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Submission of American Patent and Health Law Professors on Australian Senate Community Affairs Committee Inquiry into Gene Patents

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Submission of American Patent and Health Law Professors on Australian Senate Community Affairs Committee Inquiry Into Gene Patents

In response to the Senate Community Affairs Committee's Inquiry, the undersigned American law professors submit the following comments. (Our affiliations are provided for identification only.) In particular, we believe it would help the Senate Committee to understand the current state of American law and how the provision of patents on genetic technologies has and will continue to create serious problems for innovation, health care, and society at large.

Our submission addresses the following subjects in regard to American law, which respond generally to the issues raised by the Committee's inquiry.

1. The questionable need for patent rights in genetic sequences and other derivatives of naturally occurring materials, certain diagnostic discoveries, and other discoveries;
2. The dubious legal status of patent claims to such discoveries; and
3. The serious harms caused by granting patents on such discoveries.

The submission is not an exhaustive treatment of these issues, but rather is intended to highlight fundamental but mistaken assumptions about the need for and effects of gene patents and to identify significant problems with such patents. The undersigned would be happy to elaborate on any of the issues addressed.

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Table of Contents

American Patent and Health Law Professors Submission
Australian Senate Community Affairs Committee Inquiry Into Gene Patents

Executive Summary

The Australian Senate Community Affairs Committee Inquiry into Gene Patents is seeking information into the impact of the granting of patents over human and microbial genes, non-coding sequences, proteins, and their derivatives and the measures needed to ameliorate any harms caused by those patents. This submission provides the response to the Inquiry of American law professors who have studied these issues for the past decade.

Overview

We believe that such patents are not needed, are not valid, and are affirmatively harmful. Specifically, we have found evidence (and three U.S. Supreme Court Justices have expressed concerns) that these patents increase the cost and decrease the availability of health care, impede rather than promote important scientific and medical research, and potentially compromise the health of not only the American people, but people around the world. We also have found that such patents should not have been granted in the first place under the traditional doctrines of patent law. They reflect discoveries not inventions, they claim products of nature, natural phenomenon, and laws of nature, and they are obvious (so that patent incentives were not needed to develop and disclose the knowledge).

Harms to Patients and Medical Practice

Gene patents increase the cost of the diagnosis and treatment of genetic diseases. For up to twenty years, a gene patent holder controls *any* use of "its" gene. The patent holder can charge whatever it wants for any test analyzing the patented gene—even if that test uses a technology that was not invented by the patent holder. Myriad, which holds the patent on the BRCA1 and BRCA 2 genes, charges $2,900 for its genetic test for breast cancer. One in four laboratories in the United States has stopped performing certain genetic tests because of patent restrictions or excessive royalty costs. Further, patents reflecting genetic and other natural phenomena on which diagnostic tests or methods are based not only decrease competition and raise prices, they chill medical communication and discourage patients from obtaining needed medical care.

Harms to Research and Adverse Effects on University Scientists

Some gene patent holders have stopped research on "their" genes by researchers at top universities, such as Yale, University of California at Los Angeles and the University of Pennsylvania. One study found that 53% of genetics laboratories have stopped doing research due to concerns about gene patents. Some medical researchers have turned down funding for research on important childhood diseases because of fears of infringing patents.

Gene patents impede application of the scientific method of hypothesis generation, discovery and replication. In one survey, half of gene patent holders said they would require a license for researchers to study the prevalence of mutations in the patented gene in the population. Even more troubling is the finding that 28% of geneticists surveyed reported that

they were unable to duplicate published research because other academic scientists refused to share information, data, or materials. This goes to the heart of science, which is based on confirmation of scientific data through replication.

The grant of gene patents is contrary to long-standing patent law doctrines

Patents are supposed to be granted for an invention. Genetic sequences, proteins, and their derivatives are not inventions, but rather are products of nature. There is a long-standing legal precedent – which the language in Article I, section 8, clause 8 of the U.S. Constitution (the patent authorizing clause) reflects – that has been codified in 35 U.S.C. §101 (the Patent Act's subject matter requirements) that products of nature are not patentable.

In a series of cases over the past 150 years, the U.S. Supreme Court has held that one cannot patent products of nature, or materials isolated from products of nature, if those materials behave in the same way they would in nature. Gene patent proponents try to dilute that strong precedent by referring to the 1980 case of *Diamond v. Chakrabarty*. However, that case provided no basis for asserting that a gene sequence is patentable, even if it were isolated and purified; it involved a man-made (genetically engineered) bacterium, which the court carefully described as *not* naturally occurring. (In fact, the Court was precluded from ruling on the patentability of isolated and purified natural materials in that case when one of the petitioners withdrew its patent claim.) The Court in *Chakrabarty* stated:

> The laws of nature, physical phenomena, and abstract ideas have been held not patentable…. Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter.... Such discoveries are "manifestations of ... nature, free to all men and reserved exclusively to none."

Conclusion

Our recommendation to the Senate Community Affairs Committee is that the Patents Act of 1990 should be amended to expressly prohibit patents on genes and non-coding sequences, proteins, and their derivatives. We also recommend that the Act be amended to expressly prohibit patents on biological facts and laws of nature, such as patents on the correlation between certain gene mutations and cancer. Finally, we recommend that the Act be amended to make clear that such prohibitions cannot be avoided by clever patent claim drafting that adds trivial structures to or applications for the use of such unpatentable products, phenomena, and discoveries of nature.

1. The questionable need for patent protection for genetic and medical discoveries.

It is a commonplace to hear that patents are necessary for the biotechnology industry, and that the lack of patent protection would result in significant losses to venture and other investment capital.[1] Proponents of biotechnology patents make it appear that the industry would collapse and society would be deprived of the valuable, life-saving innovations that would otherwise occur.[2] As discussed below (in Part 3), it is not at all clear that the benefits of patents in providing incentives for investment, invention, and disclosure in genetic sequence and other discoveries outweigh the sequential innovation, competition, and social harms that result from the grant of exclusive rights. But that is beside the point here. Of greater importance is that there simply is no strong case demonstrating that the fundamental assumption that patents are needed in this field or result in significant pioneering investment, invention, and disclosure. Similar claims for software inventions have been made and criticized,[3] and the software industry in its early years developed entirely without the expectation of patent protection. Thus, it is not at all clear that patents in fact are necessary or desirable as incentives for biotechnology R&D, even without considering the overall balance of patents on sequential investment, invention, and disclosure. Nor is it clear that the absence of patents would lead to any significant reduction in pioneering investment, invention, or disclosure (or if it did so, that that would on balance be a bad thing). Of course, it is possible that venture capitalists and other financiers act irrationally and might respond by withdrawing funding because of a lack of protection where it was never really needed. But public policy should not (where reasonably possible) be based on catering to irrational behavior. As the current financial crisis demonstrates, it may not necessarily be good policy to throw good money after bad.

In any event, a significant portion of the research and development of genetic sequences and medical discoveries is funded by governmental grants to university scientists rather than through market incentives.[4] Thus, the *scientific* research funding required to provide adequate incentives for biotechnological and medical discoveries may be sufficient without patent rights at all. To the extent that denying patent rights to such discoveries might somehow *significantly* affect these incentives, numerous alternatives exist that may be preferable to exclusive patent

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[1] *See, e.g.,* Written Testimony of the Biotechnology Industry Organization (BIO) Before the United States Senate Committee on the Judiciary, Hearing Entitled "Patent Reform in the 111th Congress: Legislation and Recent Court Decisions," at 4 (March 10, 2009), available at http://www.bio.org/edocs/patent_reform_testimony_31009.pdf.

[2] *See, e.g., id.*

[3] *See, e.g.,* James Bessen, A Comment on "Do Patents Facilitate Financing in the Software Industry," available at http://www.researchoninnovation.org/comment on Mann.pdf (May 2005) ("Mann reports that 'patenting practices have at best a minuscule ability to predict the success of a venture-backed software startup' including these financing measures. In other words, Mann's evidence does not demonstrate that 'patents facilitate financing in the software industry.'").

[4] *See, e.g.,* Hamilton Moses, III, et al., *Financial Anatomy of the Biomedical Research,* 294 J.A.M.A. 1333, 1335-40 (2005) (discussing ten-year trends in industry and governmental funding of biomedical research, and noting the relative underfunding of medical services research); Tracy Hampton, *Health Research Funding Losing Ground,* 296 J.A.M.A. 1219, 1219-20 (2006) (noting that health research investment was decreasing relative to inflation since 2003).

rights. The World Health Organization is considering alternatives in regard to medical discoveries for which small markets do not provide sufficient incentives for large pharmaceutical firms to invest.[5] Different models of intellectual property rights acquisition and retention may be desirable for publicly funded research. Thus, much of the debate over patent rights in genetic sequences and discoveries is really about the role of the public sector in funding, directing, and controlling R&D. The recent history of the financial services sector suggests that a larger government role may be preferable to continued reliance on market mechanisms.

The perceived need for gene patents in the biotechnology and medical sectors also fails to account for the existing incentives that already exist for innovation. In many other economic sectors (such as open-source software, fashion, cooking, etc.), vigorous innovation exists wholly without patent rights. In fact, because of the potential for rapid and unrestricted copying, those sectors may develop innovations more quickly than in sectors protected by patent rights. Moreover, incentives to innovate already exist in the biotechnology and medical areas, because the innovators are themselves users of the innovations.[6] In recognition of this fact (and of the perceived immorality of subjecting medical *procedures* to proprietary rights), most human and animal medical, surgical, and diagnostic *methods* are not patentable throughout most of the world (and are not enforceable against most practitioners even in the United States). No one would seriously argue at this time that we need to patent such methods because without them there is insufficient investment, invention, or discovery. Yet some do make those arguments in regard to medical, surgical, and diagnostic products *that reflect the same inventive creativity!*

Finally, unlike for the pharmaceutical industry where massive costs of clinical trials require exclusive rights to protect investments, investments in R&D to *commercialize* biotechnology and medical discoveries (which largely do not entail such costs) may be more readily protected through traditional means such as lead-time advantage and complementary products and services.[7] Even to the extent that *some* biotechnological or other medical discoveries need private sector incentives in the form of patent rights, it should be clear that such needs are unlikely to be uniform and thus a patent system designed to provide exclusive rights to *all* such discoveries may be excessive.[8] Thus, if patents are to be awarded in this area, they may

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[5] *See, e.g.,* World Health Organization, Commission on Intellectual Property Rights, Innovation and Public Health, Report of the Secretariat, EB116/10, at 4 (28 Apr. 2005), available at http://www.who.int/phi/EB116_10-en.pdf (discussing alternative mechanisms to promote R&D in neglected diseases, such as modifications to exclusive rights, purchase commitments, tax incentives, more effective spending of public and non-profit money, etc.).

