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Eileen M. Kane

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Patenting Genes and Genetic Methods: What's at Stake?

ABSTRACT

THE EMERGENCE OF GENETIC MEDICINE FOLLOWING DECADES OF molecular biology research has been accompanied by the procurement of patent rights to many medically significant genes and methods for their use. The intellectual force of reductionism in the life sciences—to explain biological phenomena with molecular precision—generates direct conflicts with patent law's exclusion of basic knowledge from patenting: laws of nature, natural phenomena, and abstract ideas must remain in the public domain.

Patents have been obtained for the gene as an isolated DNA molecule, and for methods that rely on the assessment of genetic status to determine medical risk. Genetic testing can be used to identify disease susceptibility, establish diagnostic status, and design personalized therapeutic regimens in medical care. While many gene patents are managed so that wide access is facilitated, access to certain gene portfolios is quite restricted, preventing the development of a robust genetic testing climate for the relevant clinical conditions; this is most clearly observed for the BRCA1 and BRCA2 genes. This constriction affects patients seeking to make genetically-informed medical decisions, health care providers offering genetic testing options, and scientists performing genetic research. In the absence of explicit facilitated access to critical genes that are under restrictive patent management, the central question of patent eligibility and whether such patents are valid will continue to be litigated.

This is a period of renewed attention to the issue of patentable subject matter in the life sciences. It is only recently that a direct legal challenge to

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* Eileen M. Kane, Ph.D., J.D., Professor of Law, Penn State Dickinson School of Law. The author thanks Professor Lawrence Sung and the editors and staff of the University of Maryland School of Law Journal of Business and Technology Law for the invitation to participate in the April 2010 Symposium, "The Future of Genetic Disease and Diagnosis: Do Patents Matter?" The author also thanks Dennis Kergick for excellent research assistance.

the patent eligibility of a gene as an isolated DNA molecule was undertaken, in the case of *Association for Molecular Pathology v. United States Patent and Trademark Office*. Recent developments in the patent eligibility of method claims for biochemical assays, including genetic tests, have emerged in such cases as *LabCorp v. Metabolite*, *Prometheus v. Mayo*, and *Association for Molecular Pathology v. United States Patent and Trademark Office*. Identification of the relevant legal standard has implications for several kinds of method claims in genetic testing, where a patent claim may cover quantitative relationships between molecules, the mechanisms of pharmaceutical metabolism, or the cause and effect relationship between genotype and phenotype.

Further resolution of the eligibility controversies in genetic patenting has larger theoretical implications. The life sciences await a definitive and modern interpretation of the product of nature doctrine and its scope, and a contemporaneous analysis of whether and how correlations in the life sciences are defined as natural phenomena or laws of nature. The resolution of eligibility for genes has implications for the patenting of other biomolecules, while the resolution of the eligibility of genetic testing methods has implications for the contours of the preemption analysis as applied to subject matter in the life and physical sciences, including such scientific sectors as nanotechnology.

The article will outline the current legal frameworks for judging whether genetic-related inventions are patentable subject matter and identify the analytic choices available to the courts to decide the patent eligibility question for composition claims to genes and process claims to methods for genetic analysis. A central challenge to the eligibility question for genes is whether the courts should utilize a general or specific patentable subject matter theory for DNA; the choice will determine whether a decision has implications for general patenting in biotechnology. A central challenge to the analysis of life science method claims arises from the fact that the dominant analytic tests have been derived from the business method patent controversies, and illustrates how the technological neutrality of patent law causes doctrines that originate from one technical field to influence judicial review in an unrelated field.

The appellate courts confront an opportunity to update the set of “basic tools” for genetic science, and to settle these eligibility controversies for the benefit of scientists, medical practitioners, and patients who wish to use isolated genes and genetic correlations in research and medical care. As the courts enforce inventive precision through the proper application of 35 U.S.C. § 101, creative applications of fundamental knowledge will emerge

and legitimately solicit legal protection, while the intellectual foundations of genetic science remain accessible. It should be possible to reconcile the prohibitions on patenting laws of nature, natural phenomena, and abstract ideas with careful patenting practices that advance the application of genetics to medicine.

