MYRIAD & PROMETHEUS, LAWS & PRODUCTS OF NATURE: ARE THE COURTS CONSIDERING AN ECONOMIC NON-STATUTORY SUBJECT MATTER EXCLUSION?

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I. INTRODUCTION

Over the past five years, the courts have outdone themselves in establishing a tortured path to patentability for new diagnostic and therapeutic procedures. In *Association for Molecular Pathology v. U.S. Patent & Trademark Office* (hereafter "*Myriad*"),[1] the U.S. District Court for the Southern District of New York evoked the "product of nature" judicial bar in invalidating patents for a genetic test before being overturned by the Federal Circuit on appeal.[2] Subsequently, the Supreme Court in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*[3] rejected patents for a method of treating autoimmune diseases holding that it was an un-patentable "law of nature."[4] Then, on March 26, 2012, the Supreme Court vacated the Federal Circuit's decision in *Myriad* and remanded for further consideration in light of *Prometheus*.[5] For its part, the Federal Circuit, in an August 2012 ruling on the Supreme Court's remand, left its prior decision largely unchanged; allowing patents for isolated gene molecules as patentable subject matter,[6] but finding the method claims—with one exception—to be patent-ineligible for reading only to abstract mental processes.[7]

The "law of nature," "product of nature," and other non-statutory bars to patentable subject matter under 35 U.S.C. § 101 go back more than 150 years.[8] The current interpretation is set out, very influentially, in *Diamond v.*

1 702 F. Supp. 2d 181 (S.D.N.Y. 2010), *rev'd*, 653 F.3d 1329 (Fed. Cir. 2011), *vacated*, 132 S. Ct. 1794 (2012).

2 *Id.* at 227.

3 132 S. Ct. 1289 (2012).

4 *Id.* at 1294. The *Prometheus* case also consisted of a grant for summary judgment of non-patentability in the district court that was reversed by the Federal Circuit. *Id.* at 1296.

5 Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794, 1794 (2012).

6 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 689 F.3d 1303, 1333 (Fed. Cir. 2012) ("[*Prometheus*] does not change that result.").

7 *Id.* at 1333–34; U.S. Patent No. 5,747,282 col.156 l.15–26 (filed June 7, 1995).

8 Le Roy v. Tatham, 63 U.S. (22 How.) 132, 137 (1859); Corning v. Burden, 56 U.S. (15 How.) 252, 268 (1853).

Chakrabarty.[9] In this article, attention is focused particularly on the "law of nature" rather than the "product of nature" bar, as the former is the basis for the rejection of the *Prometheus* patents and the order to reassess the *Myriad* decision in that context.[10]

The depth of issues involved in these cases should not be underestimated. *Myriad* was organized by the American Civil Liberties Union, which sees the consequences of gene patents not solely as a question of patent law, but of the First Amendment's guarantee of free speech.[11]

One plaintiff in the case is the Public Patent Foundation, a not-for-profit legal services organization with a goal of protecting freedom in the patent system.[12] According to their mission statement:

> The best way to do that is to ensure that all of the interests affected by the patent system, including the public interest in freedom from unjustified restraints, are adequately represented. For example, if there are substantial questions about the validity of a patent having a significant negative impact on society, such as by limiting access, perverting markets or thwarting technological development, then we must have those questions raised and addressed.[13]

More directly, according to their patent lawyer: "The intention [of bringing *Myriad*] is to take down patents on human genes."[14]

The *Prometheus* decision has the potential to change fundamentally the analysis of what constitutes patent eligible subject matter under § 101, with particularly intense effects in the fields of diagnostics and personalized medicine.[15] It may also have profound effects on the biotechnology industry, which has relied heavily on patents claiming isolated genes and shorter DNA sequences. Leaders in the Biotechnology industry have expressed concerns as well:

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9 447 U.S. 303, 309 (1980); s*ee infra* Section II.A.

10 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1294 (2012); *Ass'n for Molecular Pathology*, 132 S.Ct. at 1794.

11 John Schwartz, *Cancer Patients Challenge the Patenting of a Gene*, NY TIMES (May 12, 2009), http://www.nytimes.com/2009/05/13/health/13patent.html.

12 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181, 183 (S.D.N.Y. 2010).

13 *About PUBPAT*, PUBPAT.ORG, http://www.pubpat.org/About.htm (last visited Jan. 10, 2013).

14 *Patent Litigation Weekly: PubPat and ACLU Aim to Take Down Gene Patents*, THE PRIOR ART (May 14, 2009), http://thepriorart.typepad.com/the_prior_art/2009/05/association-for-molecular-pathology-v-uspto.html.

15 *See Prometheus Labs.*, 132 S. Ct. at 1294.

> • "Paul Yasger, head of IP for Abbott Laboratories, stated that the *Prometheus* decision is not good for business because of the uncertainty it creates."[16]
>
> • "Phil Johnson, Chief Intellectual Property Counsel at Johnson & Johnson, pointed out that 'capital is hard to come by these days and people are reluctant.' Johnson and Johnson can invest money in R&D projects involving shampoo instead of biomarker research."[17]
>
> • "Michael Walker, Chief Intellectual Property Counsel at Dupont, pointed out that these decisions have an impact beyond personalized medicine. 60 percent % of Dupont's R&D is in Ag and Food research and industrial biosciences such as biofuels. . . . [B]usinesses have large settled business expectations in this technology and they look at *Prometheus* and *Myriad* and wonder if their technologies are just natural phenomena."[18]

Huys et al. describes the issue for industry in terms of risk: "The consequence of this high level of legal uncertainty is that either enormous risks are taken . . . or much time and energy goes into establishing patent landscapes and freedom-to-operate . . . ."[19] The Federal Trade Commission, in a 2003 hearing on patenting in the pharmaceutical and biotechnology industries, determined that "strong patent protection is essential to innovation."[20]

Considering the links among these cases, beyond the particulars of the current § 101 subject matter bars, the courts' concern "seems to be that a patent should not inhibit others from making use of natural laws"[21] by preempting subsequent research and use. In searching for a conceptual basis for this position across the several cases, I develop here the hypothesis that the courts, and the Supreme Court in particular, are in the process of evaluating a new requirement for patentable subject matter based on economics. Specifically, the courts appear to be considering as an additional patentable subject matter requirement, a quid pro quo for a patent, that a patent benefit society in proportion to the pri-

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16 Roy Zwahlen, *Mayo v. Prometheus: Thought Leaders Express Concern and Evaluate the Impact*, PATENTLY BIOTECHNOW (May 21, 2012), http://www.biotech-now.org/public-policy/patently-biotech/2012/05/mayo-v-prometheus-thought-leaders-express-concern-evaluate-business-impact-and-discuss-the-future.

17 *Id.*

18 *Id.*

19 Isabelle Huys et al., *Legal Uncertainty in the Area of Genetic Diagnostic Testing*, 27 NATURE BIOTECHNOLOGY 903, 909 (2009).

20 FED. TRADE COMM'N, TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW AND POLICY ch. 3, at 1 (2003).

21 Steven Seidenberg, *New Laws of Nature Law: Ruling Questions Scientific Patents*, A.B.A. J. (July 1, 2012), http://www.abajournal.com/magazine/article/new_laws_of_nature_law_ruling_questions_scientific_patents.

vate value it generates. This suggestion of an explicit economic public/private tradeoff arises particularly with gene-related therapies because of the belief that patents over human genes can block subsequent research to the detriment of public well-being.[22] In *Prometheus*, the concern is stated as: "[a]nd so there is a danger that the grant of patents that tie up their use will inhibit future innovation premised upon them . . . ."[23] Whether fields other than genes and gene therapy may be included in a possible new economic patentable subject matter bar remains to be seen.

Using my economic judicial patentable subject matter requirement theory, I proceed here by showing that such a bar would be ill founded; there is no basis for such a requirement in the statutes or case law.[24] Further, economic theory and empirical analysis do not elicit evidence of widespread problems with blocking gene patents as is implied in these recent court decisions.[25] And even the scientific understanding that a patent over a gene will prevent subsequent research is not sustained on the principals and available evidence.[26] If there is a reasonable concern over patenting of human genes in particular (the National Academy of Sciences in 2005 estimated about 20 percent of the genes in the human genome are patented[27]) then that concern is better addressed by a more careful attention to the initial patent grants, as well as an experimental use exemption which can selectively address rare problems rather than the blunt instrument of a non-statutory subject matter bar.[28]

This paper is structured as follows. I begin with a consideration of judicial exclusions to patentable subject matter, with emphasis on the laws and products of nature exclusions and the relevant case history. Next I review the *Myriad* and *Prometheus* case histories followed by an assessment of the legal, economic and scientific evidence for the existence of blocking gene patents. The conclusion in the final section is clear: there is no empirical basis—legal, economic, or scientific—for an additional non-statutory patentable subject matter bar, but the potential does exist for blocking patents which should be addressed on an as needed basis.

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22 *See infra* Section IV.D.

23 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1301 (2012).

24 *See* 35 U.S.C. § 101 (2006).

25 *See infra* Section IV.C.

26 *See infra* Section IV.D.

27 NAT'L RESEARCH COUNCIL, REAPING THE BENEFITS OF GENOMIC AND PROTEOMIC RESEARCH: INTELLECTUAL PROPERTY RIGHTS, INNOVATION, AND PUBLIC HEALTH 102 (2006).

28 *See infra* Section V.

II. JUDICIAL BARS TO PATENT ELIGIBLE SUBJECT MATTER

Before we can analyze whether the courts are imposing a new subject matter bar, it is useful to examine the currently established judicially-created bars. In this section, emphasis is placed on cases that apply "law of nature" subject matter bars, rather than those applying "products of nature" bars, as *Prometheus* is decided on a "law of nature" basis.[29] Leading "law of nature" cases, as identified in *Prometheus*[30] and *Myriad*,[31] include: *O'Reilly v. Morse*,[32] *Gottschalk v. Benson*,[33] *Parker v. Flook*,[34] and *Diamond v. Diehr*.[35] This section will review these cases, as well as other landmark "law of nature" decisions. I am not concerned here with whether the invention in *Prometheus* as claimed indeed constitutes a "process" under *Bilski v. Kappos*,[36] as that is not the relevant dimension of the case for my analysis.

A. Chakrabarty

As Justice Breyer noted in *Prometheus*, "[t]he Court has long held that [35 U.S.C. § 101] contains an important explicit exception. '[L]aws of nature, natural phenomena, and abstract ideas' are not patentable."[37] In its most recent and detailed form, the judicial patentable subject matter bar is set out in *Chakrabarty*:

> The Committee Reports accompanying the 1952 [Patent] Act inform us that Congress intended statutory subject matter to "include anything under the sun that is made by man." This is not to suggest that § 101 has no limits or that it

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29 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1294 (2012); *see infra* Section III.B. For more detail on the product of nature bar, see generally Daniel J. Klein, *The Integrity of Section 101: A "New and Useful" Test for Patentable Subject Matter*, 93 J. PAT. & TRADEMARK OFF. SOC'Y 287 (2011) and W. Lesser, *Nature Or Nurture: Is There A Case Basis For A Judicially Created 'Product Of Nature' Exclusion? Are Genes Somehow Different?*, 11 J. MARSHALL REV. INTELL. PROP. L. 318 (2011).

30 *Prometheus Labs.*, 132 S. Ct. at 1293.

31 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181, 218, 219, 226 (S.D.N.Y. 2010).

32 56 U.S. 62 (1854).

33 409 U.S. 63 (1972).

34 437 U.S. 584 (1978).

35 450 U.S. 175 (1985).

36 130 S. Ct. 3218, 3226–27 (2010).

37 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1293 (2012).

> embraces every discovery. *The laws of nature, physical phenomena, and abstract ideas have been held not patentable*.[38]

Chakrabarty also gives three additional clarifications on what is and is not patentable subject matter, as can be found in the Manual of Patent Examining Procedure ("MPEP"):

> [A] A "nonnaturally occurring manufacture or composition of matter—a product of human ingenuity—having a distinctive name, character, [and] use" is patentable subject matter.
>
> [B] "[A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of . . . nature, free to all men and reserved exclusively to none.'"
>
> [C] "[T]he production of articles for use from raw materials prepared by giving to these materials new forms, qualities, properties, or combinations whether by hand labor or by machinery" is a "manufacture" under 35 U.S.C. 101.[39]

B. Morse

The *Morse* case, as relates to the issues at hand, applies to claim eight of Morse's 1840 (re-issued in 1848) patent, which read:

> I do not propose to limit myself to the specific machinery or parts of machinery described in the foregoing specification and claims; the essence of my invention being the use of the motive power of the electric or galvanic current, which I call electro-magnetism, however developed for marking or printing intelligible characters, signs, or letters, at any distances, being a new application of that power of which I claim to be the first inventor or discoverer.[40]

The Supreme Court noted:

> It is impossible to misunderstand the extent of this claim. He claims the exclusive right to every improvement where the motive power is the electric or galvanic current, and the result is the marking or printing intelligible characters, signs, or letters at a distance. If this claim can be maintained, it matters not by what process or machinery the result is accomplished. . . . But yet if it is covered by this patent the inventor could not use it, nor the public have the benefit of it without the permission of this patentee.[41]

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38 Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) (emphasis added).