[6] *See, e.g.,* Katherine J. Strandberg, *Users as Innovators: Implications for Patent Doctrine,* 79 U. Colo. L. Rev. 467, 483-90 (2008) (discussing conditions under which user innovations will be disseminated and patent rights will be counterproductive).

[7] *See generally* Wesley M. Cohen, Richard R. Nelson & John P. Walsh, *Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (or Not),* NBER 7552, available at http://www.nber.org/paper/w7552 (Feb. 2000).

[8] *See, e.g.,*Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology Specific,* 17 Berkeley Tech. L.J. 1155, 1156 (2002) (discussing how the facially technology neutral patent statute actually "is technology-specific in application").

do more good than harm only in regard to certain types of discoveries (or, more likely, in regard to R&D efforts to develop commercial applications of those discoveries) where alternative incentives are insufficient and where the costs of patenting do not outweigh the benefits. It is precisely the need to differentiate discoveries from inventions in regard to business methods, software, diagnostics, and other technologies that is currently causing the U.S. courts to pay closer attention to the issue of patentable subject matter – to which the discussion now turns.

2. The dubious legal status of patent claims to genetic and many medical discoveries.

It is indisputable that for decades, the U.S. Patent Office ("USPTO") has issued patents for claims to isolated and purified genetic sequences, proteins, and other natural or synthetic derivatives of naturally occurring biological materials ("products of nature").[9] It has also issued patents for diagnostic methods based on discoveries (including accidental ones) regarding human metabolism ("phenomena of nature").[10] Given the thousands (if not tens of thousands) of patents that have now issued containing such claims, it seems odd to state that most if not all of these claims are invalid. Yet, a proper understanding of *existing* law demonstrates this fact. This unfortunate outcome has resulted largely because the USPTO has followed decisions of the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit"),[11] which has failed to follow or to properly apply binding U.S. Supreme Court precedents on patentable subject matter, as discussed below. A detailed discussion of the history of the U.S. Supreme Court's decisions on patentable subject matter and the exclusions for natural products and phenomena (including those that have been isolated and purified from their naturally occurring condition), and of the Federal Circuit's and a few other Courts of Appeals departures from these precedents is available in draft articles of the signatories.[12]

The USPTO's position in granting such patents is understandable, albeit unfortunate. For almost three decades the U.S. Supreme Court has failed to correct the Federal Circuit's rulings on patentable subject matter and other significant areas of patent law. Yet, because lower courts cannot change or alter legal rules or statutory interpretations established by superior courts, the law remains that which the U.S. Supreme Court has said it is (unless or until the U.S. Supreme Court or the Congress change the law). In areas of patent law other than patentable subject matter, however, the U.S. Supreme Court over the last six years has returned to issuing rulings on important patent law doctrines to correct the Federal Circuit's failures to follow U.S. Supreme Court precedents.[13] In particular, the recent U.S. Supreme Court decision in *KSR International, Inc. v. Teleflex Corp.* addressing the obviousness (inventive step) doctrine has made clear that the Federal Circuit has for many years been misapplying U.S. Supreme Court precedent, leading

[9] *See, e.g.*, U.S. Patent No. 4,703,008; U.S. Patent No. 5,654,155; U.S. Pat. No. 5,679,635; U.S. Patent No. 6,762,293.
[10] *See, e.g.*, U.S. Patent No. 4,940,658.

[11] *See, e.g.*, Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991); USPTO, Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (2001) ("USPTO 2001 Utility Guidelines").

[12] *See* Lori Andrews & Jordan Paradise, *Genetic Sequence Patents: Historical Justification and Current Impacts* (August 6, 2008 draft, forthcoming in conference proceedings of the Max Planck Institute), reproduced here as Appendix A; Joshua D. Sarnoff, Shaking the Foundations of Patentable Subject Matter (draft Apr. 2, 2008), available at http://www.wcl.american.edu/pijip/go/research-and-advocacy/ip-policy-and-law-reform.

[13] *See, e.g.*, John F. Duffy, *The* Festo *Decision and the Return of the Supreme Court to the Bar of Patents*, 2002 Sup. Ct. Rev. 273 (2002).

the USPTO to grant and the federal courts to uphold potentially hundreds of thousands or even millions of claims that properly should have been rejected or found invalid.[14]

The U.S. Supreme Court's correction of the Federal Circuit's obviousness doctrine (requiring federal courts and the USPTO to *properly* apply *existing* law) calls into serious question the validity of many of the genetic sequence and other natural products or phenomena claims issued by the PTO. Whether the U.S. Supreme Court will also correct the Federal Circuit's departures from U.S. Supreme Court precedent in the patentable subject matter area or will at some point retrospectively ratify them (and the patents that should not have been issued had U.S. Supreme Court precedents been properly applied) is uncertain. The most one can say now is that the applicable law has not been followed or applied, that no comprehensive challenge to the validity of gene patents on patentable subject matter grounds has been litigated, and that patents for natural products and phenomena continue to be issued even though they are not valid under the existing law.[15]

a. <u>U.S. Supreme Court precedent regarding products and phenomena of nature.</u>

In the United States, as in many other countries, natural products and natural phenomena have been considered unpatentable for centuries. Such pre-existing or fundamental basic materials and information are not patentable. "Patents cannot issue for the discovery of the 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 exclusively to none."[16] This was first expressed in early United Kingdom precedents that distinguished unpatentable ideas and philosophical (scientific) principles (i.e. discoveries of nature) from patentable principles of arranging mechanical devices (i.e. human inventions).[17] The premise was that such pre-existing natural materials and phenomena and their discovery reflected not human but rather divine creativity.[18] The exclusions were incorporated into United States law by statutory interpretation of the patentable subject matter provision of the U.S. patent law in the mid-19th Century. As

[14] *See* KSR Intl. Co. v. Teleflex, Inc., 127 S.Ct. 1727 (2007).

[15] It should not be a surprise that there have been no comprehensive judicial challenges on patentable subject matter grounds to the validity of gene patents. The United States does not have a meaningful post-grant opposition system that can bring challenges to validity unrelated to prior art. *Cf.* 35 U.S.C. §§ 302, 311(a). Nor does the USPTO play any such role after the patent is granted. See 35 U.S.C. § 303. In infringement litigation, the parties are typically already in the business of commercially making or using such inventions and themselves have an interest in maintaining such patents (as anyone else will likely avoid infringing, will not be sued, or will settle to avoid such high-cost litigation).

[16] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

[17] *See, e.g.*, Boulton v. Bull, 2 H. Bl. 463, 486 (1795) (Opinion of Buller, J.); *id.* at 495 (Opinion of Lord Eyre, C.J.); Hornblower v. Boulton, (1799) 101 Eng. Rep. 1285, 1288 (K.B.) (Opinion of Lord Kenyon, C.J.); Rex v. Wheeler, (1819) 2 B. & Ald. 345, 350-53 (K.B.) (Abbott, C.J.).

[18] *See e.g.*, 1 WILLIAM C. ROBINSON, THE LAW OF PATENTS FOR USEFUL INVENTIONS 39 (Little, Brown 1890).

stated by the U.S. Supreme Court in *O'Reilly v. Morse,*[19] which quoted from and discussed the earlier U.K. case of *Nielson v. Harford*[20] and U.S. case of *Le Roy v. Tatham*[21]:

> "[W]e think that the plaintiff does not merely claim a principle, but a machine, embodying a principle, and a very valuable one. *We think the case must be considered as if the principle being well known,* the plaintiff had first invented a mode of applying it by a mechanical apparatus." ….
> ….
> And hence it seems that the [*Nielson*] court at first doubted, whether it was a patent for any thing more than the discovery that hot air would promote the ignition of fuel better than cold. And if this had been the construction, the court, it appears, would have held his patent to be void; *because the discovery of a principle in natural philosophy or physical science, is not patentable.*
> ….
> It appeared that, in [the *Le Roy*] case, the patentee had discovered that lead, recently set, would, under heat and pressure in a close vessel, reunite perfectly, after a separation of its parts, so as to make wrought, instead of cast pipe. And the court held that he was not entitled to a patent for this newly-discovered principle or quality in lead; and that such a discovery was not patentable. But that he was entitled to a patent for the new process or method in the art of making lead pipe, which this discovery enabled him to invent and employ; and was bound to describe such process or method, fully, in his specification.[22]

Later in the 19th Century, the U.S. Supreme Court in *American Wood-Paper Co. v. Fibre Disintegrating Co.*[23] held that purification of a preexisting substance does not create a new, patentable product. The Court held that the primary characteristics and function of the product (refined cellulose – vegetable pulp – derived from straw, wood, and other fibers) were not significantly different from what existed in nature.[24]

> There are many things well known and valuable in medicine or in the arts which may be extracted from…substances. *But the extract is the same, no matter from what it has been taken.* A process to obtain it from a subject from which it has never been taken may be the creature of invention, *but the thing itself when obtained cannot be called a new manufacture.*[25]

[19] 56 U.S. (15 How.) 62 (1853).

[20] (1841) 151 Eng. Rep. 1266, 1273 (Exch.) (Parke, J.).

[21] 55 U.S. (14 How.) 156 (1853).

[22] 56 U.S. (15 How.) at 115, 117-18 (emphasis added).

[23] 90 U.S. (23 Wall.) 566 (1874).

[24] *Id.* at 594.

[25] *Id.* at 593-94 (emphasis added).