I. THE THRESHOLD DOCTRINE OF PATENT ELIGIBILITY

The boundaries of the patent system define what may be patentable, and in parallel, define what cannot be patented and belongs in the public domain. The patentable subject matter inquiry assesses the eligibility of a proposed invention for patent protection. Patentable subject matter is defined as “any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof.”¹ A gate keeping role for the patentable subject matter inquiry is legitimately inferred from its place in the numbering of statutory requirements for a patent as 35 U.S.C. § 101;² however, the grant of a patent follows an examination of a patent application for compliance with all formal statutory requirements.³ The designation of patentable subject matter as the threshold doctrine has been stated explicitly: “The first door which must be opened on the difficult path to patentability is §101,”⁴ and has been rephrased as “[w]hat *kind* of an invention or discovery is it?”⁵ In *Parker v. Flook*,⁶ the Supreme Court stated: “The obligation to determine what type of discovery is sought to be patented must precede the determination of whether that discovery is, in fact, new or obvious.”⁷ Patentable subject matter within the bounds of 35 U.S.C. § 101 must be new, nonobvious, and useful, and each of these inquiries are legally distinct.⁸ As a matter of linguistics, the term “patentable” subject matter is used both narrowly and broadly; but, formally, it represents an invention that meets the criteria of 35 U.S.C. § 101, as opposed to meeting all the other statutory requirements in order to

1. 35 U.S.C. § 101 (2006).

2. *Id.*

3. The specific provisions of the patent statute which comprise the patent prosecution requirements are: 35 U.S.C. § 101 (2006), which discusses patentable subject matter and utility; 35 U.S.C. § 102 (2006), addressing novelty; 35 U.S.C. § 103 (2006), pertaining to nonobviousness; and 35 § 112 (2006), which describes the requirements for a written description, enablement, best mode and claim definiteness.

4. *In re Bergy*, 596 F.2d 952, 960 (C.C.P.A. 1979), *aff'd*, 447 U.S. 303 (1980).

5. *Id.* (emphasis in original).

6. 437 U.S. 584 (1978).

7. *Id.* at 593.

8. *See infra* note 20.

be “patentable.”⁹ As a general matter, the threshold issue of patentable subject matter does not surface frequently. In the context of patent litigation, the doctrine is often ignored or under-litigated for reasons related to the complexity of analysis required as well as a more general disinclination on the part of potential litigants.¹⁰

Defining what is not patentable subject matter is determined by some statutory exclusions,¹¹ but more importantly, by the courts. The Supreme Court has stated that the “laws of nature, natural phenomena, and abstract ideas” are not patentable.¹² While considering whether a software-related invention might lead to the patenting of basic mathematical principles, the Court elaborated on its rationale: “Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work.”¹³ Later, as the Court encountered an invention from the emerging field of biotechnology, it further stated:

This is not to suggest that § 101 has no limits or that it embraces every discovery. The laws of nature, physical phenomena, and abstract ideas have been held not patentable. Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E = mc^2$; nor could Newton have patented the law of gravity. Such discoveries are “manifestations of nature, free to all men and reserved exclusively to none.”¹⁴

These often-quoted statements form the foundation of the Supreme Court’s attention to the task of line-drawing at the boundary of the patent system, although the practical application of these principles has proven complicated. The underlying rationale for the exclusions is that scientific

9. See *Flook*, 437 U.S. at 593, 594 n.16 (noting that a strict interpretation of §101 defines what invention is considered “patentable” notwithstanding the other statutory requirements).

