking Intellectual Property Rights" *Nature Reviews / Genetics*, Vol. 3, pg. 803-808.

<sup>10</sup> Wendell Berry, *Life is a Miracle: An Essay Against Modern Superstition*. Counterpoint, Wash., D.C. (2000).