Ten years later, the U.S. Supreme Court in *Cochrane v. Badische Anilin & Soda Fabric*[26] further held that the exclusions from patentable subject matter also applied to synthetic, non-living products that are not materially different from products of nature. The patentee had made a synthetic version of a dye that already existed in nature (alizarine), but with a brighter hue. The Court held that "calling it artificial alizarine *did not make it a new composition of matter, and patentable as such, by reason of its having been prepared artificially* for the first time from anthracine, if it was set forth as alizarine, a well known substance."[27]

In the 20th Century, the U.S. Supreme Court held that a significant change in function was required to convert an unpatentable natural material into a patentable human invention, even though the claimed material did not exist in nature. In 1931, in *American Fruit Growers, Inc. v. Brogdex Co.,*[28] the U.S. Supreme Court rejected arguments that minimal physical treatment (with mold-resistant borax) transformed a naturally occurring material (fruit) into a human "'article of manufacture,'" notwithstanding arguments that the product was "the result of a process which is defined and described and not a natural product," exhibited a property not found in naturally occurring materials (added resistance to decay), and that the "complete article is not found in nature."[29] Instead, the Court held that the treated fruit lacked "a new or distinctive form, quality, or property" even though it was "the result of treatment, labor, and manipulation."[30]

> The added substance only protects the natural article against deterioration by inhibiting development of extraneous spores upon the rind. *There is no change in* the name, appearance, or *general character* of the fruit. *It remains* a fresh orange, *fit only for the same beneficial uses as theretofore.*[31]

In 1948, the U.S. Supreme Court reiterated the distinction between patents on the discovered natural materials or scientific principles and on inventions reflecting human creativity. In *Funk Bros. Seed Co. v. Kalo Inoculant Co.,*[32] the Court held that a patent claim to a mixture of root nodule bacteria capable of inoculating the seeds of leguminous plants. The Court held that the combination of the bacteria species did not produce new bacteria, nor did it cause a change in any of the six species of bacteria, but served more of a packaging function.[33] The Court stated that "[e]ach species has the same effect it always had. The bacteria perform in

[26] 111 U.S. 293 (1884).

[27] *Id.* at 312 (emphasis added).

[28] 283 U.S. 1 (1931).

[29] *Id.* at 11.

[30] *Id.* at 11-12.

[31] *Id.* (emphasis added).

[32] 333 U.S. 127 (1948).

[33] *Id.* at 131.

their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee."[34]

The 1952 Patent Act codified the prior law on patentable subject matter without change, except to define invention as including discovery and to make clear (contrary to some earlier U.S. Supreme Court precedents) that patents could be granted for new, inventive uses of existing products.[35] But the inclusion of discoveries in the statutory definition was not meant to eliminate the exclusions for products and phenomena of nature. In 1972, the U.S. Supreme Court made clear that the 1952 Patent Act continued the pre-1952 Patent Act interpretations that discoveries of natural materials and natural phenomena were not patentable inventions. In *Gottschalk v. Benson,*[36] the Court upheld the PTO's rejection of claims to a process for converting binary data that had not practical application except in a digital computer, holding that:

> "[W]hile a scientific truth, or the mathematical expression of it, is not patentable invention, a novel and useful structure created with the aid of knowledge of the scientific truth may be." That statement followed the longstanding rule that "[a]n idea of itself is not patentable."… "A principle in the abstract, is a fundamental truth; an original cause; a motive; these cannot be patented, as non one can claim in either of them an exclusive right."…. Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work…. "He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end." We dealt [in *Funk Brothers Seed Co.*] with a "product" claim, while the present case deals with a "process" claim. But we think the same principle applies.[37]

In 1978, in *Parker v. Flook,*[38] the U.S. Supreme Court sought to provide more guidance to distinguish unpatentable scientific (or mathematical) principles from patentable applications. Taking as a point of departure *O'Reilly*'s statement that even newly discovered natural phenomena must be treated as prior art, the Court held that:

> [t]he notion that post-solution activity, no matter how conventional or obvious in itself, can transform an unpatentable principle into a patentable process exalts

[34] *Id.*

[35] *See* 35 U.S.C. §§ 100(b), 101; Patent Act of July 19, 1952, ch. 950, 66 Stat. 797, Pub. L. No. 82-593; S. REP. NO. 82-1979, at 1, 4, 6 (1952).

[36] 409 U.S. 63 (1972).

[37] *Id.* at 67-68.

[38] 437 U.S. 584 (1978).

> form over substance…. Respondent's process is unpatentable under § 101, not because it contains a mathematical algorithm as one component, *but because once that algorithm is assumed to be within the prior art, the application, considered as a whole, contains no patentable invention*…. [T]he discovery of such a phenomenon cannot support a patent unless there is some *other* inventive concept in its application.[39]

Stated differently, to make a patentable invention out of a scientific discovery requires more than mere application of the discovery to some specific, useful objective. Moreover, the inventive creativity must reside in the application; including some trivial physical transformation step in the claim will not transform an unpatentable application of a scientific discovery into a patentable invention.

In 1980, in *Diamond v. Chakrabarty*,[40] the U.S. Supreme Court held that synthetic living organisms *are* patentable subject matter. The Court upheld the patentability of claims to genetically modified bacteria based on the new function that was introduced – oil digestion – that did not exist in natural bacteria.

> Here, by contrast [to *Funk Brothers Seed Co.*,] the patentee has produced a new bacterium with *markedly* different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under § 101.[41]

However, the U.S. Supreme Court expressly reiterated the validity of the product of nature exception to patentability.

> The laws of nature, physical phenomena, and abstract ideas have been held not patentable…. Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter.... Such discoveries are "manifestations of ... nature, free to all men and reserved exclusively to none." [42]

Significantly, the U.S. Supreme Court in *Chakrabarty* did not rule on a claim to an isolated and purified natural material – a biologically pure culture of the microorganism Streptomyces vellosus, having identified characteristics – that the Federal Circuit's predecessor had ruled was patentable over the USPTO's rejection, because the petitioner (in a companion case) had moved to dismiss its application just before the U.S. Government filed its brief.[43]

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[39] *Id.* at 590, 593-94 (emphasis added).

[40] 447 U.S. 303 (1980).

[41] *Id.* at 309.

[42] *Id.* (quoting *Funk Brothers*, 333 U.S. at 130).

[43] Brief for the Respondent at *2, Diamond v. Chakrabarty, No. 79-136 (S. Ct. 1980).

Thus, *Chakrabarty* did not in any way contradict the U.S. Supreme Court's earlier precedents on isolated and purified natural materials.

In 1981, the U.S. Supreme Court found an invention patentable in *Diamond v. Diehr,*[44] the last patentable subject matter case in which it has issued a decision. The Court reiterated the general understanding of the product of nature exclusion, citing to both *Benson* and *Flook.*

> A mathematical formula as such is not accorded the protection of our patent laws … and this principle cannot be circumvented by attempting to limit the use of the formula to a particular technological environment…. Similarly, insignificant post-solution activity will not transform an unpatentable principle into a patentable process.[45]

The Court found patentable the claimed process for curing rubber using a mathematical formula for calculating temperature, on facts difficult to distinguish from those in *Flook.* The Court in *Diehr* focused on the lack of disclosed or claimed chemical processes, variables, or monitoring structures in *Flook*'s claimed process of catalytic conversion of hydrocarbons that would have distinguished that claim from mere mathematical calculation of useful temperature values.[46] Of greater importance, the Court rejected the argument that the creative contribution of a discovered natural phenomenon to the claim could not "be considered *at all"* in determining patentability, as "if [prior art treatment of the scientific discovery applied in the invention were] carried *to its extreme*, [and everything else in the claim were old, it would] make all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious."[47] *Diehr* did not repudiate *Flook*'s statement of the law, but rather only its application to certain process claims containing some unpatentable calculation steps (even if the calculation itself reflected the entire inventive creativity).

Finally, in 2006, the Court dismissed certiorari as improvidently granted in *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.,*[48] a case in which the Federal Circuit had upheld a two-step (measure and correlate) diagnostic method claim, addressing the correlation between an elevated amino acid level and a vitamin deficiency. Many gene-based diagnostic patents contain claims of this sort, because disease conditions are correlated to a particular genetic sequence or other marker. The dissent from the dismissal criticized the Federal Circuit's determination of patentability, because the two-step claim was nothing more than an application of the unpatentable (albeit newly discovered) natural phenomenon, even with the inclusion of a physical measurement step.[49]

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[44] 450 U.S. 175 (1981).

[45] *Id.* at 191-92.

[46] *Id.* at 186-87.

[47] *Id.* at 189 n.12 (emphasis added).

[48] 126 S.Ct. 2921 (2006).

[49] *Id.* at 2926-28 (Breyer, J. dissenting from dismissal of certiorari as improvidently granted).

> But one can reduce *any* process to a series of steps. The question is what those steps embody. And here, aside from the unpatented test, they embody only the correlation between homocysteine and vitamin deficiency that the researchers uncovered. In my view, that correlation is an unpatentable "natural phenomenon," and I can find nothing in claim 13 that adds anything more of significance.[50]

The dissent thus highlights the questions left unanswered by the combination of *Flook* and *Diehr* of when a claim contains steps (or structures) in addition to the scientific discovery that are not mere post- (or pre-)solution activity but rather reflect sufficient human creativity beyond the mere application of the discovery so as to warrant the grant of a patent. However, as no opinion of the Court was issued, the law remains what as it was in light of *Diehr* and the Court's earlier precedents. (A dissent in such a situation is highly unusual and does not reflect a difference from a Court opinion as no opinion has been issued. In this case, the defendant had failed to specifically identify Section 101 as a defense below, but the dissenting Justices believed the issue had been preserved and was too important not to reach.[51])

In summary, the U.S. Supreme Court's cases clearly indicate that mere isolation and purification of a naturally occurring material is not sufficient to constitute a patentable invention, but rather what is required is the creation of a synthetic material different from the natural material and having *significant* new functions not exhibited by the natural material. Similarly, for a newly discovered scientific principle to be patentable, its application to a particular context must reflect significant extra-solution activity. The significance extra-solution activity requirement is critically important, as otherwise clever claim drafting would permit applicants to avoid the prohibition on patenting natural phenomena and products through a series of narrower claims that would in piecemeal fashion encroach on the public domain of science and nature.[52]

b. Isolated and purified genetic sequences and other natural materials, diagnostic procedures, and other medical discoveries are not patentable subject matter.

