

Brave New Patents: The Law of DNA Worship

Itai Yanai

ABSTRACT

The amount of known DNA sequences has been growing exponentially in the last three decades. A tremendous amount of information is encoded in these sequences which, once deciphered, will be invaluable towards the developments of treatments for the diseases that plague us. A deciding factor in the infrastructure of this biotechnology is the form of intellectual property that supports it. In this article, I point out that the legislation of patents has precedence in an earlier revolution of information technology, software, where it has served to stifle research as opposed to spur innovation. If patents are awarded to gene sequences whose function is uncharacterized, biotechnology stands to become entangled in a legal quagmire that may hinder the realization of the benefits that knowledge of our genetic material holds.

INTRODUCTION

Patents, as the currency of intellectual property, act as fundamental support to the infrastructure of today's world economy. The biotechnology sector, in particular, stands to be strongly influenced by the ramifications of patent law as the field is currently undergoing fundamental changes, spurred by technological advancements in the sequencing of genetic information. The patentability of DNA sequences, the basic instructions for the construction and regulation of the

molecular machines that carry out nearly every biological process, stands to have major implications for the future of this field.

While intellectual property rights are admittedly central to investment and development in the biotech field, they can be detrimental when misappropriated. The "patent first, experiment later" business model of many of the biotech companies, which are geared to stake out territory in the human genome, represents a corruption of the purpose of patents. Whereas patents are intended to induce innovation, a patent for only a partially characterized gene only serves to discourage others from further experimenting with that gene.

A gene sequence, which inherently contains much information, is in itself of little value when its cellular role is only partially characterized. Many argue that patents should not be awarded to a gene of unknown function since there is no innovation there to protect. In addition, a putative, or predicted, function derived from theoretical prediction should not replace experimental evidence to support functional claims. Putative functions based on database searches should, by definition, break the criteria of novelty as they are based on the functional characterization of previously known genes.

HUMBLE ORIGINS: AN IDEA IS OWNED

Beginning with our founding fathers, the reward of monopoly over one's invention was recognized as an important catalyst of economic growth in the United States. In the first section of the Constitution, the fathers wrote that "Congress shall have the power ... to promote the progress of science and the useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries." With this provision, and perhaps beyond anything else in the entire Constitution, the fathers demonstrated an understanding of the effects of rewards on innovation to produce inventions and the way in which they may be harnessed to the greater good of the public.

The great 18th century worldly philosopher Adam Smith, in his classic treatise on *The Wealth of Nations*,¹ reasoned that:

When a company of merchants undertake, at their own risk and expense, to establish a new trade with some remote and barbarous nation, it may be not unreasonable to incorporate them into a joint stock company, and to grant them, in case of their success, a monopoly of the trade for a certain number of years. It is the easiest and most natural way in which the state can recompense them for hazarding a dangerous and expensive experiment, of which the public is afterwards to reap the benefit.

Itai Yanai is a PhD Candidate in the Graduate Program in Bioinformatics at Boston University.



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The argument is directly applicable to innovation of any kind, which can be seen as an essentially risky endeavor towards the goal of public benefit. To encourage the entrepreneur to climb this improbable mountain, the government allows for a complete but temporary monopoly over the intellectual property of the inventor, who can thus expect to recover the costs of research by selling at prices much higher than production. With such protection of the individual's property, so the argument goes, the natural desire of the individual to strike it rich will not be dampened by the fear of imitators; the sky is the limit.

The transient existence of the inventor's monopoly in the market is indicative of the tension between the need to spur innovation and at the same time to generate wealth from the industry.²

If the monopoly were to be permanent, much innovation would indeed be encouraged but the industry would not be able to fully embrace the new invention, as its use would be limited to the inventor. A discovery only fully comes of age when other scientists and engineers optimize it and extend its principles to other spheres of research. More importantly, in the evolution of technology, all inventions build upon other inventions. To allow an individual to have a permanent hold on an advancement in the field essentially locks up all further innovation and deny the benefit it may have produced to society. On the other hand, if new inventions were communicated to the industry without special claims by the inventor, the industry would be able to build upon the idea more quickly, but there would be less incentive for inventors to invent in the first place. Thus, there is a trade-off between the intellectual property rights of the individual and the free application of ideas required for a productive industry. A compromise is struck so as to optimize the growth of the market, thereby benefiting society.