39 MPEP § 2105 (8th ed. Rev. 9, Aug. 2012) (emphasis omitted).

40 O'Reilly v. Morse, 56 U.S. 62, 112 (1854).

41 *Id.* at 112–13.

The Court went on to conclude:

> Whoever discovers that a certain useful result will be produced, in any art, machine, manufacture, or composition of matter, by the use of certain means, is entitled to a patent for it; provided he specifies the means he uses in a manner so full and exact, that any one skilled in the science to which it appertains, can, by using the means he specifies, without any addition to, or subtraction from them, produce precisely the result he describes. And if this cannot be done by the means he describes, the patent is void. And if it can be done, then the patent confers on him the exclusive right to use the means he specifies to produce the result or effect he describes, and nothing more. . . . In either case he must describe the manner and process as above mentioned, and the end it accomplishes.[42]

On this basis, claim eight was declared "illegal and void."[43]

C. Benson

In *Benson*, the applicants claimed:

> a method for converting binary-coded decimal (BCD) numerals into pure binary numerals. The claims were not limited to any particular art or technology, to any particular apparatus or machinery, or to any particular end use. They purported to cover any use of the claimed method in a general-purpose digital computer of any type.[44]

In rejecting the claims the court stated:

> Here the "process" claim is so abstract and sweeping as to cover both known and unknown uses of the [binary-coded decimal] to pure binary conversion. . . . It is conceded that one may not patent an idea. But in practical effect that would be the result if the formula for converting [binary-coded decimal] numerals to pure binary numerals were patented in this case. The mathematical formula involved here has no substantial practical application except in connection with a digital computer, which means that if the judgment below is affirmed, the patent would wholly preempt the mathematical formula and in practical effect would be a patent on the algorithm itself.[45]

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42 *Id.* at 119.

43 *Id.* at 120.

44 Gottschalk v. Benson, 409 U.S. 63, 64 (1972).

45 *Id.* at 68, 71–72.

D. In re Freeman

In *In re Freeman*,[46] the Court of Customs and Patent Appeals set out a two-step analysis for determining whether a claim preempts non-statutory subject matter as a whole in light of *Benson*.[47]

> First, it must be determined whether the claim directly or indirectly recites an "algorithm" in the *Benson* sense of that term, for a claim which fails even to recite an algorithm clearly cannot wholly preempt an algorithm. Second, the claim must be further analyzed to ascertain whether in its entirety it wholly preempts that algorithm.[48]

E. Flook

In *Flook*, the inventor applied for a patent on an alarm system for use during a continuously monitored catalytic conversion process for hydrocarbons during which the temperature, pressure or flow rates may exceed prescribed limits indicating inefficiency, even possible danger.[49] Under some conditions, the prescribed limits, or "alarm limits," needed to be reset periodically.[50] The patent application described a method of updating those alarm limits.[51] The method basically consisted of three steps: (a) measuring the present value of a process variable such as temperature; (b) using an algorithm to calculate an updated alarm-limit value; and (c) re-setting the actual alarm limit to the updated value.[52] The difference between the conventional methods of changing alarm limits and that described in *Flook* is in the second step, the mathematical algorithm or formula.[53] The application did not explain how some of the parameters in the algorithm, components such as the safety margin, updating interval, or the weighing factors, are set.[54] All that it revealed was the operator inputs such as the process variables.[55] It noted that the calculations are best evaluated using a computer.[56]

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46 573 F.2d 1237 (C.C.P.A. 1978).

47 *Id.* at 1245.

48 *Id.*

49 Parker v. Flook, 437 U.S. 584, 585 (1978).

50 *Id.*

51 *Id.*

52 *Id.*

53 *Id.* at 585–86.

54 *Id.* at 586.

55 *Flook*, 437 U.S. at 586.

56 *Id.*

Further, the claims in *Flook* cover any use of the algorithm for updating the value of an alarm limit on any process variable involved in a process comprising the catalytic chemical conversion of hydrocarbons.[57] "Since there are numerous processes of that kind in the petrochemical and oil-refining industries, the claims cover a broad range of potential uses of the method, [but] not every conceivable application of the formula."[58] In response to the applicant's pointing this out, the Court noted that limiting the application to a particular technological environment does not circumvent the non-statutory subject matter bar.[59]

However, referencing *Benson* and the holding that a formula *per se* is like a law of nature and hence unpatentable under § 101, the Court did clarify that "a process is not unpatentable simply because it contains a law of nature or a mathematical algorithm. . . . The process itself, not merely the mathematical algorithm, must be new and useful. Indeed, the novelty of the mathematical algorithm is not a determining factor at all."[60] The proper procedure for evaluating a patent claim incorporating a mathematical formula for § 101 purposes is to assume the formula is within the prior art and to determine if there are other inventive concepts in the application.[61]

F. Diehr

The *Diehr* patent differs from the *Flook* patent in that it was found valid.[62] The invention enhances the "process for molding raw, uncured . . . rubber into cured precision products."[63] Achieving a perfect cure necessitates precise measures/controls of the thickness of the article, temperature and time of the molding process.[64] The well-known "Arrhenius Equation" specifies the optimal time to open the molding press, but its effective use was hampered by an inability to measure precisely the press temperature, which at times lead to products that were over or under-cured.[65]

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57 *Id.*

58 *Id.*

59 *Id.* at 590, 595.

60 *Id.* at 590–91(citing Gottschalk v. Benson, 409 U.S. 63, 67 (1972)).

61 *Flook*, 437 U.S. at 594 ("[T]he discovery of such a phenomenon cannot support a patent unless there is some other inventive concept in its application.").

62 Diamond v. Diehr, 450 U.S. 175, 192–93 (1985).

63 *Id.* at 177.

64 *Id.*

65 *Id.* at 177–78.

The patent claimed a method of continuously monitoring the inside mold temperature and feeding that and other relevant values to a computer, which, by means of the before-mentioned formula, signaled when the press should be opened.[66] In contrast to *Flook*, the majority determined that respondents "do not seek to patent a mathematical formula. Instead, they seek patent protection for a process of curing synthetic rubber."[67] Thus, the patent was upheld as not claiming a law of nature, but a process which partially *utilizes* a law of nature—the algorithm.[68]

G. Bilski

Bilski relates to a business method patent, particularly a method for minimizing price risk known as hedging.[69] The case is typically cited as holding that the "machine-or-transformation" test is not the sole test for what constitutes patentable subject matter under § 101.[70] For the present study though we are concerned only with the Court's broader pronouncements on patentable subject matter: "While these exceptions [laws of nature, physical phenomena, and abstract ideas] are not required by the statutory text, they are consistent with the notion that a patentable process must be 'new and useful.'"[71]

Based on this decision, the PTO issued a memo setting out *Bilski* "Interim Guidance" providing "factors to consider in determining whether a claim is directed to an abstract idea and is therefore not patent-eligible under 35 U.S.C. § 101."[72] Under this Guidance, "factors that weigh in favor of patent-eligibility satisfy the criteria of the machine-or-transformation test or provide evidence that the abstract idea has been practically applied . . . ."[73] Examiners are also advised to "avoid treating an application solely on the basis of patent-eligibility under 35 U.S.C. § 101 except in the most extreme cases."[74]

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66 *Id.* at 177–79.

67 *Id.* at 187.

68 *Diehr*, 450 U.S. at 192–93.

69 Bilski v. Kappos, 130 S. Ct. 3218, 3223 (2010).

70 *Id.* at 3221.

71 *Id.* at 3225.

72 Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of Bilski v. Kappos, 75 Fed. Reg. 43923 (July 27, 2010).

73 *Id.* at 43927.

74 *Id.* at 43923–24.

H. Discussion

Even from this brief case review, there are evident gaps and inconsistencies with the several courts' treatment of judicially-defined unpatentable subject matter, including laws of nature. Beginning with the *Chakrabarty* decision and its clarifications of what is and is not patent eligible,[75] as Klein notes, the pronouncement "suggests the existence [of] some inherent meaning of the categorical labels."[76] But that of course does not exist. As Justice Frankfurter pointed out forcefully in a concurring opinion in *Funk Bros. Seed Co. v. Kalo Inoculant Co.*,[77] a leading product of nature case: "It only confuses the issue, however, to introduce such terms as 'the work of nature' and the 'laws of nature'. For these are vague and malleable terms infected with too much ambiguity and equivocation."[78]

There is evident confusion even over which facts to consider. *Flook* and *Diehr*, as is discussed above, reached opposing conclusions regarding patentable subject matter because *Diehr* applied not to a formula, but a process for curing synthetic rubber.[79] But as Justice Stevens wrote in a sharply worded dissent in *Diehr*: "[the applicant's] method of updating the curing time calculation is strikingly reminiscent of the method of updating alarm limits that Dale Flook sought to patent."[80] A review of the Diehr patent indeed confirms Justice Stevens' point. "[I]f we treat the program as though it were a familiar part of the prior art—as well-established precedent requires—it is absolutely clear that their application contains no claim of patentable invention."[81] The Diehr and Flook patent applications would seem to differ by the Diehr method of "constantly determining the temperature (Z) of the mold at a location closely adjacent to the mold cavity in the press during molding."[82] However, the patent description refers to the temperature sensing being done by "[t]hermocouples, or other temperature-detecting devices" accessed separately from the claimed invention.[83]

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75 Diamond v. Chakrabarty, 447 U.S. 303, 308, 309–10 (1980).

76 Klein, *supra* note 29, at 300.

77 333 U.S. 127 (1948).

78 *Id.* at 134–35.

79 Diamond v. Diehr, 450 U.S. 175, 187 (1985).

80 *Id.* at 209 (Stevens, J., dissenting).

81 *Id.* at 216 (Stevens, J., dissenting).

82 U.S. Patent No. 4,344,142 col.7 l.1–33 (filed Aug. 6, 1975); *see also Diehr*, 450 U.S. at 207 (Stevens, J., dissenting) ("[T]here is not a word in the patent application that suggests that there is anything unusual about the temperature-reading devices used in this process . . . .").

83 U.S. Patent No. 4,344,142 col.3 l.61–62 (filed Aug. 6, 1975).

The Diehr "invention" then consists of a "standard digital computer," the Arrhenius Equation (which is acknowledged to be in the public domain[84]), the just-mentioned thermocouples, and finally a computer activat[ed] opening device.[85] Therefore, as Justice Stevens noted, there is no invention under the *Flook* test.[86]

Clearly and understandably, the courts make ongoing errors, including technical ones like this. However, by emphasizing *Flook* and *Diehr* in *Prometheus* with no evidence of a careful reassessment, the Supreme Court has doubled down on previous errors with the result of imperiling the future of the therapeutics sector over a "vague and malleable" phrase like a "law of nature."[87] In *Flook*, the Court warned, "[a specific application of a principle] would make the determination of patentable subject matter depend simply on the draftsman's art and would ill serve the principles underlying the prohibition against patents for 'ideas' or phenomena of nature."[88] But that is exactly what has been done. Yet the Court in *Prometheus* has gone far further by hinting at a new prohibition for patents.[89] Prior to examining that issue though, it is necessary to consider the *Myriad* and *Prometheus* decisions in all their complexity.

III. THE *MYRIAD* AND *PROMETHEUS* DECISIONS

A. Myriad

The Association for Molecular Pathology, a not-for-profit scientific society, along with eighteen additional plaintiffs representing other not-for-profit groups, medical societies and individual doctors and patients, sued the U.S. Patent and Trademark Office and sought to invalidate fifteen claims in seven patents owned by Myriad Genetics and the University of Utah Research Foundation.[90] The claims related to two genes, BRCA1 and BRCA2 (Breast Cancer Susceptibility Genes 1 and 2) and alleles (variants/mutations) thereof, associated

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84 *Diehr*, 450 U.S. at 209 (Stevens, J., dissenting) (explaining that the Arrhenius Equation is "pursuant to a well-known mathematical formula").

85 U.S. Patent No. 4,344,142 col. 3 l.16, 61 (filed Aug. 6, 1975).

86 *Diehr*, 450 U.S. at 216 (Stevens, J., dissenting).

87 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1298 (2012) ("The cases most directly on point are *Diehr* and *Flook* . . ."); *see also* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 135 (1948).

88 Parker v. Flook, 437 U.S. 584, 593 (1978).

89 *See infra* Section IV.A.