10. See Eileen M. Kane, *Patent Ineligibility: Maintaining a Scientific Public Domain*, 80 ST. JOHN’S L. REV. 519, 528–29 (2006) (noting the general absence of the issue in patent litigation, and discussing how the mutual disinclination of litigants to raise eligibility challenges can be traced to the potentially far-reaching consequences of ineligibility decisions).

11. There are only several instances of differential statutory treatment of technical subject matter for patent law. See, e.g., 35 U.S.C. § 287(c)(1) (2006) (limiting the enforceability of medical procedure patents against health care providers). See also 42 U.S.C. § 2181 (2006) (making inventions regarding nuclear weapons or related inventions not patentable.).

12. *Diamond v. Diehr*, 450 U.S. 175, 185 (1981).

13. *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972).

14. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (citations omitted).

advances depend on an available substrate of basic knowledge, and that, therefore, patenting the intellectual foundations of a field has an adverse effect on its progress. Lower courts have also attempted to describe this non-statutory landscape.¹⁵ The significance of line-drawing underlies Justice Kennedy's recent statement that the patentable subject matter inquiry must perform "the larger object of securing patents for valuable inventions without transgressing the public domain."¹⁶

Volatility in the judicially-created tests for patentable subject matter has been a feature of this area of patent law. The unstable nature of the patent eligibility doctrine is evident from patent law jurisprudence, as legal tests have been developed at one juncture, only to fall out of use or into explicit disregard or repudiation. Some of this history includes the mental steps exception,¹⁷ the software-generated litmus tests such as the mathematical algorithm exception,¹⁸ the *Freeman-Walker-Abele* test for identifying an unpatentable algorithm,¹⁹ and the business method-generated litmus tests such as the "technological arts" requirement,²⁰ the "useful, concrete and tangible result" test from *State Street v. Signature*,²¹ and the recent machine or transformation test elevated by the Federal Circuit and interpreted by the Supreme Court in *Bilski v. Kappos*.²² The particular cross-technical implications of evolving eligibility tests will be further discussed with respect to the analysis of life science method claims in Part III.²³

It is beyond the scope of this article to fully explore how patents have been viewed for their instrumental effect on the development of genetic science and medicine, but some brief observations can be made. Estimates of the number of gene patents vary; one study has documented that 20% of

15. Prior to the *Chakrabarty* and *Diehr* cases, it was understood that, "[T]he following are not within the statutory categories of subject matter enumerated in § 101 and its predecessor statutes as interpreted through the years: principles, laws of nature, mental processes, intellectual concepts, ideas, natural phenomena, mathematical formulae, methods of calculation, fundamental truths, original causes [and] motives. . . ." *In re Bergy*, 596 F.2d 952, 965 (C.C.P.A. 1979).

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

17. *In re Musgrave*, 431 F.2d 882, 890 (C.C.P.A. 1970).

18. *Gottschalk*, 409 U.S. at 71–72.

19. See *Arrhythmia Res. Tech., Inc. v. Corazonix Corp.*, 958 F.2d 1053, 1058 (Fed. Cir. 1992).

20. *Ex parte Lundgren*, 76 USPQ2d 1385 (B.P.A.I. 2005).

21. 149 F.3d 1368, 1373 (1998).

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

23. See *infra* Part III.

human genes are patented.²⁴ The Secretary's Advisory Committee on Genetics Health and Society (SACGHS), undertook a recent and comprehensive analysis on the need for and impact of patents affecting genetic testing.²⁵ The incentive structure of patent law as applied to genetic testing was analyzed at three junctures: the impact on inventive activity, disclosure, and product development. The SACGHS concluded that ample evidence existed that the pace and volume of genetic discovery was not a patent-induced phenomenon.²⁶ Similarly, the availability of patents was not necessary to enhance disclosure of genetic discoveries, as other incentives exist for scientists to engage in such work.²⁷ Finally, the SACGHS looked at whether investment toward the development of genetic tests was amplified by the existence of patent rights. Here, the report concluded that investment efforts could be traced to the availability of patent rights; however, there are some specific considerations applicable to genetic testing as an area of research and development.²⁸ Most genetic tests are laboratory-developed tests (LDTs), which are offered as in-house services instead of being sold through commercial test kits, thus avoiding any FDA approval process.²⁹ A key distinction where patent rights do exist in a clinical field is whether the patent owner employs exclusive licensing, effectively restricting the market or non-exclusive licensing, which allows a