Given the U.S. Supreme Court case law, it should be clear that isolated and purified genetic sequences are unpatentable in the United States. The mere fact of isolation and purification is not enough of a change, as the products *do not have any functions that they did not have already.* This is true even though the isolated and purified sequences may now be manipulated in ways that would not have occurred under natural conditions to accomplish new and useful results. Similarly, synthetic genetic sequences that are not materially different from

[50] *Id.* at 2928.

[51] *See id.* at 2925-26.

[52] *See* Brief of *Amici Curiae* Ten Law Professors in Support of Appellee Director of the United States Patent and Trademark Office, In re Bilski, Appeal No. 2007-1130 (Fed. Cir. Apr. 7, 2008), at 3-6, available at http://www.wcl.american.edu/pijip/go/research-and-advocacy/ip-policy-and-law-reform.

their naturally occurring counterparts are not patentable inventions, just as synthetic alizarine was not patentable in *Cochrane.* Treatment of cDNA as a patentable product (either as resulting from purification and isolation or because of its synthetic creation) also is a mistaken legal fiction and does not reflect scientific understandings of the nature or value of cDNA. cDNA has value only to the extent that it is a more easily manipulated version of the DNA found in nature. It does not do anything, nor contain any information that is not already present is DNA itself.

This is not to say that all synthetic genetic sequences (or other biologically active synthetic materials – including pharmaceuticals) are unpatentable. But it does mean that most of the patents that have issued claiming genetic and protein sequences are invalid, as they represent nothing more than the isolated or purified sequences or modifications to them (by removing the non-coding region of genetic sequences, preserving the functions of the naturally occurring gene, etc.) to result in materials that perform the same functions that they do in nature (even if they are now capable of manipulation in ways that would not occur without human intervention).

Nevertheless, the USPTO has granted numerous patents for an "isolated and purified DNA molecule that has the same sequence as a naturally-occurring gene … because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally-occurring compound."[53] Such DNA should not be patentable under the U.S. Supreme Court case law unless the synthetic DNA is *materially* altered from that occurring in nature (and not just isolated from it) *and* unless the synthetic DNA performs some *significant* function not occurring in the natural DNA.

The fact that some lower courts have, in a few (often factually inapposite) instances, erroneously concluded that isolated and purified natural materials by themselves are patentable[54] does not make those conclusions or factual applications into the law. Similarly, the USPTO in 2001 sought to justify the issuance of such patents in 2001 by stating that "[p]atenting compounds isolated from nature follows well-established principles, and is not a new practice."[55] The USPTO relied for these statements in particular on the 1873 patent issued to Louis Pasteur and on the federal district court decision in *Parke-Davis & Co. v. H.K. Mulford & Co.,* which found (based on two earlier appellate court precedents regarding purification of synthetic materials) that purified naturally occurring adrenaline was patentable.[56] Such "principles,"

[53] USPTO 2001 Utility Guidelines, 66 Fed. Reg. at 1093.

[54] *See, e.g.,* Kuehmsted v. Farbenfabriken of Elberfeld Co., 179 F. 701, 703-05 (7th Cir. 1910); Union Carbide Co. v. American Carbide Co., 181 F. 104, 104-07 (2d Cir. 1910); Parke-Davis & Co. v. H.K. Mulford & Co., 189 F. 95, 103 (C.C.S.D.N.Y 1911), *aff'd in part, rev'd in part,* 196 F. 496 (2d Cir. 1912); Dennis v. Pitner, 106 F. 2d 142, 143-45 (7th Cir. 1939); Merck & Co. v. Olin Mathieson Chemical Corp., 253 F.2d 156, 157-60 (4th Cir. 1958); In re Seaborg, 328 F.3d 993, 996 (C.C.P.A. 1965); In re Bergstrom, 427 F.2d 1394, 1401 (C.C.P.A. 1970); Application of deC. Kratz, 592 F.2d 1169, 1172-74 (C.C.P.A. 1979).

[55] USPTO 2001 Utility Guidelines, 66 Fed. Reg. at 1093.

[56] *See* Parke-Davis & Co. v. H.K. Mulford & Co., 189 F. at 103.

however, are anything but "well-established" as a matter of law, even if the grant of patents on isolated and purified natural materials has become common. For example, *Parke-Davis* treated the purified adrenaline as a changed product (because of the purification); different patents at issue claimed the purified active principle in both basic and salt forms and the active principle was previously extracted only as a salt.[57] Judge Hand stated that that no "rule" precluded patenting "an extracted product without change" and that the purified product was changed "not in degree, but in kind."[58] Judge Hand was wrong on both counts (regardless of whether either form was synthetic or only purified). *American Wood Products* had established that a merely purified natural product was not patentable, even if it was more useful when purified. *Cochrane* had established (and *Brogdex* later reaffirmed) that a *significant* new function was needed to make even a synthetic product (similar to a naturally occurring one) into a new patentable thing. No such significant new function was identified in *Parke-Davis*, only a greater utility (on which the novelty and patentability of purified adrenaline was based).[59]

In addition to genetic sequence claims, many diagnostic claims that have issued from the USPTO are likely to be invalid. As noted above, at least three Justices of the U.S. Supreme Court believe that measure and correlate claims like those in the *Laboratory Corp. of America Holdings* case are not even close to being considered patentable subject matter.[60] In their view, not only do such claims fail to reflect any significant inventive creativity beyond applying the newly discovered natural phenomena, but also the claim was not viewed as accomplishing a physical transformation that would impart patentability of the claim as a whole, even if the measurement step required physical transformation (in the alteration of blood samples).[61] Further, the Justices discussed numerous reasons why patents such as these are bad for society (as explained in more detail in Section 3).[62]

More recently, the Federal Circuit en banc decided *In re Bilski*,[63] enunciating a "definitive test" that a process claim reflecting "a particular application of a fundamental principle" reflects patentable subject matter if "(1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing."[64] Further, "even if a claim recites a specific machine or a particular transformation of a specific article, the recited machine or transformation must not constitute mere 'insignificant [pre- or] postsolution activity,'" and the

[57] *See id.* at 103, 106.

[58] *Id.*

[59] *See id.* at 103 ("while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically.").

[60] *See* 126 S.Ct. at 2927 ("this case is not at the boundary").

[61] *See id.*

[62] *See id.* at 2927-28.

[63] 545 F.3d 943 (Fed. Cir. 2008) (en banc).

[64] *Id.* at 954.

"transformation must be central to the purpose of the claimed process."[65] Although a petition for review by the U.S. Supreme Court has been filed, *Bilski* already has had far-reaching implications. Thus, in a recent one-paragraph unpublished opinion in *Classen Immunotherapies, Inc. v. Biogen IDEC,*[66] the Federal Circuit invalidated a patent for a method of immunization, holding that "the claims are neither 'tied to a particular machine or apparatus' nor do they 'transform[ ] a particular article into a different state or thing.'"[67] As noted by one commenter, in order to distinguish the *Classen* immunization claims from all method of human (or other living organism) treatment claims, it is necessary to conclude that the type of medical transformation accomplished by immunization "constitutes an 'insubstantial extra-solution activity.'"[68] Another pending case – *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*[69] – will test whether the *Classen* approach applies to diagnostics involving administration of non-naturally occurring substances, given that the claim may still reflect a natural phenomenon (albeit one that would not occur but for artificial conditions, such as involved in the *Cochrane* and *Brogdex* cases).

Stated differently, claims such as those in *Bilski*, *Classen,* and *Prometheus* reflect patents on information about the world and prohibit thought using such information, which may be problematic without regard to whether the conditions triggering such thought are natural or artificial. Significantly, in identifying what constitute unpatentable transformations of data (as lacking sufficient physicality),[70] the *Bilski* opinion relied on a predecessor court's decision in *In re Meyer*.[71] *Mayer* invalidated a patent for neurological diagnosis that involved identifying a malfunction in a multi-component system (the steps of which were not naturally occurring).[72] Like these diagnostic claims, genetic and other sequence claims are valuable not for their physical properties or interactions, but for their information content, regardless of whether they are natural or synthetic.

Assuming (as is likely) that *In re Bilski*'s machine-or-transformation test will now be applied by the courts and the USPTO, many (if not most) diagnostic claims and many other claims applying medical discoveries will be found unpatentable. They either do not recite machine implementation steps or physical transformation steps at all, or any such steps in the claims likely reflect either extra-solution activity or transformations that are not central to the

[65] *Id.* at 957, 962.

[66] 2008 WL 5273107 (Fed. Cir. Dec. 19, 2008).

[67] *Id.* at *1 (quoting *Bilski*, 535 F.3d at 954).

[68] Christopher M. Holman, *Classen v. Biogen: The Federal Circuit Applies Bilski to the Life Sciences*, Holman's Biotech IP Blog (Dec. 19, 2008), available at http://holmansbiotechipblog.blogspot.com/2008/12/classen-v-biogen-federal-circuit.html.

[69] No. 2008-1403 (Fed. Cir.).

[70] 535 F.3d at 962-63.

[71] 688 F.2d 789 (C.C.P.A. 1982).