90 The defendants' motion to dismiss the complaint was denied in 2009. Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 669 F. Supp. 2d 365, 370 (S.D.N.Y. 2009).

with a heightened susceptibility to a form of breast cancer and, less commonly, ovarian cancer.[91]

The initial indication of the existence of a breast cancer linked gene appeared in a landmark paper by Dr. Mary-Claire King in 1990, but the gene was un-sequenced and identified only as being in the "region of chromosome 17."[92] A subsequent founder of Myriad Genetics, Dr. Skolnick, took an interest and provided the insight of identifying and linking the Utah Mormon Genealogy with the Utah Cancer Registry to provide the large data set required for a statistical program for gene mapping.[93] The Registry allowed the identification of communities with a high prevalence for certain kinds of breast cancer, while the careful genealogical records maintained by the Mormons provided intergenerational linkages for following the transmission of susceptibility.[94] Even so, considerable effort and ingenuity was required to pinpoint the implicated gene or genes.[95] Subsequently, with the work of Dr. King and the National Institutes of Health, and utilizing venture capital funding, the BRCA1 and BRCA2 genes were sequenced in the 1990s.[96]

The plaintiffs in *Myriad* contended that the granted claims encompassed ineligible subject matter and hence violated the Patent Act, and the First and Fourteenth Amendments of the Constitution.[97] The fifteen claims at issue, contained in seven patents, are as follows: claims 1, 2, 5, 6, 7, and 20 of U.S. patent 5,747,282 ("the '282 patent") granted May 5, 1998; claims 1, 6, and 7 of U.S. patent 5,837,492 ("the '492 patent") granted November 17, 1998; claim 1 of U.S. patent 5,693,473 ("the '473 patent") granted December 2, 1997; claim 1 of U.S. patent 5,709,999 ("the '999 patent") granted January 20, 1998; claim 1 of U.S. patent 5,710,001 ("the '001 patent") granted January 20, 1998; claim 1 of U.S. patent 5,753,441 ("the '441 patent") granted May 19, 1998; and claims 1 and 2 of U.S. patent 6,033,857 ("the '857 patent") granted March 7, 2000.[98]

The case was first heard in the U.S. District Court for the Southern District of New York.[99] The court first separated the claims into two categories:

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91 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181, 184–85 (S.D.N.Y. 2010).

92 *Id.* at 201.

93 *Id.*

94 *Id.*

95 *Id.* at 202.

96 *Id.* at 201–03.

97 *Ass'n for Molecular Pathology*, 702 F. Supp. 2d at 201–03.

98 *Id.* at 212.

99 *Id.* at 181.

"composition claims and method, or process, claims."[100] It went on to discuss the scope of the claims, starting with the composition claims.

> Independent claim 1 of the '282 patent is representative of the group of composition claims and claims: "An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2."
>
> This claim is therefore directed to an isolated DNA molecule possessing a nucleotide sequence that translates into the BRCA1 protein. . . . Claim 6 of the '492 patent, however, is considerably broader than claim 1 and is directed to any DNA nucleotide encoding any mutant BRCA2 protein that is associated with a predisposition to breast cancer.[101]

Claim 6 reads: "An isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide set forth in SEQ ID NO:2, wherein said mutated form of the BRCA2 polypeptide is associated with susceptibility to cancer."[102] In light of this the Court concluded that the composition claims "reach isolated BRCA1/2 DNA obtained from any human being."[103]

The Court then discussed the method claims.

> Claim 1 of the '999 patent is representative of the group of method claims. It claims: "A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from a group consisting of the alterations set forth in Tables 12A, 14, 18, or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184–4187 of SEQ ID NO:1."
>
> Thus, claim 1 of the '999 patent covers the process of identifying the existence of certain specific mutations in the BRCA1 gene by "analyzing" the sequence of the BRCA1 DNA, RNA, or cDNA made from BRCA1 RNA obtained from a human sample.[104]

In light of these findings, on March 29, 2010, Judge Sweet granted in part the plaintiff's motion for summary judgment declaring the patent claims invalid.[105] On appeal, the Federal Circuit reversed the decision regarding the un-

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100 *Id.* at 212.

101 *Id.*

102 *Id.* at 212 n.31.

103 *Ass'n for Molecular Pathology*, 702 F. Supp. 2d at 213.

104 *Id.*

105 *Id.* at 238.

patentability of the product claims.[106] The majority made rather short shrift of Judge Sweet's analysis of the patentable subject matter issue:

> Specifically, the Supreme Court has drawn a line between compositions that, even if combined or altered in a manner not found in nature . . . and compositions that human intervention has given "markedly different," or "distinctive," characteristics. Applying this test to the isolated DNAs in this case, we conclude that the challenged claims are drawn to patentable subject matter because the claims cover molecules that are markedly different—have a distinctive chemical identity and nature—from molecules that exist in nature.[107]

The Court went on to clarify that "[i]solated DNA is not purified DNA. . . . Thus, when cleaved, an isolated DNA molecule is not a purified form of a natural material, but a distinct chemical entity."[108]

This majority view suggests that *any* physical, chemical, or structural distinction between isolated and native DNA is sufficient to establish the isolated DNA as patentable subject matter.[109] However, this conclusion is subject to the concurrence-in-part by Judge Moore,[110] and the dissent-in-part by Judge Bryson.[111]

Moore concurs with the majority regarding the potential patentability of isolated DNA, and the patentability of cDNA in particular.[112] What troubles her are the broader claims like claims 1 and 5 from the '282 patent.[113] "These include claims encompassing both the isolated full length gene sequence (e.g., claim 1 of the '282 patent), which are thousands of nucleotides, and claims to shorter isolated DNA strands, with as few as fifteen nucleotides, whose nucleotide sequence is found on the chromosome (e.g. claim 5 of the '282 patent)."[114] For her, mere differences in chemical structure of any isolated DNA may be insufficient under the "markedly different" test from *Chakrabarty*.[115] Shorter strands pass this test because they have markedly different properties "which are directly responsible for their new and significant utility," e.g., serving as

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106 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 653 F.3d 1329, 1351 (Fed. Cir. 2011).

107 *Id.* (citations omitted).

108 *Id.* at 1352.

109 *See id.*

110 *Id.* at 1358 (Moore, J., concurring-in-part).

111 *Id.* at 1373 (Bryson, J., dissenting-in-part).

112 *Ass'n for Molecular Pathology*, 653 F.3d at 1364 (Moore, J., concurring-in-part).

113 *Id.* (Moore, J., concurring-in-part).

114 *Id.* (Moore, J., concurring-in-part).

115 Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980); *Ass'n for Molecular Pathology*, 653 F.3d at 1359–60 (Moore, J., concurring-in-part); s*ee also infra* Section II.A.

probes.[116] Thus, Judge Moore believes that "isolated DNA fragments are patentable subject matter."[117] However, she feels that longer strands— "genus claims" like claim 5 of the '282 patent—are a distinct matter as they can encompass the entire isolated gene sequence.[118] "As such, the chemical and structural differences in an isolated DNA sequence which includes most or all of a gene do not clearly lead to significant new utility as compared to nature. . . . Despite the literal chemical difference, the isolated full length gene does not clearly have a new utility and appears to simply serve the same ends devised by nature, namely to act as a gene encoding a protein sequence."[119] In the end, however, Judge Moore did not wish to go against established expectations and property rights, and "these settled expectations tip the scale in favor of patentability."[120]

Judge Bryson, dissenting-in-part, was not so deferential, although he does concur with the majority decision regarding the cDNA claims.[121] For him as with Judge Moore, the issue is the claims to the BRCA genes such as claim 1 of the '282 patent.[122] In his view: "[T]hat claim covers a truly immense range of substances from the cDNA that is 5,914 nucleotides long to the isolated gene that contains more than 120,000 nucleotides. . . . Included in that set are many important molecular variations to the BRCA1 gene that Myriad had not yet discovered and could not have chemically described."[123] Further, he feels that claim 5 of the same patent is "breathtakingly broad," "so broad that it includes products of nature (the BRCA1 exons) and portions of other genes."[124] He concluded that, "[t]he naturally occurring genetic material thus has not been altered in a way that would matter under the standard set forth in *Chakrabarty*. For that reason, the isolation of the naturally occurring genetic material does not make the claims to the isolated BRCA genes patent-eligible."[125]

Both Judge Moore and Bryson concur with the patent ineligibility of the method claims as "claim[ing] only abstract mental processes."[126] However,

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116 *Ass'n for Molecular Pathology*, 653 F.3d at 1365 (Moore, J., concurring-in-part).

117 *Id.* (Moore, J., concurring-in-part).

118 *Id.* at 1366 (Moore, J., concurring-in-part).

119 *Id.* at 1366–67 (Moore, J., concurring-in-part).

120 *Id.* (Moore, J., concurring-in-part).

121 *Id.* at 1373 (Bryson, J., dissenting-in-part).

122 *Ass'n for Molecular Pathology*, 653 F.3d at 1373 (Moore, J., dissenting-in-part).

123 *Id.* at 1376 (Bryson, J., dissenting-in-part).

124 *Id.* at 1379 (Bryson, J., dissenting-in-part).

125 *Id.* at 1378 (Bryson, J., dissenting-in-part).

126 *Id.* at 1355, 1373 (Moore, J., concurring-in-part) (Bryson, J., dissenting-in-part).

knowledgeable observers have suggested that the method claims "would have been upheld if there was another step, such as sequencing the genes, in addition to just mental steps."[127]

In its most recent decision—on remand from the Supreme Court to be considered in light of *Prometheus*—the Federal Circuit concluded that the composition claims represent non-naturally occurring composition of matter, and hence are patent-eligible.[128] As with the earlier cases, several subcategories of those isolated gene claims are considered. Most observers as well as the two concurring/dissenting judges agree that cDNA is indeed manmade with characteristics and utilities not found in nature—it is "markedly different."[129] As explained by the court, "[i]solated DNA has been cleaved . . . or synthesized to consist of just a fraction of a naturally occurring DNA molecule."[130] "[I]solated DNA is not just purified DNA," as isolated DNA has been removed from its native environment and manipulated chemically through human intervention so as to have a markedly different structure.[131] Within this group, cDNA is "especially distinctive" due to greater human manipulation.[132] To indicate the magnitude of the chemical changes, the native BRCA genes have between 80 and 114 million nucleotides while the isolated genes are reduced to about 80,000 nucleotides and the cDNA to as few as fifteen nucleotides.[133]

Plaintiffs argued that isolated DNA is a product of nature due to its retaining the same nucleotide sequence as native DNA, meaning the functionality of the isolated DNA is identical to the native DNA, as indeed it must be in order to be useful.[134] For the Federal Circuit, however, it is the human-generated difference in the chemical structure that is determinate of a significant difference.[135] The court emphasized that "[u]ses of chemical substances may be relevant to the nonobviousness of these substances or to method claims embodying those uses" but not to patent eligibility.[136] "Under the statutory rubric of § 101, isolated

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127 Andrew Pollack, *Ruling Upholds Gene Patent in Cancer Test*, N.Y. TIMES (July 29, 2011), http://www.nytimes.com/2011/07/30/business/gene-patent-in-cancer-test-upheld-by-appeals-panel.html.

128 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 689 F.3d 1303, 1326 (Fed. Cir. 2012).

129 *Id.* at 1329, 1337, 1348.

130 *Id.* at 1328.

131 *Id.*

132 *Id.* at 1329.

133 *Id.* at 1328.

134 *Ass'n for Molecular Pathology*, 689 F.3d at 1330.

135 *Id.*

136 *Id.*

DNA is a tangible, man-made composition of matter defined and distinguished by its objectively discernible chemical structure."[137] The Court addressed the Supreme Court's remand in light of *Prometheus* by saying: "The answer to [the Supreme Court's concern in *Prometheus*] is that permitting patents on isolated genes does not preempt a law of nature. A composition of matter is not a law of nature."[138] Judge Moore concurred with respect to the ruling on isolated DNA to support the settled expectations of the biotechnology industry regarding property rights.[139] Judge Bryson dissented regarding the patent eligibility of isolated DNA, considering it to be a product of nature.[140]

B. Prometheus

The Prometheus patents concern the use of thiopurine drugs in the treatment of autoimmune diseases, such as Crohn's disease and ulcerative colitis.[141] A patient's body ingesting a thiopurine compound metabolizes it, forming metabolites in the bloodstream.[142] Because individuals metabolize thiopurine compounds differently, the same dose is not appropriate in all cases, but it has been difficult for doctors to determine whether, for a particular patient, a given dose is too high, risking harmful side effects, or too low, and likely ineffective.[143] At the time the Prometheus inventions were developed, scientists already knew that the levels of certain metabolites in the blood correlated with the likelihood of a particular dosage being harmful or ineffective.[144] What was unknown was the specific correlations between metabolite levels and the harm or ineffectiveness to a patient.[145]

Two U.S. patents were granted, U.S. patent 6,355,623 ("the '623 patent") granted March 12, 2002, and U.S. patent 6,680,302 ("the '302 patent") granted January 20, 2004, which specified the safe levels of metabolites of 6-TG and 6-MMP in the blood.[146] Claim 1 of the '623 patent is considered typical:

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137 *Id.*

138 *Id.* at 1331.

139 *Id.* at 1344 (Moore, J., concurring-in-part).

140 *Ass'n for Molecular Pathology*, 689 F.3d at 1348 (Bryson, J., dissenting-in-part).

141 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1294–95 (2012).

142 *Id.* at 1295.

143 *Id.*

144 *Id.*

145 *Id.*

146 *Id.*

> A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder, wherein the level of 6-thioguanine less than about 230 pmol per 8x108 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and wherein the level of 6-thioguanine greater than about 400 pmol per 8x108 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.[147]

Mayo was the sole and exclusive licensee of the '623 and '302 patents until, in 2004, it announced an intent to begin using and selling its own test, one using a slightly higher metabolite level—450 versus the 400 used by Prometheus—to indicate toxicity.[148] Prometheus sued for infringement in the U.S. District Court for the Southern District of California.[149] Mayo filed a motion for summary judgment of invalidity, arguing that the patents impermissibly claimed natural phenomena—the correlations between, on the one hand, thiopurine drug metabolite levels and, on the other, efficacy and toxicity—and that the claims wholly preempt use of the natural phenomena.[150] The court agreed that Mayo was infringing due to the lack of a significant differences in the tests.[151] However, in 2008, it granted summary judgment on the issue of patent validity, reasoning, in part, that the claimed correlations were natural phenomena and not patent-eligible inventions because the correlations resulted from a natural body process.[152] Moreover, the court determined that "[b]ecause the claims cover the correlations themselves, it follows that the claims 'wholly pre-empt' the correlations."[153]

On appeal, the Federal Circuit reversed the district court's ruling based on the machine-or-transformation test from its earlier decision in *Bilski*.[154] Following that decision, *Bilski* was appealed to the Supreme Court, where it was

147 *Prometheus Labs*, 132 S.Ct. at 1295.