Congress took advantage of its Constitutional powers through the Patent Act (35 US Code), which established the United States Patent and Trademark Office (PTO). In §101 of this act, we learn what is patentable:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent thereof, subject to the conditions and requirements of this title.

Thus, the theory of general relativity and the Mona Lisa, for example, are not patentable, despite being prized possessions of society, since they are not in themselves useful entities that can be brought to market and improve the economy. A patent must satisfy a utility clause that it is a useful invention (for example, capable of being made or used in some kind of industry). The patent must also be novel and non-obvious: novel in that it has not been in the public domain before the patent is filed, and

non-obvious in that it is actually an invention and not something that a person working in the field would find obvious.

Patents play a role that cannot be overestimated in today's marketplace. Patents represent information at a point in history when information is the distinguishing factor between the have's and the have-not's. With an army of new ".com" businesses making their way to market, it is clear that a new kind of information-based economy is in effect; where property titles and manufacturing capabilities are less important than ideas.

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As Seth Shulman, a patent scholar, reminds us, “Bill Gates made his fortune not by producing a new widget we couldn't live without but by owning a language for computers to speak.”³ IBM, currently the world leader in terms of active patents, earns about \$1 billion annually from their intellectual property alone. Patents are currently the predominant forms of control over the lucrative information behind this new economy, with trade secrets and copyrights as less powerful alternatives.

GENOMICS AND “PATENTOMICS”

A flood of data is currently being generated, including genes whose sequences are being identified for the first time and whose pharmaceutical potential is yet untapped. Advances in sequencing technology and meth-

odology are enabling the determination of complete genomic sequences of organisms, whereas one would only have had access to a few of an organism's genes a decade ago. Last June, the Human Genome Project announced a first draft of the complete genomic sequence, that is, all the genetic information contained in our cells.⁴ The sequence represents an amazing starting point for the hunt for new drug targets to cure the diseases that plague us.

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Current waves of optimism, while perfectly productive for conducting scientific research, has far-reaching implications on the business end. With the importance of the DNA sequence of a particular gene elevated to the role of complete understanding of that gene's function, patenting of DNA has become commonplace even when little is known of the biological function. Biotech companies are now staking their claim on freshly sequenced genes, often with no experiments to determine the corresponding functions.

Before the sequencing technology became sufficiently practical to perform at a large scale, biology proceeded from phenotype to genotype. In other words, working with a chosen condition, such as breast cancer, scientists would attempt to identify the gene that caused the particular condition. Once found, the gene sequence would be of immediate use as a diagnosis for the condition and was enough to warrant a patent.

Today, however, the direction of the research is completely reversed. Many drug companies are currently busy mining fresh DNA sequences and comparing them against databases of previously studied genes. If the sequence codes for a gene and has not been previously

found in the public databases, the drug company will immediately try to patent the gene. This standard practice is indicative of the new direction in which biology is moving. Given the number of sequences known, it makes more sense for pharmaceutical companies to begin directly at the DNA level and fish for sequences that appear to be involved in a disease.

Large-scale, genome-wide approaches can loosely implicate a gene in a disease by revealing that it is activated in normal cells but repressed in the disease, or vice-versa. This is one of many ways in which a given sequence can be associated with a disease and consequently patented under the disclosure that the gene may be helpful in combating the disease. In effect, the patent ceases to be

a reward for innovation and becomes an exclusion tactic to be the sole researcher of a new gene, since the actual function of the gene has not been established.

Before dealing with these issues directly, it is helpful to understand why patenting DNA is possible in the first place. In 1980, the U.S. Supreme Court, in the case of *Diamond v.*

Chakrabarty,⁵ reinterpreted what is patentable by expanding significantly the definition of what can be claimed under intellectual property. In the case, the court awarded for the first time a patent on a living organism: a modified bacterium that could break down oil. The new bacterium was a "product of human ingenuity" and thus was patentable as a new "composition of matter" under §101 of the Patent Act. The Court ruled that "anything under the sun made by man" is patentable.

Applying this ruling to DNA, if a gene is isolated and purified, or is part of a new recombinant vector, it is in a form different from the one found in nature, and thus is a new composition of matter. For example, a mouse is not patentable, but a mouse engineered to be susceptible to cancer is patentable, regardless of the fact that it is living, because its mutation has been driven by human intervention. In fact, this example is drawn from a real case. Using the argument of human intervention, it becomes possible to patent a human gene, or any stretch of DNA, simply by cloning it into a recombinant vector via established techniques. The isolated gene is now officially distinct from its natural counterpart and is fair game in the patent system.