[72] *See id.* at

claimed processes (just as the Justices in *Metabolite Laboratories* case viewed the physical measurement steps involved as not altering the unpatentable nature of the claimed invention). For example, a federal district court recently held unpatentable claims relating to a new medical discovery (fortuitously resulting from legally required clinical testing) that the bioavailability of a pharmaceutical product (for which the composition patent had expired) increased when taken with food.[73] Not only was "the food effect … an inherent property of the prior art and, therefore, unpatentable … informing a patient of that inherent property is likewise unpatentable."[74] Disseminating the new medical knowledge neither resulted in a transformation nor employed a machine (and at most was insignificant post-solution activity).[75] Moreover, "[s]uch a claim, which effectively allows a patentee to exclude others from informing people of (unpatentable) scientific discoveries is anathema to the aims of the patent statute, which favors disclosure."[76]

Although the *Bilski* decision on its face applies only to claims for processes, the U.S. Supreme Court cases addressing the exclusion for natural products and natural phenomena are not restricted to process claims and the *Bilski* decision has not been viewed by the USPTO as limited to processes. Thus, in *Ex Parte Atkin,*[77] after holding method claims unpatentable in light of *Bilski,* the USPTO also held claims to a system comprising elements for performing the functions represented by those steps similarly ineligible, because the claims as construed encompassed the same scope. (The USPTO remanded claims for a computer readable medium encoded with software for accomplishing the ineligible methods.[78]) Accordingly, many claims to diagnostic and other medical *products* will be held invalid under *Bilski*, particularly if they reflect no inventive creativity beyond the mere application of a newly discovered natural phenomenon.

c. <u>Many isolated and purified genetic sequences are not "useful".</u>

Many genetic sequence claims that previously have issued also may be unpatentable under a legal doctrine distinct from patentable subject matter contained in the same section of the Patent Act, *i.e.,* the doctrine of utility deriving from the requirement in Section 101 of the Patent Act that the patentable subject matter must be "useful."[79] As the U.S. Supreme Court held in *Brenner v. Manson,*[80] a patent may not issue on process claims unless and until they are shown to produce products having a "specific utility…. where a specific benefit exists in currently

[73] *See* King Pharms., Inc. v. Eon Labs., Inc., 593 F. Supp. 2d 501 (E.D.N.Y 2009).

[74] *Id.* (page citations not yet available)

[75] *See id.*

[76] *Id.*

[77] Appeal 2008-4352 (BPAI Jan. 30, 2009).

[78] *Id.* at *18.

[79] 35 U.S.C. § 101.

[80] 383 U.S. 519 (1966).

available form."[81] The U.S. Supreme Court specifically rejected the idea that use as "an object of scientific research" was a sufficient disclosed utility for a process, and made clear that the same requirement applied to product claims (and the mere fact that the process would produce such products could not be used to evade the utility requirement as applied to such products).[82]

The Federal Circuit recently applied *Brenner* to expressed sequence tags (EST) claims in *In re Fisher*.[83] The Federal Circuit held that the claimed genetic sequences were unpatentable as they had no known function at the time of filing. The Federal Circuit rejected arguments that the disclosed sequences possessed sufficient utility, because they acted "as no more than research intermediates that may help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes."[84] It repudiated the asserted comparison to microscopes useful for further research, because the claimed EST "can only be used to detect the presence of genetic material having the same structure as the EST itself. It is unable to provide any information about the overall structure let alone the function of the underlying gene."[85] The Federal Circuit also rejected the idea that "hypothetical possibilities" or identified "objectives which the claimed ESTs … could possibly achieve" can provide the required sufficient disclosed utility.[86] Although some patent applications and some issued patents may have disclosed functions for ESTs (or other sequence claims) that might be found to constitute a sufficient disclosed utility (particularly if they were tied to research identifying the function of the genes or proteins for which they code), many (if not most) of the claims that reflected large-scale sequencing may not have done so. Thus, any such applications should be denied and any patents issued for such claims are invalid.

d. <u>Many genetic sequences, diagnostics, and other medical discoveries are "obvious".</u>

In 2007, in *KSR International Co. v. Teleflex, Inc.*,[87] the U.S. Supreme Court made clear that the Federal Circuit (and thus the USPTO) had for many years (perhaps decades) been applying an excessively strict standard for determining the obviousness of claims. The Federal Circuit's approach had undermined the "principle reason for declining to allow patents for what is obvious," *i.e.*, that such patents withdraw "'what is already known into the field of [their] monopoly and diminish[] the resources available to skillful men.'"[88] Stated differently, obvious patents tax the public for disclosed knowledge that is already within its constructive possession

[81] *Id.* at 534-35.

[82] *Id.* at 535.

[83] 421 F.3d 1365 (Fed. Cir. 2005).

[84] *Id.* at 1373.

[85] *Id.*

[86] *Id.*

[87] 127 S.Ct. 1727 (2007).

[88] *Id.* at 1739 (quoting Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152 (1950)).

and thus that needs no such incentives to be developed and disclosed. Such patents provide no present innovation benefits while discouraging future innovation. The magnitude of patent claims that improperly issued (or improperly were found to be valid) and have caused such harms cannot be determined. But there are good reasons to believe that gene patents, diagnostics, and many other medical patents are among the most likely to fall into that category.

In *KSR*, the U.S. Supreme Court rejected the "rigid rule" for proving obviousness that had been adopted by the Federal Circuit, which had required identification in the prior art of a specific "teaching, suggestion, or motivation" to combine the elements found in a claim.[89] The U.S. Supreme Court faulted the Federal Circuit for its narrow focus on the motivations and problems of inventor, its failure to look beyond elements of the prior art designed to solve those specific problems, its rejection of an "obvious to try" analysis where finite predictable and feasible solutions exist, and its exclusion of common sense when seeking to prevent hindsight bias.[90] Following *KSR*, the USPTO issued guidance that dramatically revised the analysis that examiners apply to determining the obviousness of claims. The USPTO identified seven ways that examiners can support obviousness rejections, which focus on the predictability of the result achieved or a reasonable expectation of success in achieving some desired result.[91]

Applying *KSR* and the USPTO's guidance, many genetic sequence, diagnostic, and other medical discovery claims should be found obvious. This is because once the scientific discovery task is specified: (1) obtaining the desired isolated and purified sequence requires no meaningful inventive creativity and achieves predictable results; (2) adding to discoveries of natural phenomena trivial physical steps or structures so as to create diagnostic methods or products is what persons of ordinary skill can and would be motivated to do; and (3) creating a new synthetic product or process may reflect only the application of ordinary skill to a defined problem. For example, in 1979 the Federal Circuit's predecessor court had noted – in a case frequently cited to support the argument for patent eligibility of isolated and purified synthetic chemicals resembling natural materials – that the USPTO had rejected the claims as obvious. "The analysis of the natural constituents of foods is now conventional," and the synthetic or substantially pure compound is thus obvious in light of the natural constituent.[92] Similarly, in a recent pharmaceutical case that closely preceded the Supreme Court *KSR* decision, the Federal Circuit held that a motivation to combine structural elements found in the prior art was sufficient to demonstrate obviousness based on the nature of the problem itself, and not the problem that the inventor was trying to solve.[93] The Federal Circuit also rejected the lower court's holding that the properties of the combination were unpredictable and lacked an expectation of success, and even rejected the patent holder's argument that the combination was at most obvious to try

[89] 127 S.Ct. at 1741.

[90] *See id.* at 1741-43.

[91] USPTO, Examination Guidelines for Determining Obviousness Under 35 U.S.C. § 103 in View of the Supreme Court Decision in KSR International Co. v. Teleflex, Inc., 72 Fed. Reg. 57526, 57529-34 (2007).

[92] Application of deC. Kratz, 592 F.2d 1169, 1172 (C.C.P.A. 1979).

[93] Pfizer, Inc. v. Apotex, Inc. 488 F.3d 1377, 1364 (Fed. Cir. 2007).

but not obvious in light of the limited number of parameters and prior art uses.[94] (As the case preceded *KSR*, the Federal Circuit had required an improperly high standard of proof, stating that an obvious to try standard for proving obviousness was "impermissible."[95]; the claim nevertheless was obvious.)

More recently, the Federal Circuit held a claimed isolated and purified active pharmaceutical ingredient to be obvious over the prior art chemical that contained it, stating that one expects "a concentrated or purified ingredient to retain the same properties it exhibited in a mixture, and for those properties to be amplified when the ingredient is concentrated or purified" (which thereby provides the obvious motivation to do so).[96] Further, "[i]solation of interesting compounds is a mainstay of the chemist's art," and "[i]f it is known how to perform such an isolation, doing so 'is likely the product not of innovation but of ordinary skill and common sense.'"[97] The active ingredient either was known or there was sufficient reason to look to it, and there were no unexpected results of purification that would rebut the prima facie determination of obviousness.[98] Genetic sequences are similarly likely to be obvious because: (1) the desirable property of a gene is derived from its coding region, therefore creating a prima facie case of obviousness; and (2) a prima facie case of obviousness may not be rebutted by arguing unexpected results if the "isolated" and a "purified" gene retains the properties it exhibited in its natural form.

Isolated and purified genetic sequences also are likely to be obvious because isolation, purification, and identification do not require (particularly in recent decades) anything beyond ordinary mechanical skill. Typically, such isolation and purification required only the application of techniques fully disclosed (and made operable) by the prior art, which merely needed to be applied to the target under investigation. As the USPTO's guidance has long made clear:

> the mere purity of a product, by itself, does not render the product unobvious…. Factors to be considered … include whether the claimed chemical composition has the same utility as closely related materials in the prior art make, and whether the prior art suggests the particular form or structure of the claimed material or suitable methods of obtaining that form or structure.[99]

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[94] *See id.* at 1365-66.

[95] *Id.* at 1365.

[96] Aventis Pharm Deutschland v. Lupin, LTD., 499 F.3d 1293, 1302 (Fed.Cir. 2007).

[97] *Id.* (quoting *KSR Int'l. Co.*, 127 S.Ct. at 1742).

[98] *See id.*

[99] USPTO, Manual of Patent Examining Procedure, § 2144.04 at 2100-150 (8th ed. Rev. 6 Sept. 2007) ("Purifying an Old Product").

This guidance, moreover, predates the expansive understanding of the ways to demonstrate obviousness now permitted by *KSR*.

Although selection of the target might possibly involve some creativity, *KSR* made clear that obviousness does not depend on creativity in the selection of the problem that the inventor was seeking to solve, but rather requires only an objective basis in the field for achieving the solution to any problem that would arrive at the claimed invention. And as a matter of practice, isolation and purification of genetic sequences does not even need to address an identified problem. A founder of a company selling genetic sequencing hardware recently noted that the use of an "ultra-high-throughput sequencing machine" permits a single machine operator only two weeks to obtain a "tenfold coverage" of a particular human genome.[100] For such sequencing discoveries, and particularly in recent years where automation has replaced human labor, no sufficient inventive creativity is involved.