148 *Id.* at 1295–96.

149 *Id.* at 1296.

150 *Id.*

151 *Id.*

152 Prometheus Labs., Inc. v. Mayo Collaborative Servs., No. 04CV1200 JAH (RBB), 2008 U.S. Dist. LEXIS 25062, at *46 (S.D. Cal. Mar. 28, 2008).

153 *Id.* at *35.

154 Prometheus Labs., Inc. v. Mayo Collaborative Servs., 581 F.3d 1336, 1349–50 (Fed. Cir. 2009).

reversed on the basis that the machine-or-transformation test is not the sole, exclusive test for examining patent eligibility under § 101, and holding, rather, that the test is a useful, investigative tool.[155] The Federal Circuit's decision in *Prometheus* was then vacated and remanded for reconsideration based on the *Bilski* decision.[156] The Federal Circuit again determined that the Prometheus method claims were patentable subject matter, leading to the Supreme Court again granting certiorari.[157]

Citing principally to *Morse*, *Chakrabarty*, *Benson*, *Flook*, *Diehr*, and *Bilski* the Supreme Court determined that the

> relation itself [between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm as claimed in the Prometheus patents] exists in principle apart from any human action. . . . The question before us is whether the claims do significantly more than simply describe these natural relations.[158]

The Supreme Court's answer to this question was: no.[159] As justification, the court stated:

> [The claimed process recites] an "administering" step, a "determining" step, and a "wherein" step. . . . First, the "administering" step simply refers to the relevant audience, namely doctors who treat patients with certain diseases with thiopurine drugs. . . . Second, the "wherein" clauses simply tell a doctor about the relevant natural laws, at most adding a suggestion that he should take those laws into account when treating his patient. . . . Third, the "determining" step tells the doctor to determine the level of the relevant metabolites in the blood, through whatever process the doctor or the laboratory wishes to use. As the patents state, methods for determining metabolite levels were well known in the art. . . . Fourth, to consider the three steps as an ordered combination adds nothing to the laws of nature that is not already present when the steps are considered separately. . . . To put the matter more succinctly, the claims inform a relevant audience about certain laws of nature; any additional steps consist of well understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately.[160]

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155 Bilski v. Kappos, 130 S.Ct. 3218, 3227 (2010).

156 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 130 S. Ct. 3543, 3543 (2010).

157 Prometheus Labs., Inc. v. Mayo Collaborative Servs., 628 F.3d 1347, 1355 (Fed. Cir. 2010) (citations omitted).

158 Prometheus Labs., Inc. v. Mayo Collaborative Servs., 132 S. Ct. 1289, 1297 (2012).

159 *Id.*

160 *Id.* at 1297–98.

The Justices rejected the Federal Circuit's upholding of the patents based on the *Bilski* machine-or-transformation test by noting: "we have neither said nor implied that the test trumps the 'law of nature' exclusion."[161] The Court also rejected the defendant's position that "the particular laws of nature that its patent claims embody are narrow and specific" encouraging the courts "to draw distinctions among laws of nature."[162] It stated:

> [c]ourts and judges are not institutionally well suited to making the kinds of judgments needed to distinguish among different laws of nature. And so the cases have endorsed a bright-line prohibition against patenting laws of nature, mathematical formulas and the like, which serves as a somewhat more easily administered proxy for the underlying "building block" concern.[163]

Yet as was discussed in Section II, the case law prohibition against the patentability of laws of nature is anything but "bright-line."[164]

Based on this decision, the Patent Office developed a memo for providing preliminary guidance to the examining corps in conjunction with the *Bilski* "Interim Guidance."[165] Examiners are advised to ensure that claims, and particularly process claims, are

> not directed to an exception to eligibility such that the claim amounts to a monopoly on the law of nature, natural phenomenon, or an abstract idea *itself*. In addition, to be patent-eligible, a claim that includes an exception should include other elements or combination of elements such that, in practice, the claimed product or process amounts to significantly *more than* a law of nature, a natural phenomenon, or an abstract idea with conventional steps specified at a high level of generality appended thereto.[166]

C. Brief for the United States

Noting that the Supreme Court's resolution on this case would significantly affect the work of the Patent and Trademark Office, the government filed

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161 *Id.* at 1303.

162 *Id.*

163 *Id.*

164 *See supra* Section II.

165 Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of Bilski v. Kappos, 75 Fed. Reg. 43923 (July 27, 2010).

166 Memorandum from Andrew H. Hirshfeld, Exec. Comm'r for Patent Examining Procedure, to Patent Examining Corps of the USPTO (Mar. 21, 2012) (regarding the Supreme Court Decision in Mayo Collaborative Servs. v. Prometheus Labs., Inc.) (emphasis in original).

an amicus brief supporting neither party.[167] The position taken supports the invalidation of the Prometheus patents, but on 35 U.S.C. §§ 102 and 103 grounds, not § 101.[168] For the government, "Section 101 is, by design, a 'coarse filter' [] [while] [t]he remaining provisions of the Patent Act permit nuanced, fact-intensive distinctions necessary to separate patentable from unpatentable inventions."[169] That is, the government concurs with the Federal Circuit's machine-or-transformation test-based decision on patentable subject matter, noting a transformation does take place, as required of the test, and the fact that it occurs within the human body fits into a long line of decisions supporting the patentability of methods of treating patients.[170] Moreover, it concludes that the process is not a natural phenomenon as the thiopurine metabolites are synthetic compounds.[171]

The Brief also includes extensive comments on the preemption matter: "the claims do not preempt all practical applications of the relationship between thiopurine drugs and human health. . . . [T]here remain substantial opportunities to derive practical value from knowledge of that relationship without infringing [Prometheus's] patents."[172] Those opportunities include higher correlates used for organ-transplant patients than recommended for auto-immune disorders.[173] Additionally, applications to a related thiopurine drug, tioguanine, are not claimed in the patents.[174] Indeed, it is only when the correlations are described in a patent at a high level of particularity that preemption becomes an issue.[175]

Rather, the government calls for rejection under 35 U.S.C. §§ 102 and 103.[176]

> Here, the patents themselves make clear that the "administering" and "determining" steps of the disputed claims were part of the prior art, and the inventors' only asserted innovation is the specific metabolite ranges cited in the "wherein" clauses of the claims. . . . Rather, to be patentable over the prior art, a process claim must recite a series of steps in the physical world that differs

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167 Brief for the United States as Amici Curiae Supporting Neither Party at 1, Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289 (2012) (No. 10-1150), 2011 WL 4040414 at *1 (hereinafter "Amicus Brief for the U.S.").

168 *Id.* at *26.

169 *Id.* at *11.

170 *Id.*

171 *Id.* at *8, *9, *25.

172 *Id.* at *10.

173 Amicus Brief for the U.S., *supra* note 167, at *21.

174 *Id.*

175 *Id.* at *23.

176 *Id.* at *26.

> from any series of steps that was previously known. [But] the "wherein" clauses of [Prometheus's] claims do not recite any physical step to be performed by a doctor (or anyone else) [so] they add no patentable weight to the "administering" and "determining" steps.[177]

In brief, the government argues that the claims are not novel.[178]

The Supreme Court, for its part, rejects favoring 35 U.S.C. §§ 102, 103 and 112 over § 101 exclusions as being inconsistent with prior law.[179] Section 102 exclusions of natural laws would also—in their view—be problematic if a newly discovered law were novel.[180] The Court stated that: "These considerations lead us to decline the Government's invitation to substitute §§ 102, 103, and 112 inquiries for the better established inquiry under § 101."[181]

D. Discussion

The matter of judicial bars to patentable subject matter described as "products of nature" and "laws of nature" has been left in a confusing state by the Supreme Court; requiring that practice be "consistent" with prior law. But that statutory law is unclear itself, and the case law is inconsistent on where the line is drawn between what is and is not patentable subject matter. With this equivocal history on defining non-statutory subject matter bars one might imagine that the courts would be extremely careful not to suggest an additional one be added. Yet that is just what the Supreme Court seems to be suggesting in *Prometheus*, something I refer to here as an economic § 101 requirement.[182]

I turn now to developing an argument for the Supreme Court's seeming predilection for an economic § 101 subject matter patentability requirement, at least for (human) genes. Subsequently, I evaluate such a possible requirement from legal, economic and scientific perspectives.

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177 *Id.* at *27–*29.

178 *See id.*

179 Prometheus Labs., Inc. v. Mayo Collaborative Servs., 132 S. Ct. 1289, 1304 (2012).

180 *Id.*

181 *Id.*

182 *See generally id.*

IV. AN ECONOMIC § 101 JUDICIAL REQUIREMENT FOR PATENT ELIGIBLE SUBJECT MATTER?

A. Hints for Such a Requirement in Myriad *and* Prometheus

The Supreme Court, of course, has not yet considered *Myriad,* and the Federal Circuit's decision considered largely legal issues. However, the initial district court action directed considerable attention to the consequences of the decision.[183] Judge Sweet considered arguments of the effects of the patents on Myriad's testing procedures, as well as the advancement of science and medical treatments.[184]

Typically, the Supreme Court makes relatively few references to economic issues and monopoly in patent cases, but it did so repeatedly in *Prometheus*:

> • "The Court has repeatedly emphasized this last mentioned concern, a concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature."[185]
>
> • "There is a danger that the grant of patents that tie up their use will inhibit future innovation premised upon them . . . or otherwise foreclose more future invention than the underlying invention could reasonably justify."[186]
>
> • "[Prometheus' patents] threaten to inhibit the development of more refined treatment recommendations . . . ."[187]
>
> • "[The respondent] encourages us to draw distinctions among laws of nature based on whether or not they will interfere significantly with innovation in other fields now or in the future."[188]
>
> • "But the underlying functional concern here is a relative one: how much future innovation is foreclosed relative to the contribution of the inventor."[189]
>
> • "Patent protection is, after all, a two-edged sword. On the one hand, the promise of exclusive rights provides monetary incentives that lead to creation, invention, and discovery. On the other hand, that very exclusivity can impede the flow of information that might permit, indeed spur, invention, by, for ex-

183 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181, 206–10 (S.D.N.Y. 2010).

184 *Id.*

185 *Prometheus Labs.*, 132 S. Ct. at 1301.

186 *Id.*

187 *Id.* at 1302.

188 *Id.* at 1303.

189 *Id.*

> ample, raising the price of using the patented ideas once created, requiring potential users to conduct costly and time consuming searches of existing patents and pending patent applications, and requiring the negotiation of complex licensing arrangements."[190]

The final quote is of course a restatement of the economic justification for patents and the inherent societal tradeoff when creating even a partial, temporary monopoly.[191] The other quotes, however, read directly to the court's very specific concern of a patent inhibiting future research. GenScott observes that the potential for the Myriad and Prometheus patents to affect innovation and diagnostic research is "remarkably similar."[192] "This similarity is most likely the driving force behind the Supreme Court's decision to vacate and remand the Federal Circuit's decision in *Myriad*."[193]

As noted, the original *Myriad* lawsuit was initiated to "take down" patents for human genes to prevent the thwarting of technological progress.[194] That conceptualization of the issue is further developed in an amicus curiae brief by the Information Society Project ("ISP") at Yale Law School.[195] The amicus brief ("ISP Brief") includes the following points:

> • Evidence establishes that the Myriad patents limit genetic research, stifling the dissemination of information required for scientific progress;[196]
>
> • Because there are "a finite number of genes, it is impossible to invent around" them, creating what is called a "double monopoly";[197]
>
> • Human genetic research is not as costly as the development of pharmaceutical patents; moreover, gene patents are not "patent-driven," in part due to public funding;[198]

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190 *Id.* at 1305.

191 *See infra* Section IV.C.

192 GenScott, *Supreme Court Vacates Federal Circuit Decision in Case Challenging Patents on Breast Cancer Genes*, INFO. SOC'Y PROJECT AT YALE L. SCH. (Apr. 11, 2012), http://yaleisp.org/2012/04/supreme-court-vacates-federal-circuit-decision-in-case-challenging-patents-on-breast-cancer-genes/.

193 *Id.*

194 *See supra* note 14 and accompanying text.

195 Brief of Amici Curiae, Info. Soc'y Project at Yale Law Sch. Scholars in Support of the Petition at 1, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012) (No. 11-725), 2012 WL 166995 at *2 [hereinafter Info. Soc'y Project Brief].

196 *Id.* at *7, *10, *11, *19.

197 *Id.* at *5, *6.

198 *Id.* at *5, *8.