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SOFTWARE PATENTS: THE PREVIOUS GENERATION

The Biotech Century, to use the phrase of Jeremy Rifkin,⁶ promises to introduce revolutionary new drug products and even redefine the way we look at ourselves as a species. To consider what effect patent law might bear on this plan, it is helpful to compare it to the earlier revolution of computation. The two fields are similar in terms of their exponential growth. Following a surprisingly accurate empirical law known as "Moore's Law," the computer industry has managed to double the amount of information it can store per unit of space about every 18 months since the 1960's. The increase in known genetic sequences has followed a similar trend since sequencing became possible in the early 1970's.

Computer software was originally unpatentable by the USPTO, since it was seen as a mathematical algorithm and thus a kind of law of nature as unpatentable as Newton's laws of gravity. Under 35 USC §101, patents could only be granted to "processes, machines, articles of manufacture, and compositions, of matter," whereas inventions of computer software were seen as a scientific truth. Computer programs could be copyrighted like a book or piece of music, but the actual idea underlying a particular program could not be. In *Gottschalk v. Benson*,⁷ the U.S. Supreme Court denied a patent for an algorithm to convert binary numbers to decimal numbers. The "patent would wholly preempt the mathematical formula" for other uses the court said, thereby setting a trend against the patenting of software when described as straight mathematical algorithms.

What opened the door to software patents was the Supreme Court decision of *Diamond v. Diehr*,⁸ granting a patent for a process for "curing" synthetic rubber involving a computer program. The inventors disclosed a method for simultaneously recording the temperature of the rubber, dispatching it to a computer executing a mathematical equation to calculate the cure time based on the temperature, and then sending a signal back to the press to open when ready. The court ruled that:

When a claim containing a mathematical formula implements or applies the formula in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect (e.g., transforming or reducing an article to a different state or thing), then the claim satisfies 101's requirements.

In other words, the algorithm executed by the computer in calculating the equation was not only a mathematical abstraction, but an actual, real-world method for curing rubber, and hence was patentable.

From that case on, a software patent would be awarded given that its claims showed it was not just an algorithm but actually connected to some real world process. For example, one patent ("A system and method for superimposing images"⁹) was awarded for a computer program that could, given a picture of a person's face, simulate any hairdo for it. Here, the real-world application is the simulation of a new hairdo, potentially a lucrative feature for a hair salon that wishes to offer the service to clients, and the computer program is simply a method for accomplishing this.

A main problem with software, and, with gene patents, is that the novelty of the entire field renders it rather simple to obtain broad patents on innovations. A well known and frightening example is the 1993 award to Compton's New Media (as in Compton's Interactive Encyclopedia) of a patent broadly covering any multimedia database which allows users to simultaneously search for text, graphics, and sounds. The company was quick to gloat about their new patent, quoting to the press, "We have invented multimedia,"¹⁰ and, before the audience of the annual Comdex trade show, they announced the patent with a veiled threat to sue any company that infringes on their patent.

Compton's certainly did not discover multimedia: the same idea had already been on the market and in the literature for two years when Compton's went to the USPTO.³ However, Compton's was the first to consider multimedia as an idea that could sneak through the USPTO and perhaps allow the company to gain some edge in the field, considering the amount of royalties to be collected on an idea so fundamental. As it turns out, the patent was eventually rejected when the USPTO "discovered" evidence of prior art, but the issue remains that many of the patents granted are old-hat tricks that are part of the basic tools of the trade. The computer software industry can now boast patents to find a word in a document, to automatically generate footnotes in a document, and for many other subroutines that should not have passed the non-obvious requirement of patenting.

Perhaps precisely because many patents seem to be so obvious, the application of a patent system to this field should be questioned. The symptom of obvious patents is a sign of a very fast-paced field, one with an explosion of technology and innovation. Under such conditions, the award of a full monopoly over the invention for 20 years may not be necessary, as the field may advance unaided with its own momentum. Built into the patent system is an acknowledgment that a monopoly will negatively influence the industry for the duration of the patent. This shelf life of the patent may be inappropriate for faster-paced areas of research. In particular, the

enormous amount of litigation involved in enforcing and contesting the patents are enough to drive an entire business of ventures to collect undue royalties and of barring new start-up competitors from the field.