[100] Steven Quake, Guest Column: Genome Mania, NYTimes.com (Mar. 3, 2009), at http://judson.blogs.nytimes.com/2009/03/03/guest-column-genome-mania.

3. The serious harms caused by granting patents on genetic and similar medical discoveries.

As three U.S. Supreme Court Justices stated in the *Laboratory Corp. of America* case, just making clear the legal status of diagnostic claims based on newly discovered natural phenomena would benefit "those who engage in medical research, who practice medicine, and who as patients depend upon proper health care."[101] But the Justices also emphasized the serious harms that such patents impose on patients, doctors, medical practice, and medical innovation. Such patents:

> may inhibit doctors from using their best medical judgment; they may force doctors to spend unnecessary time and energy to enter into license agreements; they may divert resources from the medical task of health care to the legal task of searching patent files for similar simple correlations; they may raise the cost of healthcare while inhibiting its effective delivery."[102]

Similarly, such patents:

> can discourage research by impeding the free exchange of information, for example by forcing researchers to avoid the use of potentially patented ideas, by leading them to conduct costly and time-consuming searches of existing or pending patents, by requiring complex licensing arrangements, and by raising the costs of using the patented information, sometimes prohibitively so.[103]

Not only were Supreme Court Justices concerned, but the American medical, patient, and industrial communities also were concerned, as reflected in amicus briefs filed in that case by the American Medical Association and other medical groups, by the AARP, and by the American Clinical Laboratories Association.[104] These concerns were and are not merely speculative. Detailed evidence of the harms such patents cause is discussed below, and we focus (given the

[101] Lab. Corp. of America Holdings v. Metabolite Labs., Inc.,126 S.Ct. 2921, 2922 (Breyer, J., dissenting from dismissal of cert. as improvidently granted).

[102] *Id.* at 2928-29.

[103] *Id.* at 2922.

[104] *See* Brief for the American Medical Association, the American College of Medical Genetics, the American College of Obstetricians and Gynecologists, the Association for Molecular Pathology, the Association of American Medical Colleges, and the College of American Pathologists as *Amicus Curiae* in Support of Petitioner, Lab. Corp. of America Holdings v. Metabolite Labs., Inc., No. 04-607, available at http://www.ama-assn.org/ama1/pub/upload/mm/395/labcorp.pdf ; Brief *Amicus Curiae* of AARP in Support of Petitioner, Lab. Corp. of America Holdings v. Metabolite Labs., Inc., No. 04-607, available at http://www.wcl.american.edu/ipclinic/documents/LabCorpMetabolite-Dec2005.pdf?rd=1 ("AARP Brief"); Brief of the American Clinical Laboratory Association as *Amicus Curiae* in Support of Petitioner, Lab. Corp. of America Holdings v. Metabolite Labs., Inc., No. 04-607, available at http://www.robbinsrussell.com/pdf/319.pdf.

Inquiry) principally on the harms of gene patents. However, the harms extend to many other patents reflecting discoveries of nature and of medicine, and additional comprehensive data gathering and analysis of the harms would clearly be warranted to demonstrate just how pernicious such patents may be.

Before discussing the concrete evidence of harms, it is important to note that additional legal doctrines and licensing practices compound the harms that such patents may cause. We identify but do not elaborate these doctrines and practices here, because we are recommending that such genetic, diagnostic, and other discovery-based patents be prohibited entirely. But to the extent that they are not so prohibited, we then would recommend that Australia assure that its corresponding patent law doctrines avoid exacerbating the harms that such patents cause.

First, because the experimental use doctrine has been seriously constricted by interpretations of the Federal Circuit,[105] scientific research and experimentation in general has been adversely affected. In fact, the only reason it has not been affected to a more serious degree is that scientists (and their institutions) routinely flout the law and ignore their potential liability, based in part on the general reluctance of patent holders to sue research scientists and medical practitioners[106] (and the preclusion of remedies against most medical practitioners contained in the U.S. Patent Act[107]). As discussed below, such routine forbearance does not apply to the genetics and diagnostics industries, and thus for the patents of concern here the costs to innovation, competition, and medical care are truly serious.

Second, the over-extension of indirect liability for patent infringement seriously compounds the problems of genetic, diagnostic, and other medical care patents. Such expansive liability not only chills medical communication and medical practice, but also significantly increases the costs of medical care. Under current U.S. law, a person may be found liable for infringement indirectly, either by contributing articles that have no uses except to facilitate infringement by others or by inducing others to infringe. The standards for finding a sufficient contribution or inducement, and the requisite knowledge and intent of the contributor and inducer, however, have recently been set at an extremely low level. Thus, in the *Laboratory Corp.* case in the district court, the diagnostic supplier of an unpatented assay (which, although new, performed in a better way functions that were also performed by prior art assays) was found to be liable both as a contributor and as an inducer of doctors who performed a patented

[105] *See, e.g.*, Madey v. Duke Univ., 307 F.3d 1351 (Fed. Cir. 2002).

[106] *See, e.g.*, Joshua D. Sarnoff & Christopher M. Holman, *Recent Developments Affecting the Enforcement, Procurement, and Licensing of Research Tool Patents*, 23 Berkeley Tech L.J. __ (forthcoming 2008) (citing, inter alia, John P. Walsh, Charlene Cho, & Wesley M. Cohen, *View from the Bench: Patents and Material Transfers*, 309 Science 2002 (2005) ("*View from the Bench*"); Sci. & Intellectual Prop. in the Pub. Interest, Am. Ass'n for the Advancement of Sci., Effects of Intellectual Property Protections on the Conduct of Scientific Research: Results of a Survey of U.S. AAAS Members 2-3 (2007); and Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, 76 U. Mo.-Kan. City L. Rev. 295 (2007)).

[107] *See* 35 U.S.C. § 287(c); Misha Angrist and Robert M. Cook-Deegan, *Who Owns the Genome?* 11 The New Atlantis 87 – 96 (Winter 2006) (stating that purportedly "contradictory" statements in the law have led "academic genome researchers [to] feel more protected from litigation" than they actually are).

measure-and-correlate claim. (The doctors ordered the new unpatented assay to obtain the same measurement as previously done in the prior art, and then unavoidably made the mental correlation that completed the claimed method.) Significantly, such secondary liability not only impermissibly withdraws the use of unpatented prior art medical practices from the public domain, but also chills medical communication. Given the low threshold for inducement, doctors and suppliers may be liable for communicating the medical knowledge that the patent itself discloses. The threat of inducement liability (or of direct liability for patients who would perform such patented methods themselves and are not shielded by the statutory provision applicable to medical practitioners) discourages proper medical treatment. A detailed discussion of these issues can be found in the U.S. Supreme Court amicus brief of the AARP in that case.[108]

Third, patents provide the potential for discriminatory licensing and other harmful behaviors that may adversely affect research and development or commercialization of important new technologies. Because the underlying reasons for decisions to refuse to license patent rights need not be made public, any patent presents the potential for the patent holder to disfavor particular kinds of research (e.g., research that might assist abortions) or to disfavor particular individuals or classes of people (e.g., people having rare diseases or people of a distinct racial group) by refusing to grant access to and use of patented technologies. Such practices are of particular concern in the health-care field. Antitrust and competition laws are not well suited to policing such harmful discriminatory conduct, even when it becomes identifiable. This is particularly true in the United States, where patent immunity from antitrust scrutiny is broad and unilateral refusals to license are not considered problematic by antitrust enforcement agencies.[109]

In contrast to such covert discriminatory licensing practices, there is now an overt practice of seeking biotechnological patents on the basis of racial and ethnic categories (racialized patents), highlighting the problems of discriminatory creation and licensing of property rights in a highly visible and notoriously problematic context. Racialized patents may reflect socially constructed understandings of race, but "corporations … are literally 'investing' their patents and products with race to gain commercial advantage in the research, development, and marketing of new biotechnology products."[110] Not only do the restrictions imposed by such patents impose discriminatory burdens on those who may be least able to afford the restrictions on access and increased market prices for the technologies protected, but also such patents may "have profound implications for both the equitable distribution of benefits derived from biotechnology and for broader social understandings and mobilizations of race. In this context, law and commerce are driving the use of race in science and medicine."[111]

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[108] *See* AARP Brief, *supra*, at 10-20.

[109] *See, e.g.,* U.S. Department of Justice and Federal Trade Commission, Antitrust Enforcement and Intellectual Property Rights: Promoting Innovation and Competition (April 2007), Introduction at 5-6, available at www.usdoj.gov/atr/public/hearings/ip/222655.pdf; In re ISO Antitrust Litigation, 203 F.3d 1322 (Fed. Cir. 2000); Virginia Panel Corp. v. MAC Panel Corp., 133 F.3d 860 (Fed. Cir. 1999).

[110] Jonathan Kahn, *Race-ing Patents/Patenting Race: An Emerging Political Geography of Intellectual Property in Biotechnology*, 92 Iowa L. Rev. 353, 355 (2007).

[111] *Id.*

a. Gene patents interfere with medical care.