- The patents are used to inflate the cost of genetic testing and inhibit its progress; less costly and more comprehensive tests can be developed absent the patents;[199] and
- These patents contribute to the "patent thicket" which stifles research.[200]

Most of these points of course could apply to patents in any subject area, and indeed largely describe the market-reward base of patents, good or bad.[201] However, to initiate the assessment of the legal basis for an economic § 101 subject matter patentability requirement, it is appropriate to begin with the first point made in the ISP Brief, that "the central concern of patent law is the difficult business of drawing a line between those things which are worth to the public the embarrassment of an exclusive patent and those which are not."[202]

B. The Legal Basis for an Economic § 101 Requirement for Patent Eligible Subject Matter

The economic rationale for U.S. patent law as established in the Constitution is well known: "To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[203] By granting property rights,[204] patents give authors and inventors the opportunity to benefit financially from their creations, with all remuneration derived from the market. The monopoly rights so granted are restricted in time ("limited Times") and scope.[205] In this way, "[t]he Patent Clause itself reflects a balance between the need to encourage innovation and the avoidance of monopolies which stifle competition without any concomitant advance in the 'Progress of Science and useful Arts.'"[206]

Regarding terminology, the courts have been inconsistent in the use of the term "monopoly" to refer to patent rights. "Letters patent are not to be re-

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199 *Id.* at *6, *17.

200 *Id.* at *14.

201 *See infra* Section IV.C.

202 Info. Soc'y Project Brief, *supra* note 195, at *3 (quoting Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 148 (1989)) (internal quotations omitted).

203 U.S. CONST. art. I, § 8, cl. 8.

204 *See* United States v. Dubilier Condenser Corp., 289 U.S. 178, 187 (1933) ("A patent is property . . . ").

205 *See* Graham v. John Deere Co., 383 U.S. 1, 6 (1966) ("Congress may not authorize the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials already available.").

206 *Bonito Boats*, 489 U.S. at 146.

garded as monopolies . . . but as public franchises granted to the inventors of new and useful improvements . . . ."[207] In *United States v. Dubilier Condenser Corp.*,[208] the Supreme Court eschews the very concept of monopoly: "[A] monopoly takes something from the people. An inventor deprives the public of nothing which it enjoyed before his discovery, but gives something of value to the community by adding to the sum of human knowledge."[209] Conversely, in *Precision Instrument Mfg. Co. v. Automotive Maintenance Machinery Co.*,[210] the potential harm of patents is particularly emphasized.[211] "[A] patent is an exception to the general rule against monopolies . . . . The far-reaching social and economic consequences of a patent, therefore, give the public a paramount interest in seeing that patent monopolies . . . are *kept within their legitimate scope*."[212] Notably, *Prometheus* appears to take the latter position, emphasizing the potential cost of a patent monopoly by restricting future research.[213]

To economists, terms like "legitimate scope,"[214] "balance,"[215] and "foreclose[] more future invention than the underlying discovery could reasonably justify,"[216] refer to equilibration on financial value terms, broadly assuming that market prices reflect societal value.[217] That is, over the long term and through the availability of the product/process itself and derivations therefrom, does a patent generate more benefits for society than private value for the inventor? That, however, is the economists' take on the terms. Here, we must consider how they are treated in case law, and what that teaches about a possible economic § 101 subject matter patentability requirement?

Reiffin v. Microsoft Corp.[218] uses similar terminology in suggesting an "economic balance" is part of establishing the scope of a patent: "The purpose of [the written description] provision is to ensure that the scope of the right to

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207 Seymour v. Osborne, 78 U.S. 516, 533 (1870).

208 289 U.S. 178 (1933).

209 *Id.* at 186.

210 324 U.S. 806 (1945).

211 *Id.* at 816.

212 *Id.* (emphasis added).

213 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1301–02 (2012).

214 *Id.*

215 Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 146 (1989).

216 *Prometheus Labs.*, 132 S. Ct. at 1301.

217 Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998) ("A proliferation of intellectual property rights upstream may be stifling life-saving innovations downstream in the case of research and product development.").

218 214 F.3d 1342 (Fed. Cir. 2000).

exclude, as set forth in the claims, *does not overreach the scope of the inventor's contribution to the field of art . . . .*"[219] However, the sentence finishes with "as described in the patent specification," making it clear that the reference to "overreach" is with regard to the adequacy of the written description required by 35 U.S.C. § 112(a).[220]

Bonito Boats, Inc. v. Thunder Craft Boats, Inc.[221] also uses similar terminology describing the balance of costs and benefits from a patent: "The federal patent system thus embodies a carefully crafted bargain . . . ."[222] Again, however, the completion of the sentence makes it clear that the "carefully crafted bargain" is a reference to the statutory limits of patent law, and in particular the incentives for inventors to reveal their inventions rather than rely on secrecy. "The federal patent system thus embodies a carefully crafted bargain for encouraging the creation and disclosure of new, useful, and nonobvious advances in technology and design in return for the exclusive right to practice the invention for a period of years."[223]

At the same time, the courts have been emphatic that mere investment, through effort, in creating a product is itself not sufficient for a patent.[224] Clearly, and appropriately from a societal perspective, a patent is not a reward for diligence; it must be something more. At the same time, it is important to recognize that the courts are potentially establishing a highly non-symmetric requirement; investment cost is not a consideration when awarding a patent, but the relationship between the inventor's investment and the public benefit may be.

The utility requirement under § 101 is an additional patentability requirement where one might reasonably anticipate a balance between the grant and the "immediate benefit to the public" in some tangible, economic sense.[225] In *Brenner v. Manson*,[226] the court states that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility."[227]

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219 *Id.* at 1345 (emphasis added).

220 *Id.*

221 489 U.S. 141 (1989).

222 *Id.* at 150.

223 *Id.* at 150–51.

224 Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 132 (1948) ("Even though it may have been the product of skill, it certainly was not the product of invention.").

225 *See* Nelson v. Bowler, 626 F.2d 853, 856 (C.C.P.A. 1980).

226 383 U.S. 519 (1966).

227 *Id.* at 534.

Additionally, *In re Fisher*[228] established that utility must be specific ("provide a well-defined and particular benefit to the public") and substantial ("useful to the public . . . in its current form").[229]

A product or process must be operable to have utility.[230] What is not required is that the invention be somehow efficient or otherwise preferential for the public over available competing products.[231] The courts have stated:

> An invention does not lack utility merely because the particular embodiment disclosed in the patent lacks perfection or performs crudely. A commercially successful product is not required. . . . [P]artial success [is] sufficient to demonstrate patentable utility. In short, the defense of non-utility cannot be sustained without proof of total incapacity.[232]

Nor is it clear to whom the utility must apply.[233] The courts have noted that "[t]he Patent Office position seems to have been that there must be a presently existing 'practical' usefulness to some undefined class of persons. We have never received a clear answer to the question. 'Useful to whom and for what?'"[234] Clearly, the courts are not holding inventors to a high standard when balancing the patent property right with usefulness to the public.

Consider next the research or experimental use exemption, defined as not-for-profit research or experimentation, which, by allowing researchers access to the Myriad genes without the requirement for its prior consent, would alleviate many of the concerns voiced in the *Myriad* and *Prometheus* decisions.[235] In *Prometheus*, for example, the court stated:

> Exclusivity can impede the flow of information that might permit, indeed spur, invention, by, for example, raising the price of using the patented ideas once created, requiring potential users to conduct costly and time consuming

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228 421 F.3d 1365 (Fed. Cir. 2005).

229 *Id.* at 1371.

230 *See In re* Harwood, 390 F.2d 985, 989 (C.C.P.A. 1968) ("An inoperative invention, of course, does not satisfy the requirement of 35 U.S.C. 101 that an invention be useful.").

231 *In re* Nelson, 280 F.2d 172, 180 (C.C.P.A. 1960), *overruled by In re* Kirk, 376 F.2d 936 (C.C.P.A. 1967).

232 *Id.* (citations omitted).

233 *Id.* at 180.

234 *Id.*

235 For example, one of the stated concerns is "[Prometheus' patents] threaten to inhibit the development of more refined treatment recommendations…" due to the lack of experimental use access for the genes. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1301 (2012). By definition, an experimental use exemption would permit such access making the development of improved tests possible.

> searches of existing patents and pending patent applications, and requiring the negotiation of complex licensing arrangements.[236]

Of course, if a use discovered under a research exemption is to be commercialized, an agreement with the patent holder is still required, but research can proceed unimpeded.[237]

Court consideration of the experimental use exemption goes back to 1813 and *Whittemore v. Cutter*,[238] where the issue was whether making without use was an infringement.[239] Justice Story ruled that "it could never have been the intention of the legislature to punish a man, who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects."[240] Justice Story's reference to "philosophical experiments" was prophetic, as similar terminology reappeared in the pivotal *Roche Products, Inc. v. Bolar Pharmaceutical Co.*,[241] which dealt with experimental use of a patented pharmaceutical product to prepare a generic substitute for when the patent expired.[242] The Federal Circuit refused to apply the experimental use exception in that situation, holding that Bolar's "use was solely for business reasons and not for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry."[243]

One may ask if there is any basis for a de minimis "common law experimental use" exemption? Not according to Judge Rader in *Embrex Inc. v. Service Engineering Corp.*[244]

> Because the Patent Act confers the right to preclude 'use,' not 'substantial use,' no room remains in the law for a de minimis excuse. . . . When in-

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236 *Id.* at 1305.

237 A common example is the material transfer agreement as epitomized by the Uniform Biological Materials Transfer Agreement which: (1) allows the recipient's institution the right to use the provider's material for academic research purposes only; (2) covers the ownership of derivatives, progeny, and modifications of the original materials; and (3) consists of legal language on liability, warranty, publication rights, and intellectual property, etc. *Uniform Biological Materials Transfer Agreement (UBMTA)*, AUTM, http://www.autm.net/AM/Template.cfm?Section=Technology_Transfer_Resources&Template=/CM/ContentDisplay.cfm&ContentID=2810 (last visited Jan. 16, 2013).

238 29 F. Cas. 1120 (C.C.D. Mass. 1813).

239 *Id.* at 1121.

240 *Id.*

241 733 F.2d 858 (Fed. Cir. 1984), *superseded by statute*, Act of Sept. 24, 1984, Pub. L. No. 98–417, 98 Stat 1585.

242 *Id.* at 860.

243 *Id.* at 863 (internal quotations omitted).

244 216 F.3d 1343, 1352 (Fed. Cir. 2000) (Rader, J., concurring).

> fringement is proven either minimal or wholly non-commercial, the damage computation process provides full flexibility for courts to preclude large (or perhaps any) awards for minimal infringements.[245]

What though of research conducted by a research institution like a university or research hospital? The district court and the Federal Circuit in *Madey v. Duke University*[246] split over that issue when considering Duke University researchers' use of electron laser equipment.[247] The district court recognized a "common law" defense and rejected the patent owner's contention of commercial intent based on statements in Duke's patent policy indicating the potential to develop commercial applications based on its academic research.[248] The court cited another clause in the patent policy describing Duke as "dedicated to teaching, research, and the expansion of knowledge . . . not undertak[en] . . . principally for the purpose of developing patents and commercial applications."[249]

However the Federal Circuit saw matters differently:

> In short, regardless of whether a particular institution or entity is engaged in an endeavor for commercial gain, so long as the act is in furtherance of the alleged infringer's legitimate business and is not solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry, the act does not qualify for the very narrow and strictly limited experimental use defense. . . . [T]he profit or non-profit status of the user is not determinative.[250]

This brings us to the question of whether there is an economic base to the patent eligible subject matter requirement of § 101? Here, again, the courts are mixed in their opinions. In a lengthy concurrence in *Bilski*, Justice Stevens suggests that non-statutory bars are in fact based on the statutes:

> The statute thus authorizes four categories of subject matter that may be patented: processes, machines, manufactures, and compositions of matter. Section 101 imposes a threshold condition. "[N]o patent is available for a discovery, however useful, novel, and nonobvious, unless it falls within one of the express categories of patentable subject matter."[251]

Additionally, he references another scholar's likening of knowledge to a pyramid with basic ideas at the top and broadening out at the base with applica-

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245 *Id.* at 1352 (Rader, J., concurring).

246 307 F.3d 1351 (Fed. Cir. 2002).

247 *Id.* at 1356, 1362.

248 *Id.* at 1355–56.

249 *Id.* at 1356.

250 *Id.* at 1362.

251 Bilski v. Kappos, 130 S. Ct. 3218, 3236 (2010) (Stevens, J., concurring) (quoting Kewanee Oil Co. v. Bicron Corp., 416 U.S. 470, 483 (1974)).

tions.[252] "The higher up a patent is on the pyramid, the greater the social cost and the greater the hindrance to further innovation."[253] Of course, inventions higher up on this knowledge pyramid can also bring the greatest social value, which is why patents are not limited to iterative applications.[254] However, the treatment of patents as a right that the Patent Office has the responsibility to refute works against the legal/economic concept that the hindrance of future invention should be a criterion for patentability.[255] Early applications in the development of a new technology (pioneer inventions) are typically broad for the simple reason that, by definition, there is little prior art.[256] This does not say that broad claims are necessarily socially beneficial, but indicates that the statute does not define non-statutory subject matter as based predominately on economic considerations. Rather, the issue is one of encouraging products accessible for public use.