The case of patenting in software allows for a negative control. Before 1981, virtually no software patents were awarded, while about a thousand a year have been issued since. Even without the incentives of patents, software writing was at a golden age before 1981 and produced such innovations as Windows, virtual reality, spreadsheets, and networks.³ Since patents, the software business has become very complicated, with any newly written program having a probability very close to certainty that it is infringing on at least one patent. Richard Stallman, a well-respected programmer, has likened the writing of a computer program to crossing a minefield; every step in the program runs a risk of exploding the entire venture.¹⁰

FROM COMPUTERS TO BIOTECH: LESSONS LEARNED

From this case study in the computer software business, which is in some respects technological predecessor of the biotech field, we come away with several basic notions that may be applied to avoid fundamental mistakes in gene patenting. Each of the three lessons from software is discussed in detail in following sections.

1. Firstly, we have seen that a patent is often awarded for inventions where the criteria of non-obviousness is not very rigorously maintained. For example, the “discovery” of protein function based on sequence similarity is a routine step of the trade, and a patent should not reward the brainless application of this analysis.¹¹
2. Secondly, in a related issue as we saw above, Compton’s broad patent on multimedia threatened to monopolize an entire field to which it actually had no due claim. Similarly, in the gene business, broad patents are indicative of undue monopoly. An example is the case of CCR5, a gene whose sequence was patented with no known function, and later determined by other groups to be of tremendous importance to HIV infection.
3. A final, third lesson from software patents is the cross-litigation nightmares produced when one program infringes upon numerous patents. In the biotech sector, this situation occurs when one gene may find itself with more than one owner. At times, there may be different owner for different parts of the gene. In other cases, two owners may find themselves with the nearly the same gene and the same exact application for it.

REWARDING THE ROUTINE

In January 1995, the Human Genome Organization (HUGO), facing the threat of a general privatization of genetics research due to patents from the private sector, stated:

It would be ironic and unfortunate if the patent system were to reward the routine while discouraging the innovative. Yet that could be the result of offering broad patent rights to those who undertake massive but routine sequencing efforts.¹²

The routine endeavor to which HUGO was referring is the sequencing of genomic DNA followed by its putative functional annotation by similarity searches against databases of known sequences. The process is so well characterized that it is even completely automated in the software “pipelines” of leading pharmaceutical companies.

The USPTO has attracted much criticism for its loose utility guidelines. In response, last December, the USPTO revised its guidelines from requiring an “invention [that] is useful for any particular purpose” to an “invention useful for any particular practical purpose.”¹³ In other words, not only must the invention be specific, but it must also be significant.

Yet even according to this revision, the guidelines give an example that continues to provide support to empty claims. Example 10 of the utility guidelines¹³ instructs the patent examiner, when reviewing an application, what to do in the case of a “DNA fragment encoding a full open reading frame” (for example, a whole gene). In this scenario, a sequence is disclosed whose corresponding amino acid sequence has a 95% similarity with a member of the ligase family (for example, they are 95% identical). A ligase is a protein that can glue together two nucleic acid molecules. The pedagogical example concludes with the following synopsis of the decision:

Based on the record, is there a “well established utility” for the claimed invention? Based upon applicant’s disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO: 2 encodes a DNA ligase. Further, DNA ligases have a well-established use in the molecular biology art based on this class of protein’s ability to ligate DNA. Consequently the answer to the question is yes.¹³

By jumping past this most difficult hurdle of demonstrating utility, this patent has a good chance of succeeding at the PTO. The problem is that there is absolutely nothing new in the patent. Amazingly, the tutorial itself states that “there is no reason to doubt” that the protein is a ligase. Ligases are well-studied proteins whose func-

tion has already made them valuable enough to put them on the market. The logic of the PTO is that the new gene, which shares a 95% sequence similarity with the known gene, is useful because the known one has been shown to be useful. The fatal flaw, however, is that given such a high sequence identity, the new sequence is exactly the same as the known sequence, thus making it trivial yet very harmful to patent a new version of it. The only exception would be if the new ligase showed any new and useful properties relative to the old ligase. However, as the applicants never tested this possibility, the patent attempts to ride completely on the back of an old innovation and is thus completely superfluous.