24. Kyle Jensen & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, 310 SCIENCE 239, 239 (2005).

25. SECRETARY'S ADVISORY COMM. ON GENETICS, HEALTH, AND SOCIETY, U.S. DEP'T OF HEALTH & HUM. SERVS., GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS (2010), available at http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_patents_report_2010.pdf [hereinafter SACGHS Report]; see also Neil A. Holtzman & Michael S. Watson, *Promoting Safe and Effective Genetic Testing in the United States*, NATIONAL HUMAN GENOME RESEARCH INSTITUTE, (1997), available at <http://www.genome/10001733> (defining genetic testing as "[t]he analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes or karyotypes for clinical purposes. Such purposes include predicting risk of disease, identifying carriers and establishing prenatal and clinical diagnosis or prognosis").

26. See *id.* at 23 ("[T]his information suggests that scientists are motivated to conduct genetic research by reasons other than patents, suggesting that discoveries will be sought regardless of the availability of intellectual property rights.").

27. See *id.* at 28 ("[I]t appears that scientists have sufficient reasons independent of patents to disclose gene-disease associations and that patent claims to genes may be diminishing research that builds on disclosed genetic discoveries.").

28. See *id.* at 30 (concluding that there is a correlation between intellectual property, licensing and accompanying investment incentives).

29. See, e.g., Gail H. Javitt et al., *Direct-to-Consumer Genetic Tests, Government Oversight, and the First Amendment: What the Government Can (And Can't) Do to Protect the Public's Health*, 57 OKLA. L. REV. 251, 272-73 (2004); Eileen M. Kane, *Patent-Mediated Standards in Genetic Testing*, 2008 UTAH L. REV. 835, 839-43 (2008).

competitive market to flourish.³⁰ The SACGHS did find that investment toward the commercialization of genetic testing was stimulated in some instances by patent rights managed through an exclusive licensing model; however, in other instances, genetic testing services were developed where no patent rights were available, or where non-exclusive patent licensing was the dominant model.³¹ Therefore, the overall conclusion was measured:

*Based on all of the above information, patent-derived exclusive rights are neither necessary nor sufficient conditions for the development of genetic test kits and laboratory-developed tests. In the area of laboratory-developed tests particularly, where development costs are not substantial, patents were not necessary for the development of several genetic tests.*³²

A separate analysis of litigation involving gene patents—which might be expected to reveal critical instances where patent rights influence the market structure—revealed few instances where patent rights were asserted by gene patent holders, and the overall conclusion was that gene patents collectively have not created significant obstacles to the development of genetic science.³³ Nonetheless, independent empirical studies document where gene patents are managed by patent owners to the detriment of a robust genetic testing climate for some diseases, such as the BRCA1 and BRCA2 patents and their use for determination of risk for early onset breast and ovarian cancers.³⁴

The application of the various patent law doctrines to patents that involve gene sequences has evolved through a series of cases that tested issues of patentability and patent claim scope.³⁵ This line of cases is now

30. See SACGHS Report, *supra* note 25, at 38–39 (discussing previous studies’ conclusions on the effect patents and exclusive licenses have on the competitive market).

31. See *id.* at 28–35 (discussing how exclusive and non-exclusive patent licensing impact genetic testing services).

32. *Id.* at 35.

33. See Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, 76 UMKC L. REV. 295, 360–61 (2007) (noting that gene patents have posed few obstacles to the development of genetic science).