Another opinion comes from Bohannan and Hovenkamp, who interpret the non-statutory patent bars as "based mainly on the idea that these things [natural phenomena, laws of nature, abstract ideas] are not 'new'."[257]

Justice Breyer frames the issue differently in a dissent dismissing a writ of certiorari.[258]

> The problem arises from the fact that patents do not only encourage research by providing monetary incentives for invention. Sometimes their presence can discourage research by impeding the free exchange of information, for example by forcing researchers to avoid the use of potentially patented ideas, by

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252 *Id.* at 3255 (Stevens, J., concurring) (citing Rochelle Cooper Dreyfuss, *Are Business Method Patents Bad for Business?*, 16 SANTA CLARA COMPUTER & HIGH TECH. L.J. 263, 275 (2000)).

253 *Id.* (citing Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 873–79 (1990)).

254 Merges & Nelson, *supra* note 253, at 848–49.

255 *See First Office Action Estimator*, USPTO, http://www.uspto.gov/patents/stats/first_office_action_estimator.jsp (last visited Jan. 16, 2013) ("An Office action is a document written by a patent examiner in the course of examination of a patent application. The Office action many cite prior art and give reasons why the examiner has allowed (approved) the applicants' claims, and/or rejected the claims.").

256 For example, U.S. Patent No. 4,736,866 claims "A transgenic non-human mammal." U.S. Patent No. 4,736,866 col.9 l.35 (filed Apr. 12, 1988). This is the famous "Harvard mouse" patent which led to the patentability of higher animals and, under license to DuPont, became notorious for restrictive licensing practices. *See generally* Heller & Eisenberg, *supra* note 217.

257 CHRISTINA BOHANNAN & HERBERT HOVENKAMP, CREATION WITHOUT RESTRAINT: PROMOTING LIBERTY AND RIVALRY IN INNOVATION 119 (2012).

258 Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 125 (2006) (Breyer, J., dissenting).

> 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.
>
> Patent law seeks to avoid the dangers of overprotection just as surely as it seeks to avoid the diminished incentive to invent that underprotection can threaten. One way in which patent law seeks to sail between these opposing and risky shoals is through rules that bring certain types of invention and discovery within the scope of patentability while excluding others.[259]

Complicating the matter of preemption of future research is the issue of the requisite degree of preemption. Conceivably, the higher the degree of preemption (sometimes referred to by the less formal term "tie up") the more likely the invention is to involve a law or product of nature. But that is not what the case law shows. In *Flook*, the claimed process "cover[ed] a broad range of potential uses . . . . [It did] not, however, cover every conceivable application of the formula."[260] Yet the application was still rejected.[261] *Prometheus* touched on the preemption issue several times, giving a relativistic answer: "[T]he underlying functional concern here is a relative one: how much future innovation is foreclosed relative to the contribution of the inventor."[262] The brief for the United States, however, noted that "the claims do not preempt all practical applications of the relationship between thiopurine drugs and human health" and would have to be defined in "a very fine degree of particularity" to do so.[263]

Thus, while the degree of preemption is relevant to an undue monopoly argument, the Supreme Court suggests that any degree of preemption is unacceptable.[264] Overall, the courts have left the matter of the critical level entirely open and case specific.[265]

> Courts and judges are not institutionally well suited to making the kinds of judgments needed to distinguish among different laws of nature [and consequential preemption]. And so the cases have endorsed a bright-line prohibition against patenting laws of nature, mathematical formulas and the like, which serves as a somewhat more easily administered proxy for the underlying "building block" concern.[266]

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259 *Id.* at 127.

260 Parker v. Flook, 437 U.S. 584, 586 (1978).

261 *Id.* at 594–96.

262 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1303 (2012).

263 Amicus Brief for the U.S., *supra* note 167, at *10.

264 *See Prometheus Labs.*, 132 S. Ct. at 1303.

265 *Id.*

266 *Id.*

But as the case law has shown, the line is anything but bright, meaning the permissible level of preemption is indeterminate as well.

And then there are the instances when judges question the very need for patents to incentivize invention at all. The *Myriad* plaintiffs asserted in the district court that gene patents are not necessary to create innovation, and indeed that two-thirds of such patents are based on research funded by the government.[267] In a current paper, Professor Eisenberg indicates that:

> courts in the past "implicitly analyzed" the economic effects of patents by subject matter area in developing rules that "distinguish, albeit not explicitly, efficient from inefficient subject matter for patentability," but beginning with the 1980 decision of the Supreme Court in *Diamond v. Chakrabarty* courts have "largely abandoned any gatekeeping role" in favor of a broad reading of statutory standards for patentable subject matter.[268]

Judge Posner in a recent media interview noted, "It's not clear that we really need patents in most industries," but he did acknowledge that "some industries, like pharmaceuticals, had a better claim to intellectual property protection because of the enormous investment it takes to create a successful drug."[269] Judge Posner is recognized for being outspoken, but he is also the author of a well-known book on the economics of intellectual property rights.[270]

However, before the courts start down the path of attempting to determine when patent rights may or may not be necessary, it is important to recall that Congress passed the Bayh-Dole Act[271] expressly because government-funded university research was not being commercialized because it was in the public domain, providing no incentive for firms to invest in bringing those products to market.[272] The Act allows universities and other research institutions to claim ownership over the products of federal research with the obligation to

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267 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181, 210 (S.D.N.Y. 2010).

268 Rebecca S. Eisenberg, *Wisdom of the Ages or Dead-Hand Control? Patentable Subject Matter for Diagnostic Methods After* In re Bilski, 3 CASE W. RES. J. L. TECH. & INTERNET 1, 45 (citations omitted) (quoting David S. Olson, *Taking the Utilitarian Basis for Patent Law Seriously: The Case for Restricting Patentable Subject Matter*, 82 TEMPLE L. REV. 181, 205–15 (2009)).

269 Dan Levine, *Judge who Shelved Apple Trial Says Patent System Out of Sync*, REUTERS (July 5, 2012), http://www.reuters.com/article/2012/07/05/us-apple-google-judge-idUSBRE8640IQ20120705.

270 *See generally* WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW (2003).

271 35 U.S.C. §§ 200–212 (2006).

272 Robert Cook-Deegan & Christopher Heaney, *Patents in Genomics and Human Genetics*, 11 ANN. REV. OF GENOMICS AND HUM. GENETICS 383, 383 (2010).

commercialize when feasible.[273] Typically this is done through patenting,[274] and it is of note that the Act is generally considered to be very successful in achieving those objectives.[275]

C. Economic Theory and Empirical Evidence for an Economic § 101 Requirement for Patent Eligible Subject Matter

The economic issues raised in *Prometheus* relate to ways that patents can reduce future research, rather than incentivize as intended.[276] According to the literature, there are three principal ways that can happen: very broad patents; conglomerations of multiple patents combined in a single product; and patents on research tools.[277] Each is examined here through both the theoretical and empirical evidence. I then turn to the particular issues identified in *Myriad* and *Prometheus.*

Using economic theory, the Constitutional mandate "[t]o promote the Progress of Science and useful Arts"[278] by creating a property right prohibiting direct copying can be readily substantiated for discrete (non-sequential), single-product inventions, e.g., the "better mouse trap" of patent lore.[279] However, once the complexities of cumulative knowledge and/or multiple patents incorporated into a single product are added to the analysis, the issue becomes far more complex and ambiguous. Theoretical (and practical) problems arise as each subsequent inventor attempts to maximize his or her share of the value, which leads to too high a price ("double marginalization").[280] Multiple patents necessitate difficult negotiations over cross-licensing terms, which can break down because of high negotiation transaction costs, different goals of patent owners, and overestimates of value.[281] In the extreme of multiple overlapping patents, those for which the value created by one patented component can benefit anoth-

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273 WENDY H. SCHACHT, CONG. RESEARCH SERV., RL32076, THE BAYH-DOLE ACT: SELECTED ISSUES IN PATENT POLICY AND THE COMMERCIALIZATION OF TECHNOLOGY 7 (2005).

274 *Id.*

275 *Id.* at 8.

276 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1301–02 (2012).

277 Merges & Nelson, *supra* note 253, at 865.

278 U.S. CONST. art. I, § 8, cl. 8.

279 *See generally* LANDES & POSNER, *supra* note 270, at 297–300.

280 *See* Bronwyn H. Hall & Dietmar Harhoff, *Recent Research on the Economics of Patents* 10 (Nat'l Bureau of Econ. Research, Working Paper No. 17773, 2012), *available at* http://www.nber.org/papers/w17773.

281 Heller & Eisenberg, *supra* note 217, at 700–01.

er patent owner, the existence of patents can actually reduce the incentive to invest compared to the no-patent case.[282]

Heller and Eisenberg use the term "anticommons" to refer to the case where multiple owners have the right of exclusion but none the privilege of use.[283] Sometimes the term "patent thicket" is used.[284] Heller and Eisenberg identify Cetus Corporation as one case where a firm used an upstream invention (polymerase chain reaction) to claim benefits from subsequent downstream discoveries (using "reach-through licenses"), leading to stacked licenses.[285] However, the authors do recognize that reach-through agreements reduce the royalty cost to each generation of licensees.[286] In any case, the PTO's 2001 revised written description guidelines limit reach-through claims to products and data for insufficiently described molecules.[287] Heller and Eisenberg also found 100 extant patents using the term "adrenergic receptor" and interpreted that to represent a bargaining challenge.[288] The case of sequential, multi-component patent products is relevant to both *Myriad* and *Prometheus* (see examples below) and to biomedical research in general, so the courts have a basis for concern. But is the concern realized in practice?

It is evident that economic theory is a limited guide to understanding the practical details of the problem, and so I turn to the empirical evidence. At the most general level, it is clear that broad patents can indeed block advances. Merges and Nelson describe the cases of automobiles (the Selden patent), airplanes (the Wright Brothers patents), lighting (the Edison patent), and radio (the Marconi patent).[289] Note that these are all cumulative inventions, although most are pioneering patents which raise particular issues regarding breadth.[290] The

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282 *See* Hall & Harhoff, *supra* note 280, at 9–12 (discussing how businesses can benefit from a lack of patent protection in cases Eisenberg of sequential innovation).

283 Heller & Eisenberg, *supra* note 217, at 698.

284 ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT, GENETIC INVENTIONS, INTELLECTUAL PROPERTY RIGHTS AND LICENSING PRACTICES: EVIDENCE AND POLICIES 61 (2002) [hereinafter OECD].

285 Heller & Eisenberg, *supra* note 217, at 699.

286 *Id.*

287 Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001).

288 Heller & Eisenberg, *supra* note 217, at 699; *see generally* NATIONAL RESEARCH COUNCIL, INTELLECTUAL PROPERTY RIGHTS AND RESEARCH TOOLS IN MOLECULAR BIOLOGY: SUMMARY OF A WORKSHOP HELD AT THE NATIONAL ACADEMY OF SCIENCES, FEB. 15–16, 1996 40–56 (1997).

289 Merges & Nelson, *supra* note 253, at 884–93 (1990).

290 *See supra* Section IV.B.

real issue, though, is not if patents can restrict future research, but the *degree* to which they do so in practice. There are two threads of empirical results, those based on the analysis of secondary data and those using surveys.

Hall and Harhoff cite a study of how the Celera Corporation's use of its intellectual property indeed led to reductions in subsequent scientific research and product development.[291] However, another cited study found that such practices "had little impact thus far due to the work-arounds adopted by university researchers: taking out licenses, inventing around, using an informal research exemption, and developing publicly available research tools."[292]

Huang and Murray attempted to measure the effects of gene patenting on the production of public information, as proxied by paper citations referring to the patented gene for at least one of the identified inventors before and after the patent issued.[293] They found a statistically significant five percent reduction in publication numbers post-patent, which was more pronounced for private than public sector researchers.[294] Studies like these, though, which involve a number of assumptions, such as the distribution of citations and the representativeness of the sample, not to mention the absence of a control group, are somewhat difficult to assess and often require a replication to make the results more robust.

More of a case study than empirical research is Maurer's analysis of the breakdown of an attempt to establish a unified database of the connections between genetic mutations and particular diseases.[295] The issue was how to coalesce multiple small participants who maintained databases limited to their own research findings.[296] Those databases were operated on a volunteer, noncommercial basis with the frequent limitation of varying data protocols and standards, making comparisons across databases complex.[297] There were also a handful of large participants, but neither they nor the commercial users had an incentive to merge the available data.[298] The described efforts at collaboration to

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291 Hall & Harhoff, *supra* note 280, at 27.

292 *Id.*

293 Kenneth G. Huang & Fiona E. Murray, *Does Patent Strategy Shape the Long-Run Supply of Public Knowledge? Evidence from Human Genetics*, 52 ACAD. MGMT. J. 1193, 1194 (2009).

294 *Id.* at 1209.

295 *See* Stephen M. Mauer, *Inside the Anticommons: Academic Scientists' Struggle to Build a Commercially Self-Supporting Human Mutations Database, 1999–2001*, 35 RES. POL'Y. 839, 839–40 (2006).

296 *Id.* at 840.

297 *Id.* at 840–41.

298 *See id.* at 839–40.

create such a unified source are replete with suspicion, efforts to dominate, concerns about access, and differences in assessed value of individual contributions; in short, the kinds of anticommons problems of fragmented ownership described by Heller and Eisenberg.[299] Many of the anticommons problems were visible, but, critically, patents and other forms of intellectual property rights were not an issue.[300] So yes, the anticommons certainly can and does occur, but patents are neither a necessary nor sufficient condition.