Gene patents increase the cost of the diagnosis and treatment of genetic diseases. For up to twenty years, a gene patent holder controls *any* use of "its" gene. The patent holder can charge whatever it wants for any test analyzing the patented gene—even if that test uses a technology that was not invented by the patent holder. Myriad, which holds the patent on the BRCA1 and BRCA 2 genes, charges $2,900 for its genetic test for breast cancer. One in four laboratories has stopped performing certain genetic tests because of patent restrictions or excessive royalty costs.[112]

Plus, when a single entity controls all testing of a gene sequence, it might not provide the highest quality test or it may decide, for commercial reasons, not to offer testing for all the known mutations in the gene sequence. According to a study published in 2006, the test Myriad employs to detect breast cancer risk can miss mutations that help cause the disease. Myriad's protocol is to "sequence the exons and flanking regulatory regions of each gene and … to test for 5 specific larger mutations in BRCA1."[113] Because many mutations are inherently undetectable by short-range polymerase chain reaction (PCR)—the process Myriad uses—Myriad's test was unable to detect them.[114]

In the study, researchers sampled DNA from 300 members of high-risk families in which four or more members had been diagnosed with either breast or ovarian cancer.[115] All 300 patients had received negative test results from Myriad.[116] The research team used 6 methods to search DNA for breast cancer gene mutations.[117] The researchers found that 12% of the patients studied carried rearrangements of BRCA1 or BRCA2 that were not included in Myriad's array.[118]

Some believe the number of missed mutations to be even higher.[119] According to Institut Curie geneticist Dr. Dominique Stoppa-Lyonett, the Myriad test may miss up to 20% of the expected BRCA1 mutations.[120] Myriad's patents extend to all methods of diagnosing the risk for

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[112] *See* Mildred K. Cho, Samantha Illangasekare, Meredith A. Weaver, Debra G.B. Leonard, and Jon F. Merz, *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services,* 5 Journal of Molecular Diagnostics 3-8, 3 (2003) ("*Effects of Patents and Licenses"*).

[113] *See* Tom Walsh, Silvia Casadei, Kethryn Hale Coats, Elizabeth Swisher, Sunday Stray, Jake Higgins, Kevin Roach, Jessica Mandell, Ming Lee, Sona Ciernikova, Lenka Foretoca, Pavel Soucek, and Mary-Claire King, *Spectrum of Mutations in BRCA1, BRCA2, CHEK2, and TP53 in Families at High Risk of Breast Cancer,* 295 JAMA 1379-1388 (2006).

[114] *See id.*

[115] *See id.*

[116] *See id.*

[117] *See id.*

[118] *See id.*

[119] *See* Steve Benowitz, *French Challenge to BRCA1 Patent Underlies European Discontent,* 9 Journal of the National Cancer Institute 80-81 (2002).

[120] *See id.*

hereditary breast and ovarian cancers based on comparing an individual's sequence with the company's BRCA sequences.[121] Stoppa-Lyonett claims that the company's patent is too broad because it prohibits alternative techniques, such as DNA combing, from being used to detect mutations.[122]

Although alternative, less expensive methods exist to identify breast cancer gene mutations in a patient's DNA that could identify more mutations, they are not used clinically for genetic testing for breast cancer in countries covered by the Myriad patents.[123] Since Myriad does not make use of the other methods the researchers used, they are effectively cutting off the public from their use entirely. Dr. Mary-Claire King, a senior author of the 2006 study, maintained in an interview that "a fuller testing process would include more than one technology, and competition would enable that to develop."[124]

The example of Myriad's BRCA patents also indicate how the ability to patent genes can produce perverse incentives to frame scientific data in problematic and sometimes very troubling ways. In response to European Patent Office actions limiting the scope of their BRCA patents, Myriad filed and won a more narrow patent to cover genetic testing for particular BRCA2 alleles specifically in women of Ashkenazi Jewish descent. The rationale was that these particular variations occurred at a higher frequency in Ashkenazi Jewish women than in the general population. Yet, since knowledge of these mutations was already generally available, the patent promoted no medical innovation. Its only innovation was to protect a share of the market for such gene tests. Such commercialization of basic genetic information here carries the additional problem of characterizing Jews as a distinct genetic group. Not only is such a characterization scientifically unwarranted, it is affirmatively dangerous given the obvious recent history of the European Holocaust of World War II, which was, in part, premised on a genetic construction of Jews as an "alien" race. As Gert Matthijs, of the Catholic University of Leuven (KUL) in Belgium and a member of the European Society of Human Genetics, said at the time of the Myriad controversy, "we believe there is something fundamentally wrong if one ethnic group can be singled out by patenting…. It means that someone is exploring the limits of what is acceptable legally and ethically."[125] The classic rationale for patenting is that it provides a spur to innovation. The case of Myriad exemplifies a new dynamic that is becoming increasingly common: using patents to exploit race and ethnicity in ways that do not spur the invention of new products, but rather the reinvention or recharacterization of existing products as racial or ethnic.

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[121] *See id.*

[122] *See id.*

[123] *See* Erik Stockstad, *Genetic Screen Misses Mutations in Women at High Risk of Breast Cancer,* 311 Science 1847 (2006).

[124] Andy Pollack, *Flaw Seen in Genetic Test for Cancer Risk,* The New York Times (Mar. 22, 2006), at 20.

[125] "Patent Singles Out Ashkenazi Jewish Women. *New Scientist,* 9 July 2005. http://www.newscientist.com/article/mg18725073.300.

The ability of a patent holder to prevent health care providers from using a patented genetic sequence also denies people crucial medical information. Most drugs only work on a percentage of patients who use them. An asthma inhaler might only work on three of ten people to whom it is prescribed, causing the other seven to suffer symptoms of asthma and pay for an inappropriate drug until the right medication can be found. Genetic testing can help to distinguish those people for whom a drug will work from those people for whom it will not work, but, if the same entity holds the patents on the drugs and the gene sequences, it may prevent use of the gene sequence because the identification of people for whom the drug will not work will limit the market for the drug.

One company has filed for patent protection on a genetic sequence that could be tested to determine the effectiveness of its asthma drug in a prospective patient.[126] The company, however, has said that it will not develop the test - or let anyone else develop the test. While such a test would be crucial to doctors in determining which patients would benefit from the use of the asthma inhaler and which patients would benefit from a different drug or treatment, it would also diminish the market for the drug because a trial use of the asthma inhaler would no longer be needed to know if it would be an effective treatment.

In addition to the negative impact that gene patents have on access to and the quality of genetic testing, the possibility of patenting genes has caused some physicians and university researchers to view patients as treasure troves. Doctors, health care institutions, researchers and hospitals have gone to court to gain ownership of patients' cell lines, tissue, and genes in order to commercialize them, even over the patients' objections. Genetic research is being undertaken on people without their consent as researchers prospect for genes.

b. <u>Gene patents impede research and affect university scientists' conduct.</u>

Given the constricted experimental use exception in the U.S., if a researcher wants to study a patented gene, he or she must either obtain a license or infringe and risk treble damages. In fact, the researcher may have to obtain multiple licenses if patents have been granted on mutations in the gene. Some gene patent holders have stopped research on "their" genes by researchers at top universities, such as Yale, University of California at Los Angeles and the University of Pennsylvania. When a non-profit foundation and the American Neurological Association wanted to finance research to find a cure for a particular genetic disease, researchers were unwilling to undertake the work because of the potential for legal action against them by the holder of the patent. SARS research was slowed down because of concerns about the patents on the genetic sequence of the SARS organism.

The barriers to research caused by patents are even greater in genetics than in other areas of science. In a study of members of the American Association for the Advancement of

[126] *See* Geeta Anand, *Big Drug Makers Try to Postpone Custom Regimens*, Wall Street Journal (Jun. 18, 2001), at B.1.

Science,[127] 35% of scientific researchers had difficulty related to being allowed to use a patented invention. The number was even higher – 76% – for bioscience researchers. As a result, 58% of scientific researchers responded that they delayed their research, 50% responded that they changed their research, and 28% reported abandoning their research.[128]

One study found that 53% of genetics labs have stopped doing research due to concerns about gene patents.[129] Another found that 49% of American Society of Human Genetics members have had to limit their research due to gene patents.[130] Moreover, once a patent is granted in the area of biotechnology, there is a chill on future research using the patented

[127] A random sample of 4,017 of 88,117 eligible members was selected and the answers of 843 who actively engaged in research were analyzed.

[128] *See* Stephen Hansen, Amanda Brewster, Jana Asher & Michael Kisielewski, The Effects of Patenting in the AAAS Scientific Community (American Association for the Advancement of Science 2005), available at http://sippi.aaas.org/survey/AAAS_IP_Survey_Report.pdf .

[129] *See Effects of Patents and Licenses*, *supra*, at 5, 7.

In contrast, a September 2006 article by some leading analysts cited the results of a study conducted in the fall of 2004 and published in 2005 that asked "academic biomedical researchers in the United States" to self-report instances when they had delayed or abandoned a project because of a gene patent. *See* Timothy Caulfield, Robert M. Cook-Deegan, F. Scott Kieff, and John P. Walsh , *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 Nature Biotechnology 1091-1094 (2006) ("*Evidence and Anecdotes*") (citing *View from the Bench*, *supra*, at 2002). According to the study "only 1%" of academic researchers reported that a patent had caused them to delay a project, and "none" reported abandoning a project because of a patent. *Id.* When examined and put into context, this statistic does not support the proposition that gene patents are not slowing the development of and access to genetic technology and thus pose no significant concerns. First, as noted above, the same study noted that these relatively low rates of adverse effects relied on the willingness (after the *Madey* decision) of academic researchers to infringe or ignore the patents. Second, the investigators did not necessarily ask those likely to be most affected by gene patents. Over 75% of those polled were academics who reported doing basic research. *See* John Walsh, Charlene Cho, and Wesley Cohen, Report to the National Academy of Sciences' Committee on Intellectual Property Rights in Genomic and Protein-Related Inventions, Patents, Material Transfers, and Access to Research Inputs in Biomedical Research at 10 (Sep. 20, 2005). With a majority of the academic researchers doing basic research, it is expected that few patent holders would attempt to enforce their rights against the respondents in ways that would cause them to abandon or delay a project.

Genetic diagnostics, unlike most other tools of DNA-based science, are widely-marketable to the public. And while there is a real effect by patents on researchers working in the area of diagnostic tool development, few of the researchers in the study above worked in that field. Diagnostic labs have reported being affected by patents with at least 25% of diagnostic labs having "abandoned one or more genetics test as a result of patents" by 2001. *Evidence and Anecdotes*, *supra*, at 1092 (citing *Effects of Patents and Licenses* at 5). Caulfield's group has acknowledged the credibility of these studies and the conclusion that gene patents have had a negative impact on researchers who use genetics to develop diagnostic tools. *See Evidence and Anecdotes*, *supra*, at 1091-92 (citing *Effects of Patents and Licenses*, *supra*, and Jon F. Merz, Antigone G. Kriss, Debra G.B. Leonard, and Mildred K. Cho, *Diagnostic testing fails the test*, 415 Nature 577–579 (2002) ("*Diagnostic testing*")). The implication of such impacts is to adversely affect access to and development of diagnostic tools. And it is to be expected that such effects will also develop when patent holders exercise their rights in regard to other widely marketable products that emerge that are protected by gene patents.