34. See, e.g., Robert Cook-Deegan et al., *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers with Colon Cancers*, 12 GENETICS IN MEDICINE S15, S15 (2010) (comparing the effects of patenting on the availability of several cancer-related genetic tests).

35. See generally Kenneth J. Burchfiel, *BIOTECHNOLOGY AND THE FEDERAL CIRCUIT* (2d ed. 2010).

almost twenty years old.³⁶ Interestingly, the threshold issue of patentable subject matter was not the earliest doctrinal battle, but the latest. The earlier doctrinal highlights include the following issues: the scope of claims to DNA sequences under the disclosure doctrines of 35 U.S.C. § 112 (*Fiers v. Revel*,³⁷ *Amgen v. Chugai Pharmaceutical Co.*,³⁸ and *Regents of the University of California v. Eli Lilly & Co.*³⁹); the evolving obviousness of cloning methods under 35 U.S.C. § 103 (*In re Deuel*⁴⁰ and *In re Kubin*⁴¹) and the utility of gene excerpt sequences under 35 U.S.C. § 101 (*In re Fisher*⁴²).

The direct legal challenge to the patent eligibility of a DNA molecule encoding a gene is presented by the recent case, *Association for Molecular Pathology v. United States Patent and Trademark Office (AMP)*.⁴³ The case is a vehicle for presenting the long-standing controversy over the patent eligibility of purified DNA, and will be further discussed in Part II, *infra*.⁴⁴ Recent developments in the patent eligibility of method claims in biochemical assays, including genetic tests, have emerged in such cases as *LabCorp v. Metabolite*,⁴⁵ *Prometheus v. Mayo*,⁴⁶ and *AMP*⁴⁷ and will be discussed in Part III, *infra*.⁴⁸ These cases occur against the backdrop of evolving legal standards for method claims, most clearly drawn from *State Street v. Signature*⁴⁹ and *Bilski v. Kappos*,⁵⁰ both involving business method patents. These latter cases contributed new standards for identifying eligible patentable subject matter, particularly for intangible inventions less related to physical technology. Identification of the relevant legal test for considering the eligibility of method claims in genetic testing can be outcome-determinative, and the influence of the tests derived from business

36. The first major patent infringement litigation involving a gene patent was *Amgen v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991).

37. 984 F.2d 1164 (Fed. Cir. 1993).

38. *Amgen*, 927 F.2d at 1200.

39. 119 F.3d 1559 (Fed. Cir. 1997).

40. 51 F.3d 1552 (Fed. Cir. 1995).

41. 561 F.3d 1351 (Fed. Cir. 2009).

42. 421 F.3d 1365 (Fed. Cir. 2005).

43. 702 F. Supp. 181 (S.D.N.Y. 2010).

44. See *infra* Part II.

45. 548 U.S. 124 (2006) (per curiam).

46. 581 F.3d 1336 (Fed. Cir. 2009).

47. 702 F. Supp. 2d 181 (S.D.N.Y. 2010).

48. See *infra* Parts III.B–D.

49. 149 F.3d 1368 (Fed. Cir. 1998).

50. 130 S. Ct. 3218, 3227 (2010).

method patent cases can be seen in the recent life science litigations involving the use of scientific correlations in patent method claims.⁵¹

This recent cluster of patent eligibility cases from the life sciences has finally generated the legal momentum that is likely to result in definitive interpretations of the eligibility of genes and genetic methods for patenting. For the life sciences, the common-law exclusions from patentable subject matter that coexist with the statutory categories means that there are compositions of matter that would formally qualify but may be barred as products of nature, and there are methods that would formally qualify but may be barred because they preempt natural phenomena or laws of nature. The article will outline the current analytic framework for judging whether genetic-related inventions are patentable subject matter and identify the analytic choices available to decide the patent eligibility question for composition claims to genes and process claims to methods for genetic analysis. The technological-neutrality of patent law coexists with field-specific controversies over patentable subject matter, and the current legal framework reflects this complicated set of realities.