Patent applications such as this one should be disqualified simply due their obvious nature. James Watson, co-discoverer of the structure of DNA, has said that automatic procedures using computers can be done by anyone, even a monkey.¹⁴ Thus, the non-obvious requirement of a patent does not seem to be met, in a similar manner in which we have seen the USPTO fail to acknowledge in the case of software patents. Perhaps understandably, the remoteness of the USPTO from the trends of the field put into question its ability to distinguish what is obvious from what it is not. As the criteria of non-obviousness itself is defined according to what an artisan in the field would consider the invention, given all the currently known tools of the trade, I propose actually asking such an artisan in the field this very question. Such peer review, if it can be made fair to the applicant, may be invaluable in determining the actual strength of the invention. The proposed peer review could be embodied as a collection of experts in the field and may not even demand special consideration for each case as many of the patents fall into a manageable number of distinct clusters.

BROAD PATENTS TO STIFLE RESEARCH

Parallels to the broad patent of multimedia sought by Compton's New Media exist in gene patenting and also threaten to sneak by the US PTO and wreak havoc on the field. In some respects, though, the field is better equipped to handle these types of patents. For example, the new utility guidelines¹³ discuss one case in which the applicant discloses 4332 fragments of genes (cDNA library) as well as a method for (1) obtaining the corresponding full length genes, (2) using them recombinantly to obtain purified proteins which can then (3) be used to determine "the cellular mechanisms and activities in which the proteins are involved." The three-step method disclosed is not new and only serves to stress the indirect utility of the gene fragments. The guidelines demonstrate that such an application cannot

show either a specific or substantial utility for the fragments. The utility is not specific because any fragment could be made into a protein whose function could then be studied. The utility is also not substantial as no "real-world" use is given for the fragments, only that they will be used to determine function, which belongs to the world of science, not business.

When no "real world" use is shown, the USPTO can also refer to the 1966 U.S. Supreme Court ruling of *Brenner v. Manson*.¹⁵ In this case, a patent application for the preparation of a steroid was rejected for failing to disclose a utility for this compound except for inclusion in a screen for possible tumor-inhibiting activity. The Court ruled that "Congress intended that no patent be granted on a chemical compound whose whole 'utility' consists of its potential role as an object of use-testing" and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful completion" because the "patent system must be related to the world of commerce rather than the realm of philosophy." A patent thus needs to carry a substantial utility in order to be considered applicable to the "real world."

Even with these guidelines, however, the USPTO often grants patents on ill-characterized genes, which stands to question the entire system. One such case includes that of the CCR5 gene, first sequenced by Human Genome Sciences Inc. (HGS) in June 1995. A computational search of similarities between this sequence and others from a comprehensive database revealed that the sequence belonged to a family of chemokine receptors, which are traditionally successful pharmaceutical targets. Given the sequence and the results of this search, the USPTO awarded HGS a patent on the gene.¹⁶ A year later, a string of international discoveries by five teams (not including HGS) revealed that this same sequence, CCR5, codes for the immune system cell receptor that lets the HIV virus into the cell and thus initiates the onset of AIDS.¹⁷ This essentially made CCR5 the single most important sequence in all of biology. Though the initial patent had no insight into this important function, HGS now stands to reap all of the financial rewards resulting from therapeutic and diagnostic applications based on discoveries made by others.¹⁸

The problem raised by the CCR5 case is the USPTO's recognition of the upstream, relatively easier findings, which then serves to stifle research down the line when the real scientific discoveries are made. Considering the timeline of knowledge of genes, the standard milestones are as follows: raw DNA sequence, gene identification, putative theoretical function, and then function. The first three steps are all very close to being completely automated, while the last step remains one where the

creativity and perseverance of the researcher are still the predominant factors. By awarding the CCR5 patent at the automated or routine portion of this timeline, the USPTO is essentially crediting the mundane. Such a measure provides less incentive for the real innovative task of working out the function of the gene and perhaps applying the function to some real-world problem, such as curing AIDS. In effect, the USPTO is working against the original intentions of the patent system, which is to reward innovation.

A solution to this problem is to raise the bar on patentability. Such a measure would give the prize of monopoly to the true innovators while also decreasing the number of patents. With fewer patents, the USPTO would be less likely to award too broad a patent.

VARIATIONS UPON A THEME

The threat of litigation, so widely scorned in the software business, seems to be the destiny of the biotech sector as well. Just like any new software program must cross-license many patents to avoid infringements, a developer of a new drug wishing to use a certain gene may need to deal with many owners.