[130] *See* Issac Rabino, *How Human Geneticists in U.S. View Commercialization of the Human Genome Project*, 29 Nature Genetics 15-16 (2001).

information, including a statistically significant decline in scientific publications using the patented information.[131]

Gene patents also impede the application of the scientific method of hypothesis generation, discovery and replication. In one survey, half of gene patent holders said they would require a license for researchers to study the prevalence of mutations in the patented gene in the population.[132] Even more troubling is the finding that 28% of geneticists surveyed reported that they were unable to duplicate published research because other academic scientists refused to share information, data, or materials.[133] This goes to the heart of science, which is based on confirmation of scientific data through replication.

Researchers with commercial interests – who are now the majority of academic genetics researchers – protect their interests in ways that are fundamentally changing the nature of science. They keep information confidential that they used to readily share, since, if the invention has been disclosed in a publication for more than a year before the patent application is filed, a patent will not be granted.[134] For example, the scientific report of the discovery of the hemachromatosis gene was not submitted for publication until over a year after the patent on the gene was filed.[135] During that time, people with the disease could have been diagnosed and cured.

David Blumenthal and his colleagues at the Harvard Institute of Health Policy found that one of every five professors in the life sciences had delayed publication of research results for at least half a year in order to protect financial interests in various ways.[136] Those scientists who directly engaged in the commercialization of their research were three times more likely to delay

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[131] Gene patents have increased the cost of building on this particular source of knowledge. A study evaluated the existence of the anti-commons effect on scientific knowledge by examining 340 peer-reviewed scientific articles appearing between 1997 and 1999 in Nature Biotechnology. *See* Fiona Murray & Scott Stern, Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis, Prepared for the NBER Academic Science and Entrepreneurship Conference (June 2005). The study looked at patent-paper pairs—scientific articles that have corresponding patents on the knowledge covered in the article—and compared them to scientific articles that do not have corresponding life science patents. *See id.* The authors reported that "there is robust evidence for a quantitatively modest but statistically significant anti-commons effect; across different specifications, the article citation rate declines by 9 to 17% after a patent grant." *Id.* The authors concluded that intellectual property rights have had a measurable impact on the diffusion of scientific knowledge. *See id.* at 31.

[132] *See* Timothy Caulfield, E. Richard Gold, and Mildred K. Cho, *Patenting Human Genetic Material: Refocusing the Debate*, 1 Nature Reviews Genetics 227-231, 230 (2000).

[133] *See* Eric G. Campbell, Brian R. Clarridge, Manjusha Gokhale, Lauren Birenbaum, Stephen Hilgartner, Neil A. Holtzman, and David Blumenthal, *Data Withholding in Academic Genetics*, 287 JAMA 473, 478 (2002).

[134] *See* 35 U.S.C. §102(b).

[135] *See Diagnostic Testing*, *supra*, at 579.

[136] *See* David Blumenthal, Eric G. Campbell, Melissa S. Anderson, Nancyanne Causino, and Karen S. Louis, *Withholding Research Results in Academic Life Sciences. Evidence from a National Survey of Faculty*, 277 JAMA 1224 (1997).

publication and twice as likely to refuse to share information than those doing basic work. Among the life scientists, geneticists were the most likely to withhold data.

Much of this counterproductive behavior has been spurred by the possibility of patenting genes. In 2006, Blumenthal and colleagues reported on their survey of life scientists at the 100 most research-intensive universities in the U.S.: 44% of geneticists and 32% of other life scientists reported that they had withheld data, either in verbal exchanges or as part of the publishing process. The research being published in the literature was incomplete – 16% had withheld information in their manuscripts to protect their lead, 12% to protect trade secrets, 6% to allow time for patents, and 2% to protect commercial value.[137]

The training of the next generation of scientists also is affected by the potential for patent rights and its affect on publication. In a survey of over 1000 doctoral students and post-docs in life sciences, 49% said withholding of information had a negative effect on the rate of discovery in their laboratory and 33% felt it interfered with their education.[138]

c. <u>Patents on genes are not like patents on drugs.</u>

Some proponents of gene patents argue that the rationales for patent protection for drugs support the patenting of genes. But genes are inherently different than drugs. The main function of genes is as encoded information.[139]

There are fewer downsides to granting a patent on a drug or a medical device than granting a patent on a gene. The nature of genes makes them impossible to invent around.[140] In the case of drugs and pharmaceuticals, the disclosure of a new drug in a patent may motivate other researchers to find chemical analogs that may work better or in slightly different ways.[141]

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[137] *See* David Blumenthal, Eric Campbell, Manjusha Gokhale, Recai Yucel, Brian Clarridge, Stephen Hilgartner, and Neil Holtzman, *Data Withholding in Genetics and the Other Life Sciences: Prevalences and Predictors*, 81 Academic Medicine 137, 140-142 (2006).

[138] *See* Christine Vogeli, Recai Yucel, Eran Bendavid, Lisa Jones, Melissa Anderson, Karen S. Louis, and Eric Campbell, *Data Withholding and the Next Generation of Scientists: Results of a National Survey*, 81 Academic Medicine 128, 131-132 (2006).

[139] *See, e.g.*, Comments of Rochelle Dreyfuss in Transcript, The Brookings Institution, The Limits of Patents in an Intangible Economy (Jan. 14, 2009), at 92 ("these products are not valuable for their physicality, for say their chemical reactivity in the body, what they're valuable for is the information that they convey."), *at* http://www.brookings.edu/~/media/Files/events/2009/0114_patents/0114_patents_transcript.pdf; The True Cost of Gene Patents: The Economic and Social Consequences of Patenting Genes and Living Organisms Patents – A Greenpeace Document, at 2, *at* http://weblog.greenpeace.org/ge/archives/1Study_True_Costs_Gene_Patents.pdf.

[140] *See* Gert Matthijs, and Dicky Halley, *European-wide Opposition Against the Breast Cancer Gene Patents*, 10 European Journal of Human Genetics 783, 784 (2002) ("*European-wide Opposition*").

[141] *See* Sarah Boseley, *Scientists On A Mission To Bring Cheap Drugs To The World's Poorest Countries*, The Guardian (Jan. 2, 2007), *available at* http://www.guardian.co.uk/medicine/story/0,,1981152,00.html.

Patented genes invite no such innovation. A patent for a particular gene sequence patents the *sequence itself*, and there is therefore no way to invent around that discovery.[142]

The discovery of genes does not require the same incentives as drug development. Molecular biologists were attempting to identify genes long before the U.S. Patent and Trademark Office adopted the position that genes could be patented. Also, the discovery of genes has been undertaken with vast quantities of public funds, as opposed to the development of drugs, which is undertaken primarily with private funds (for which investors expect a commercial return).

Moreover, there are no expensive clinical trials when a gene is discovered and knowledge about the sequence of the gene is used to identify whether a particular patient has a mutation in that gene. In some cases, testing has begun almost immediately after a disease gene has been identified. Because the FDA does not regulate the clinical services of genetic tests (as opposed to the sale of genetic diagnostic kits or gene therapies), there is no costly FDA approval process, as there would be for drugs. Thus, even if there were a need to provide financial incentives to incent such inventions, there is much less of a need to financially compensate a gene-discoverer than the developer of a drug, who must take it through costly clinical trials with only a small number of drugs actually becoming commercially-viable products.

Gene patents also do not appear to be necessary to encourage technology transfer in the move from gene discovery to the availability of a genetic diagnostic test. As soon as information about the discovery of the hemachromatosis gene was published, laboratories began testing for mutations in the gene. After a patent on the gene was granted seventeen months later, 30% of the 119 U.S. laboratories surveyed reported discontinuing or not developing a genetic test for the disease. The patent holder was asking for an up-front fee of $25,000 from academic laboratories and as much as $250,000 from commercial laboratories, plus a fee of $20 per test.[143] The patent interfered with clinical adoption of the test and potentially compromised the quality of testing by limiting the development of higher quality or lower cost alternative testing methods.

In conclusion, it bears repeating that prohibiting gene patents and patents on medical discoveries will not remove the existing incentives for investment, invention, and disclosure, and alternatives to patents for any perceived need for such incentives may be preferable. First, many related aspects of these discoveries may lead to patentable inventions. Thus, in the *Laboratory Corporation* case, the natural phenomenon discovery was a fortuitous consequence of the efforts to test a newly invented gas chromotography-mass spectrometry machine for assaying the relevant amino acid. That invention was undoubtedly patentable, and provided all the incentives needed for the invention and the fortuitous discovery; Laboratory Corporation took a license from the patent holder to pay 27.5% of its revenues on that test (which it used for many years

[142] *See European-wide Opposition , supra,* at 784.

[143] *See Diagnostic Testing, supra,* at 578.

before simultaneously offering a new unpatented assay method).[144] Of greater importance, such innovations are produced because they are needed, and incentives already exist for investment, invention, and dissemination. Finally, much of the investment for such inventions comes from governmental funding. To the extent that additional funding is needed for such important scientific research with such widespread public benefits, additional government funding from tax revenues would be a preferable and cheaper solution than exclusive rights with market and innovation harms. This has been widely recognized in the pharmaceutical context, where estimates are that increased prices from patent exclusivity have cost the public eight or nine dollars for every dollar of research and development expenditure incented (including funding the high costs of clinical trials).[145]

[144] *See* Lab. Corp. of America Holdings v. Metabolite Labs., Inc., 126 S.Ct. at 2923.

[145] *See, e.g.*, James Love & Tim Hubbard, *The Big Idea*, 82 Chicago-Kent L. Rev. 1520, 1523 (2007).