II. THE GENE: PRODUCT OR LAW OF NATURE?

A. Background of the Problem

The patent eligibility of DNA as a product—in the form of genes—has been debated for several decades in U.S. patent law, as well as other fora including the bioethical and scientific communities.⁵² At first glance, DNA can be simply classified as a molecule which fits into the patent-eligible category of composition of matter.⁵³ DNA is often claimed as a molecule in a purified state, which distinguishes it from its native form.⁵⁴ Such claim language is intended to obviate any objection based on lack of novelty.⁵⁵ The United States Patent Trademark Office has endorsed the eligibility of a purified gene for patenting, relying on the reasoning that purification of the DNA molecule results in an isolated form of the molecule that does not

51. See *infra* Part III.A for a discussion of the analytic background and Parts III.B–D for discussions of the application of existing legal tests.

52. See Kane, *supra* note 10, at 521–22 (discussing the debate regarding the patentability of DNA and how it was not resolved by cases such as *Chakrabarty*).

53. 35 U.S.C. § 101 (2006).

54. See Eileen M. Kane, *Splitting the Gene: DNA Patents and the Genetic Code*, 71 TENN. L. REV. 707, 738–39 (2004) (discussing the use of a purified compound as a patentable entity).

55. 35 U.S.C. § 102 (2006).

exist in nature.⁵⁶ In *Amgen v. Chugai*,⁵⁷ where patentable subject matter was not challenged, the Federal Circuit acknowledged the standard claiming practice: “The claims of the ‘008 patent cover purified and isolated DNA sequences encoding erythropoietin [. . .]”⁵⁸ In a later statement reflecting a view that DNA might present some unique analytic challenges for patent law, the court noted that “[A] gene is a chemical compound, albeit a complex one [. . . .].”⁵⁹

Sharp criticism of the issuance of patents on genes has been maintained for years by many genetic testing advocates, who cite particular fields where genetic testing and research has been impeded by patenting.⁶⁰ An academic legal debate over DNA eligibility has focused on the nature of the DNA molecule, with scholars noting that while DNA fits into the category of composition of matter under 35 U.S.C. § 101, its function as an information carrier complicates the analysis.⁶¹ Some have argued for renewed attention to the product of nature doctrine from patent law, a doctrine which has historically been interpreted to exclude the patenting of unaltered natural products,⁶² and asserted its relevance for testing the

56. USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092–02 (Jan. 5, 2001) (“An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound.”).

57. 927 F.2d 1200 (Fed. Cir. 1991).

58. *Id.* at 1203–04.

59. *Id.* at 1206.

60. See, e.g., Lori B. Andrews, *The Gene Patent Dilemma: Balancing Commercial Incentives with Health Needs*, 2 HOUS. J. HEALTH L. & POL’Y 65, 89 (2002) (describing the inhibiting effects of patents to the breast cancer genes on genetic research); John H. Barton, *Emerging Patent Issues in Genomic Diagnostics*, 24 NATURE BIOTECHNOLOGY 939, 940 (2006) (examining the effects of gene patents on genome-wide testing protocols); Jon F. Merz et al., *Diagnostic Testing Fails the Test*, 415 NATURE 577, 577 (2002) (discussing the inhibiting effect of patents on the HFE genes on the availability of diagnostic tests for hereditary haemochromatosis).

61. See Rebecca S. Eisenberg, *Molecules vs. Information: Should Patents Protect Both?*, 8 B.U. J. SCI. & TECH. L. 190, 196 (2002) (characterizing DNA as “a tangible storage medium for information”); Arti K. Rai, *Intellectual Property Rights in Biotechnology: Addressing New Technology*, 34 WAKE FOREST L. REV. 827, 836 (1999) (stating that “[a]lthough DNA is, obviously enough, a chemical compound, it is more fundamentally a carrier of information.”).