Generally, empirical research is no more illuminating of the practical costs of patents than is economic theory. This brings us to survey results as the basis for most of our understanding of the effects of patents on research productivity. Surveys have been instrumental in identifying pharmaceuticals, biotechnology, and medical instrument fields as the areas where patents are most critical in increasing innovation.[301] Since genomics, which underlies the Myriad and Prometheus patents, fits into those fields, the use of patents can presumably have a significant effect on innovativeness and openness.

Cho et al. surveyed 122 directors of clinical genetic testing services, concluding that "virtually all laboratory directors felt that patents have had a negative effect on all aspects of clinical testing, except on the quality of testing."[302] The ability to conduct research was decreased modestly:

> • 65 percent were contacted regarding potential infringement by performance of a genetic test (including for BRCA1 and BRCA2);
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> • 25 percent were prevented from continuing a test or service they had developed; and
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> • 53 percent decided against performing or developing a test or service because of a patent.[303]

However, it is important to recognize that the respondents (all but one) were involved in genetic testing for fee-based clinical purposes rather than research.[304] It is unsurprising that patent holders prevented that group from using the patented technologies for no charge and thwarted the development of alternative tests.

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299 *Id.* at 843–49; *see also* Heller & Eisenberg, *supra* note 217, at 699.

300 Mauer, *supra* note 295, at 845.

301 *Id.* at 839–40.

302 Mildred K. Cho et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3, 4, 5 (2003).

303 *Id.*

304 *Id.* at 7.

The distinction between fee-based use and academic research is evident in the control Myriad applied to its patents.[305] Cease-and-desist letters sent to alleged infringers who were providing clinical BRAC genetic testing services also contained an experimental use exemption. "[T]he cease-and-desist notification did not apply to research testing 'for the purpose of furthering non-commercial research programs, the results of which are not provided to the patient and for which no money is received from the patient or the patient's insurance.'"[306] In the judgment of the Federal Circuit, "[P]atents are rarely enforced against scientific research, even during their terms."[307]

For broader survey results, I turn to Walsh, Arora, and Cohen, who contacted 70 attorneys, business managers, and scientists from pharmaceutical and biotech firms and universities for in-depth personal interviews.[308] As the authors note, a patent, by definition, suggests restricted access, so the real issue is the "degree" of restriction.[309] Their focus was on the more extreme forms.[310]

First considered is the sheer number of patents potentially burdening research.[311] This is one factor specifically highlighted by Heller and Eisenberg when they identified 100 extant patents using the term "adrenergic receptor" and thus potentially encumbering research in the area.[312] Respondents to Walsh et al.'s surveys, however, saw matters quite differently.[313] Of the 100 patents identified by Heller and Eisenberg (subsequently increased to 135 by another researcher), only a "small number" of licenses was found to be required in order to conduct research involving the "adrenergic receptor."[314] Generally, complicated cases involved 6-12 key patents, but "more typically the number was zero."[315] Jenson and Murray did find that "some genes have up to 20 patents asserting rights to various gene uses and manifestations," suggesting additional

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305 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 689 F.3d 1303, 1315 (Fed. Cir. 2012).

306 *Id.*

307 *Id.* at 1331.

308 John P. Walsh et al., *Effects of Research Tool Patents and Licensing on Biomedical Innovation, in* PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285, 292 (W.M. Cohen & S.A. Merrill eds., 2003).

309 *Id.* at 291.

310 *Id.*

311 *Id.* at 292–93.

312 Heller & Eisenberg, *supra* note 217, at 699.

313 *See* Walsh et al., *supra* note 308, at 294–95.

314 *Id.* at 294.

315 *Id.*

freedom-to-operate issues for researchers.[316] But, presumably, those patents are included in the industry assessment of key patent numbers.[317]

Next assessed were research tools (upstream inventions).[318] This too was a problem area identified by Heller and Eisenberg, who particularly noted the Cetus and OncoMouse patent kafuffles.[319] Walsh et al., however, found "almost no evidence of such [negotiation] breakdowns" that led to a project's cessation.[320] Nor was royalty stacking found to be a practical barrier; while the royalty burden could at times become onerous, "the research always went forward."[321] Reasons for this outcome include the common practice of offering discounts to university and government researchers, as well as the employment of various negotiation strategies.[322] The strategies include establishing a "ceiling" (as well as a "floor" for individual components) for combined royalties; the choice of a lump-sum payment or use of a patent pool, in which a broad group of technologies is provided at a fixed unit cost;[323] or employing field-of-use licenses when exploitation in all possible fields is not feasible for a single firm.[324] The Federal Trade Commission in a follow-up study of patenting in the biotech industries concluded that expressed concerns that the patenting of research tools would obstruct the commercialization of new products "ha[ve] yet to materialize."[325]

Additionally, for universities and other non-profits there is always the possibility, in case of infringement, for avocation of the self-serving experimental use exception.[326] Generally, if their work does not involve fees (such as

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316 Kyle Jenson & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, 310 SCI. 239, 239 (2005).

317 Walsh et al., *supra* note 308.

318 *Id.* at 296.

319 Heller & Eisenberg, *supra* note 217, at 699–700.

320 Walsh et al., *supra* note 308, at 298.

321 *Id.* at 299–300.

322 Keith J. Jones et al., *Problems with Royalty Rates, Royalty Stacking, and Royalty Packing Issues*, *in* INTELLECTUAL PROPERTY MANAGEMENT IN HEALTH AND AGRICULTURAL INNOVATION: A HANDBOOK OF BEST PRACTICES 1121, 1121 (A. Krattiger et al. eds., 2007); Walsh et al., *supra* note 308, at 302.

323 Jones et al., *supra* note 322, at 1121.

324 Sandra L. Shotwell, *Field-of-Use Licensing*, *in* INTELLECTUAL PROPERTY MANAGEMENT IN HEALTH AND AGRICULTURAL INNOVATION: A HANDBOOK OF BEST PRACTICES, 1113, 1131 (A. Krattiger et al. eds., 2007).

325 FED. TRADE COMM'N, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION 32 (2009).

326 Walsh et al., *supra* note 308, at 324–25.

for clinical tests, recognizing the distinction between research and clinical testing is not necessarily a clear one), such organizations are largely ignored; some may receive a cease-and-desist notification, but notifications are rare and frequently ignored.[327] Myriad, for example, allowed tests so long as fees were not charged.[328] Patent holders seem to be making business decisions that suing universities for infringement makes no economic sense and is poor public relations.[329]

Where an issue may exist is in the cost of licensing for small, start-up research firms, if not for large pharmaceutical companies. But there is no evidence these issues have increased in the "recent past."[330] Costs include cash payments as well as the time involved in negotiating license agreements and even accessing materials (material transfer agreements), along with ensuing delays.[331] Delays are particularly prevalent when university technology transfer offices become involved.[332] But again, there is no indication that these costs and delays are specifically patent-related.[333]

Related to research tools are the effects of patents on research targets, defined as a "cell receptor, enzyme, or other protein implicated in a disease."[334] Limited access to targets because of restrictive licensing could indeed slow research progress.[335] Walsh et al., though, quote industry respondents as preferring broad licensing, which enhances the opportunity for identifying a drug. "With an exclusive license, the odds of finding an active drug, let alone the best, are not good. Therefore we [the target owner] want the target technology broadly available. Broad licensing only makes economic sense in our view."[336] More generally, while Walsh et al. identified "some evidence of researchers being excluded [from access to targets], [they did] not find a failure to exploit the target."[337]

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327 *Id.* at 317–19.

328 *Id.* at 312, 318.

329 *Id.* at 325.

330 *Id.* at 316.

331 *Id.* at 314, 319.

332 Walsh et al., *supra* note 308, at 319–20.

333 *Id.* at 317–22.

334 *Id.* at 310.

335 *Id.* at 310–11.

336 *Id*. at 311 (alteration in original).

337 *Id.* at 314–15.

Walsh, Cohen, and Cho subsequently interviewed 507 academic biomedical researchers with similar results.[338] That is, patents in the field do not regularly prevent academic researchers from accessing the knowledge inputs for their research.[339] None abandoned a research project due to impediments from patents, while few noted delays caused by the same source.[340] However, nearly 20 percent indicated that requests for materials or data had been denied.[341] The cause was not patents per se, but rather scientific competition, a history of business activity, and the time and effort needed to fulfill the request, among other causes.[342]

In 2002, the Organisation for Economic Co-Operation and Development (OECD) conducted an international workshop on just these topics; its conclusions included the following:

> • The transaction costs of negotiating arrangements within the complexity of overlapping patent claims are real and should not be ignored;[343]
>
> • "The available evidence does not suggest a systematic breakdown in the licensing of genetic inventions";[344]
>
> • Evidence of fragmented patent rights, blocking patents, uncertainty, and abuses of the patent "monopoly positions appear anecdotal and are not supported by existing economic studies";[345]
>
> • "In specific areas there is evidence of problems associated with the numbers and breadth of gene patents . . . although the exact cause of those problems has not been fully elucidated";[346] and
>
> • "[F]reedom to operate is not unduly impeded."[347]

Overall, there is no real evidence that research access has been thwarted or even significantly delayed except in rare instances.[348] However, the increased

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338 John P. Walsh, Wesley M. Cohen & Charlene Cho, *Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research*, 36 RES. POL'Y 1184, 1184 (2007).

339 *Id.*

340 *Id.* at 1190.

341 *Id.* at 1200.

342 *Id.* at 1199–1200.

343 OECD, *supra* note 284.

344 *Id.* at 77.

345 *Id.*

346 *Id.*

347 *Id.* at 79.

348 *See supra* text accompanying notes 289–342.

complexity of agreements, only partly patent-related, does raise costs and causes some delays, creating a societal as well as a private cost.[349] The potential also exists for a patent holder to withhold or burden access to a key tool; it has happened in the past and could happen again in the future.[350] But it should be stressed that the problem is not nearly as widespread as the Supreme Court in *Prometheus* appears to be convinced it is.[351] The Court was clearly aware of the potential problem, but seemingly did not evaluate the actual record.[352] Policy responses to rare, if potentially extreme, cases always present difficult choices. Here I argue that an economic, judicially created § 101 subject matter bar is not the appropriate approach. But first I shall consider the particular access issues identified in *Myriad* as well as in several amicus briefs.

Judge Sweet draws on amicus briefs (including from the American Medical Association[353]) and depositions to identify claims that gene patents have impeded critical data sharing, and, in particular, that Myriad withheld critical data concerning genetic predispositions to breast cancer.[354] Gene patents additionally stand accused of impeding the development of improved genetic testing.[355] Myriad contested those assertions, noting it freely allows research studies (if not clinical testing) on the BRCA1 and BRCA2 genes.[356] Eight plaintiffs were involved in operating clinical laboratories and testified in regards to stopping screening of the BRCA1 and BRCA2 genes in response to letters from Myriad, or to halting the development of alternatives tests.[357] Six plaintiffs were breast or ovarian cancer sufferers who noted the high cost of the Myriad tests, including problems with insurance payments, as well as the absence of confirming test availability.[358] Notably, the Leahy-Smith America Invents Act calls on the PTO to "conduct a study on effective ways to provide independent, confirming genetic diagnostic test activity where gene patents and exclusive licensing

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349 *See* Walsh et al., *supra* note 308, at 314–15.

350 *See, e.g.*, Merges & Nelson, *supra* note 253, at 865.

351 *See supra* Section IV.A.

352 *Id.*

353 *See generally Gene Patenting*, AMERICAN MEDICAL ASSOCIATION, http://www.ama-assn.org/ama/pub/physician-resources/medical-science/genetics-molecular-medicine/related-policy-topics/gene-patenting.page (last visited Jan. 9, 2013).

354 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181, 208–10 (S.D.N.Y. 2010).

355 *Id.* at 206.

356 *Id.* at 210.

357 *Id.* at 187–88.

358 *Id.* at 188–89.

for primary genetic diagnostic tests exist."[359] The PTO has recently informed Congress that the report will be delayed beyond the June 2012 deadline.[360]

Judge Sweet concludes by noting, "[T]here exists a sharp dispute concerning the impact of patents directed to isolated DNA on genetic research and consequently the health of society. . . . [T]he resolution of these disputes of fact and policy are not possible within the context of these motions."[361] Nor is their resolution possible within the context of this paper, but it is equally infeasible to substantiate the concerns expressed by the Supreme Court in *Prometheus* regarding gene patents impeding subsequent research.[362] Impediments can occur and have occurred, but as rare exceptions and not common practice that would seem to require a drastic remedy like a new category of unpatentable subject matter.[363] I now consider the issue from a scientific perspective.

D. The Scientific Factors Related to an Economic § 101 Requirement for (Human) Gene Patents

The preceding analysis has primarily been focused on access issues. Here I consider whether there are particular attributes of genes that would indicate their patenting should be treated differently from other sectors. In particular, two issues are explored: (1) Does the uniqueness of a gene prevent "patenting around" it (the "double monopoly" the Information Society Project refers to);[364] and (2) Do patents on genes prevent the sequencing of an individual's genome—a promising new field of medical treatment ?[365] This latter concern was expressly stated by the district court in *Myriad*:

> [A]s new sequencing technologies offer the possibility of faster and less expensive sequencing of a patient's genes, patents on one or more genes may impede scientists' ability to develop a comprehensive test for complex diseases or provide a person with an analysis of his or her entire genome.[366]

Huys et al. approached the issue by examining extant patents related to 22 diseases with genetic bases, diseases like cystic fibrosis, Huntington's dis-

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359 Leahy-Smith America Invents Act, Pub. L. No. 112-29, § 27, 125 Stat. 284, 338 (2011).