Single nucleotide polymorphisms (SNP's), or the units of change in a gene sequence, are the stuff that ultimately distinguish us as individuals; blue eyes vs. brown eyes, for example. A SNP in one gene could even be the cause of a disease such as breast cancer. In fact, with the case of breast cancer, a race to identify BRCA1, a gene that increases a woman's risk of having breast cancer, led to the patent of this gene along with many of the harmful mutations (SNP's) for diagnosis.¹⁹

The USPTO, however, also awarded a patent to another company for the "consensus sequence" of the normal version of the gene drawn from harmless genetic variations it had identified.²⁰ This "consensus sequence" thus corresponds to the most likely BRCA1 sequence in

the population. As this grant was also given for the utility of genetic testing, the USPTO decisions left two companies each with a slightly different version of the same gene. Apparently, the USPTO failed to notice that testing an individual for a lack of a harmful mutation is identical to testing for the presence of the normal version of the gene.

Such a mess will now leave a legacy of overlapping patents to muddle the legal waters of genetic testing. Had the USPTO examiner of these patents kept better counsel on the science of these sequences, the second patent could have been avoided. One way to keep the USPTO better informed of issues in the practice is to establish, again as suggested above, a peer-review process, whereby a committee of experts would meet to decide on the patentability of certain inventions. Another method is make the patent applications open to the public (they are currently confidential) so that members of the community can voice their concerns while the patent is being considered.

CONCLUSION: THE NEED FOR REFORM

In summary, it is not doubted that patents stimulate growth by allowing entrepreneurs the motivation to produce innovation. However, as with any new field, such as the software business, patents that are inappropriately awarded threaten to stifle the growth of the field. Patents should not be granted for genes of uncharacterized function, as this will effectively reward the trivial while ignoring real achievements of innovation. Patents based on sequence similarity results should be coupled with some other experimental evidence that the sequences will be of marketable value. Otherwise, the patent is not demonstrating any new function. The establishment of a peer-review system would allow the USPTO to catch such obvious mistakes as handing down two patents for the same invention. ■

ENDNOTES

- 1 A. Smith, *The Wealth of Nations*. Prometheus, 1776.
- 2 S. Sherry, "The Incentive of Patents," in *Genetic Ethics: Do the ends justify the genes?*, R. D. P. John F. Kilner, and Frank E. Young, Ed. Michigan: Paternoster, 1997, pp. 113-123.
- 3 S. Shulman, *Owning the Future*. Boston: Houghton Mifflin Company, 1999.
- 4 F. Collins, "A new 5-Year Plan for the United States Human Genome Project," *Science*, vol. 262, pp. 43-46, 1993.
- 5 *Daimond v. Chakrabarty*, 477 U.S. 303 (1980)
- 6 J. Rifkin, *The Biotech Century*. New York: Putnam, 1998.
- 7 *Gottschalk v. Benson*, 409 U.S. 63 (1972)
- 8 *Diamond v. Diehr*, 450 U.S. 175 (1981)
- 9 US 5060171
- 10 S. L. Garfinkel, "Patently Absurd," *Wired*, vol. July, pp. 109, 1994.
- 11 S. F. Altschul, T. L. Madden, A. A. Schaffer, J. Zhang, Z. Zhang, W. Miller, and D. J. Lipman, "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs," *Nucleic Acids Res*, vol. 25, pp. 3389-3402, 1997.
- 12 HUGO, "HUGO Statement of the Patenting of DNA sequences," 1995.
- 13 USPTO, "Revised Interim Utility Guidelines Training Materials," 2000.
- 14 K. Nawa, "Patenting Human DNA," presented at Second International Bioethics, Fukui, 1992.
- 15 *Bremner v. Manson*, 383 U.S. 519 (1966)
- 16 WO9639437, I. Human Genome Sciences, Human G-Protein Chemokine Receptor, 1995.
- 17 E. Marshall, "HIV Experts vs. Sequencers in Patent Race," *Science*, vol. 275, pp. 1261-1264, 1997.
- 18 E. Marshall, "Patent on HIV Receptor Provokes an Outcry," *Science*, vol. 287, pp. 1375-1377, 2000.
- 19 P. D. Murphy, "Coding sequences of the human BRCA1 gene, US5750400," 1997.
- 20 E. Marshall, "The Battle Over BRCA1 Goes to Court," *Science*, vol. 278, pp. 1874, 1997.