360 *AIA Studies and Reports*, USPTO (Jan. 4, 2013, 3:42 PM), http://www.uspto.gov/aia_implementation/aia_studies_reports.jsp#heading-3.

361 *Ass'n for Molecular Pathology*, 702 F. Supp. 2d at 190, 210.

362 *See supra* Section IV.C.–IV.D.

363 *See supra* text accompanying notes 289–342.

364 Info. Soc'y Project Brief, *supra* note 195, at *5, *6.

365 *Ass'n for Molecular Pathology*, 702 F. Supp. 2d at 210.

366 *Id.*

ease, and, of course, familial breast and ovarian cancer.[367] The researchers examined both U.S. and European patents (European patents are excluded from the present analysis for obvious reasons) directed to genes, primers and probes, diagnostic methods, and diagnostic kits.[368] In this article, patents applied to genes are considered, as they are most closely associated with "laws of nature" and "products of nature," as well as method patents, i.e., the categories for the Myriad patents. The analysis involved identifying the relevant patents and patent applications using both key-word and patent classifications, with the selected patents scrutinized by knowledgeable researchers to categorize "the necessity of having access to the technology" for carrying out the diagnosis.[369] Three levels were established: easily circumvented; circumvention "requires a substantial investment of money and time"; and nearly impossible to circumvent (called "blocking claims").[370]

In total, 118 U.S. patents (nearly 60 percent of the U.S. and EU total) were identified, 38 percent were method patents and 25 percent were gene patents (primarily "isolated" cDNA).[371] Notably, 62.5 percent originated from the non-profit sector, primarily universities.[372] Only three percent of the gene patents were considered to be "blocking," too few to constitute a patent thicket.[373] Conversely, 30 percent of the method claims were categorized as blocking, enough to constitute a thicket.[374] Overall the authors concluded: "[T]he present analysis and accompanying observations do not point to the existence of a wide patent thicket in genetic diagnostic testing. Rather, they highlight a problem of lack of transparency and clarity, leading to legal uncertainty."[375] The "legal uncertainty" refers for example to the granting of a diagnostic testing method claim that "broadly formulates the link between mutation and disease" making it "unclear when a diagnostic testing method is infringing."[376] While "it should be almost impossible to construe a claim so broadly that it would cover an infinite

367 Huys et al., *supra* note 19, at 903, 904.

368 *Id.*

369 *Id.* at 903, 904–05.

370 *Id.*

371 *Id.* at 906.

372 *Id.*

373 Huys et al., *supra* note 19, at 906, 908.

374 *Id.* at 905–06, 908.

375 *Id.* at 909.

376 *Id.* at 908.

number of tests, the examples show that nevertheless, such claims are granted."[377]

One of the issues considered by a Department of Health and Human Services Advisory Committee is the effect of gene patents on individual whole genome sequencing.[378] The Committee recognized that there is considerable uncertainty over this issue in the legal community, enhanced by differences in claim languages leading to different infringement determinations.[379] Nonetheless, the report identifies a "distinct possibility" of infringement, meaning that gene patents are seen as a potential barrier to the development of whole-genome sequencing.[380] Additionally, as widespread parallel gene sequencing is expected to be undertaken prior to whole-genome sequencing, the parallel sequencing itself may infringe gene patents.[381]

The Committee was particularly concerned about broad patent claims, pointing to claims 1 and 2 of U.S. patent 5,508,167 as an example.[382] Since those claims apply to unspecified detection methods, and whole-genome sequencing is one of many such methods, whole-genome sequencing would likely infringe the patent.[383] Note though that the 1994 application date of that patent is well prior to the *Bilski* decision which would at minimum have likely limited its claim scope.[384]

Henner, senior vice president of research at Genentech, Inc., sees the issue as much more straightforward: "[A] gene patent—properly examined—should not enable its owner to prevent parties from doing research, such as sequencing or studying a portion of the genome of an organism."[385] This perception is closer to actual experiences involving the Myriad patents.[386] Myriad law-

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377 *Id.*

378 *See* DEP'T OF HEALTH AND HUM. SERVS., SECRETARY'S ADVISORY COMMITTEE ON GENETICS, HEALTH, AND SOCIETY, GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 3 (2010).

379 *Id.* at 58.

380 *Id.*

381 *Id.* at 59.

382 *Id.* at 58–59.

383 *Id.*

384 Bilski v. Kappos, 130 S. Ct. 3218, 3218 (2010); U.S. Patent No. 5,508,167, at [22] (filed Apr. 13, 1994).

385 *Gene Patents and Other Genomic Inventions: Hearing Before the Subcomm. on Courts and Intellectual Property of the H. Comm. on the Judiciary*, 106th Cong. 89 (2000) (testimony of Dennis J. Henner, Ph.D., Senior Vice President, Research, Genentech, Inc.).

386 *See* Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 689 F.3d 1303, 1322 (Fed. Cir. 2012).

yers pointed out that since the BRAC discoveries were reported, more than 18,000 scientists have conducted research on them, with more than 8,600 research papers published.[387] Moreover one of the plaintiffs conceded that her lab continues to conduct the sequencing of the BRAC genes, patents or no patents.[388]

In any case, before widespread individual genetic testing can advance, Kingsmore and Saunders identify four key hurdles:

> • "First, no clinical-grade general database of disease-associated mutations currently exists."[389]
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> • "Second, consensus strategies for standardized, high-throughput interpretation of genetic variants of unknown significance . . . must be developed and implemented."[390]
>
> • "Third, genomic training programs must be designed . . . ."[391]
>
> • "Finally, before clinical practice guidelines can be defined . . . , many questions must be answered: What are the analytical gold standards? What are the benefits and harms of using genomic information in health care, and how are these maximized and minimized, respectively? Which sets of disorders benefit from NGS-based diagnostic testing in terms of cost and improved outcomes?"[392]

Resolving these matters will clearly take time.[393]

E. Discussion

A detailed review of the literature identifies there is indeed a basis for a concern that patents on genes and gene-based diagnostic procedures can, and in a few cases have, restricted subsequent research.[394] That evidence, though, is limited, spotty, and anecdotal.[395] The broader record indicates that patent thickets are more potential than reality; research progresses, whether through busi-

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387 *Id.*

388 *Id.*

389 Stephen F. Kingsmore & Carol J. Saunders, *Deep Sequencing of Patient Genomes for Disease Diagnosis: When Will it Become Routine?*, SCI. TRANSLATIONAL MED., June 15, 2011, at 1, 3.

390 *Id.*

391 *Id.*

392 *Id.* at 1.

393 *See id.*

394 *See supra* Section IV.C.

395 *Id.*

ness decisions by firms that widespread licensing makes economic sense, creative approaches to patenting around obstacles, or accommodation of minor infringement, especially by the non-profit sector.[396] The research process has become more complex as a result of expanded patenting, but other factors and changes are involved as well, so a cessation of gene patenting would not return research to the terms of decades past.[397] Overall, the biogenetics research system is coping.[398]

This is a fortuitous finding, for patent law and case history provide no basis for curtailing patentable subject matter based on an informal societal cost-benefit analysis of whether the costs of patent rights to society exceed the benefits generated. Nonetheless, the potential for holdups to research do exist.[399] Possible remedies are evaluated in Section V immediately below.

V. CONCLUSIONS AND A WAY AHEAD

The muddle in the courts over § 101 patent ineligible subject matter has been set forth in all its painful details. Observers have noted that the bars form anything but a clear line; the very terminology is vague, and the uncertainty created in the therapeutics and biotech industries is all too real.[400] Hopes are that a Supreme Court review of *Myriad* will clarify the issues. Yet the Court's record on § 101 is not encouraging; in *Prometheus*, it accepted conceptual statements of problems with gene patents restricting future research without the due diligence of investigating whether those problems are realized in fact.[401] The literature reviewed here indicates that, as a practical matter and due to a number of coping strategies, blocking or even notable delay of subsequent research due to gene patents is at best rare.[402]

Under those circumstances one might imagine the courts would proceed with great caution when considering expanding the scope of non-statutory subject matter under § 101. Yet that seems not to be the case.[403] The Supreme Court appears to be very focused on the research preemption issue to the degree that its use of a "law of nature" bar seems more like an economic bar (a required

396 *See supra* Section IV.C.–IV.D.

397 *Id.*

398 *Id.*

399 *Id.*

400 *See supra* Section IV.B.

401 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1303 (2012).

402 *See supra* Section IV.C.–IV.D.

403 *See generally Prometheus Labs.*, 132 S.Ct. at 1289.

quid pro quo for public and private value).[404] The case history and literature review provided here indicates there is no basis or broad need for such a requirement, and it is something beyond the scope of the Patent Office and courts. Overall, it is a bad idea.

Yet, at its base, the research preemption concern expressed by the court does resonate, all the more because the cases relate to human health. The evidence decidedly indicates that blocking of biomedical research due to patent thickets and the like is rare, but it could occur, as it has occurred (if rarely) in other sectors.[405] I turn next to approaches for dealing with rare, if still possible, blockages. As a starting point, the efficient approach is decidedly *not* to avert the problem by prohibiting all patenting in a field. Overall, the cost in economic and human health terms would likely be far greater than the value of the research preemption averted. What is needed is a more nuanced policy approach.

The field of workable approaches can be further reduced by rejecting the recommendation from the report to the Department of Health and Human Services.[406] It recommends "[t]he creation of an exemption from liability for infringement of patent claims on genes for anyone making, using, ordering, offering for sale, or selling a test developed under the patent for patient-care purposes."[407] This recommendation is unsatisfactory because it effectively removes patent protection for genes and treatments related to genes.[408]

In its amicus brief, the Government argues that, "[p]roperly conceived, however, petitioners' objections [in *Prometheus*] arise not under Section 101, but under the novelty and nonobviousness requirements of 35 U.S.C. 102 and 103[sic]. Although the claims are likely invalid under those provisions, the claims describe patent-*eligible* subject matter."[409] Other observers agree that the Prometheus patents are likely invalid on §§ 102 and 103 grounds.[410] The general conclusion is that "invalidation under the 'law of nature' exception should be reserved for very unusual circumstances."[411] That comports with statements from the case history. In the *Bilski* "Interim Guidance," examiners are advised to "avoid treating an application solely on the basis of patent-eligibility under 35

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404 *See id.*

405 *See supra* Section IV.C.–IV.D.

406 *See* DEP'T OF HEALTH AND HUM. SERVS., *supra* note 378, at 97.

407 *See id.*

408 *See id.*

409 Amicus Brief for the U.S., *supra* note 167, at *8–*9 (emphasis in original).

410 *See* Seidenberg, *supra* note 21, at 20 ("[Many legal experts] concede that the patents at issue were dubious and probably should have been struck down . . . .").

411 Amicus Brief for the U.S., *supra* note 167, at *23.

U.S.C. § 101 except in the most extreme cases."[412] And in *Classen Immunotherapies, v. Biogen IDEC,*[413] the court states that "patentability of subject matter that is facially within the classes set forth in § 101 is most reliably resolved in accordance with the conditions of §§ 102, 103, and 112."[414]

The advice to emphasize the §§ 102, 103, and 112 requirements over § 101 is appropriate as many "law of nature" issues and, more broadly, research preemption in general have arisen as a consequence of overly broad patents.[415] However, that recommendation was pointedly rejected by the Supreme Court in *Prometheus* and so has little standing.[416]

Finally, the Congress, courts and the PTO should reconsider the experimental use exemption, which is to say reassess *Roche* and *Duke*. At a minimum, a general exemption would allow research to move forward unimpeded by transaction costs, and should a useful product be discovered, the owner of the underlying patent would have a distinct economic incentive to license. The Community Patent Convention allows a broad experimental use exemption for research on a patented invention, so an exemption is indeed workable in an industrialized economy.[417]

Non-statutory unpatentable subject matter is one area where the newly activist Supreme Court needs to act with caution. Recent decisions over laws and products of nature have upset long-standing understandings of what is and what is not patentable, creating great uncertainty within research programs that have a long gestation. Business, it is often said, hates uncertainty and may well hold back research funding in genomics until the patentability uncertainties are resolved. In that context, adding even a suggestion of some kind of economic test for patentability would only exacerbate the current confusion. Rather, the best course is a renewed effort to avoid errors in patent grants. If the courts seek further assurances of avoiding patent thickets, an appropriate direction for their activism is expanding the experimental use exemption.

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412 Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of Bilski v. Kappos, 75 Fed. Reg. 43922, 43924 (July 27, 2010).

413 659 F.3d 1057 (Fed. Cir. 2011).

414 *Id.* at 1066.

415 Amicus Brief for the U.S., *supra* note 167, at *8–*9.

416 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1304 (2012) ("These considerations lead us to decline the Government's invitation to substitute §§ 102, 103, and 112 inquiries for the better established inquiry into § 101.").

417 Council Agreement 89/695, art. 27(b), 1989 O.J. (L 401) ("acts done for experimental purposes relating to the subject-matter of the patented invention").