62. There is substantial scholarship on the product of nature doctrine, both historically and in modern application. See, e.g., Karl Bozicevic, *Distinguishing “Products of Nature” from Products Derived from Nature*, 69 J. PAT. & TRADEMARK OFF. SOC’Y 415, 425–26 (1987); John M. Conley & Roberte Makowski, *Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents (Part I)*, 85 J. PAT. & TRADEMARK OFF. SOC’Y 301, 319 (2003); John M. Conley & Roberte Makowski, *Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents (Part II)*, 85 J. PAT. & TRADEMARK OFF.

eligibility of genes for patenting.⁶³ An alternative analytic approach identifies the specific ineligibility of genes for patenting as a consequence of the fact that the molecule functions as a template to execute the genetic code; patenting preempts the use of the genetic code, which is a law of nature.⁶⁴ These several theories of gene ineligibility are general (product of nature) and specific (preemption of a law of nature), and illustrate how nuances in the legal analysis result from the singular complexity of the DNA molecule.

B. The Patenting of Two Genes Linked to Cancer Risk: AMP v. USPTO

In *Association for Molecular Pathology v. United States Patent and Trademark Office*,⁶⁵ (*AMP*) a formal challenge to the legitimacy of genes as patentable subject matter was brought by a coalition of professional medical organizations, medical providers, researchers and patients against Myriad Genetics (Myriad) and the USPTO.⁶⁶ Myriad holds significant patent portfolios for the BRCA1 and BRCA2 genes, which have been linked to an elevated risk of developing early-onset breast and/or ovarian cancer.⁶⁷ The Myriad patents are directed to the isolated BRCA1 and BRCA2 genes,⁶⁸ several clinically relevant mutations in the genes,⁶⁹ and short fragments of

SOC'Y 371, 390 (2003); Michael D. Davis, *The Patenting of Products of Nature*, 21 RUTGERS COMPUTER & TECH. L.J. 293, 320 (1995).

63. See, e.g., Conley & Makowski, *supra* note 62, at 397–98 (2003) (revisiting *Chakrabarty* and asserting that many biotechnology patents would be invalid if the product of nature doctrine were to be applied as the Supreme Court intended); Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303, 334–90 (2003) (reviewing the distinction between impure and purified natural products, as well as introducing a “substantial transformation test” for patenting natural products); Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289, 299 (2003) (proposing a “reinvigoration” of the product of nature doctrine for application to DNA patenting).

64. See Kane, *supra* note 54, at 752–53 (arguing for the patent ineligibility of DNA because it embodies the genetic code, which is a law of nature).

65. 702 F. Supp. 2d 181 (S.D.N.Y. 2010).

66. *Id.*

67. See Yoshio Miki et al., *A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene BRCA1*, 266 SCIENCE 66, 66 (1994) (identifying BRCA1 mutations as a significant indicator for early-onset breast and/or ovarian cancer); Richard Wooster et al., *Identification of the Breast Cancer Susceptibility Gene BRCA2*, 378 NATURE 789, 790 (1995) (identifying BRCA2 mutations as increasing the risk of breast and/or ovarian cancer).

68. See *AMP*, 702 F. Supp. 2d at 212 (“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.”).

69. See *id.* at 212 n.29. Claim 7 of the ‘282 patent reads:

the genes used in laboratory assays.⁷⁰ In addition to challenging the composition claims, the suit further alleged the ineligibility of the method claims directed to testing for BRCA1 and BRCA2 mutations.⁷¹ The history of the acquisition and management of these patents has been well documented, and significant criticism of Myriad's practices has followed.⁷² Myriad chose to use its patent rights so that most clinical testing could only be procured through the laboratory services offered by Myriad, which has heightened the scientific and medical concerns over the lack of a competitive genetic testing market.⁷³ Relevant to this suit was that Myriad had targeted some of the plaintiffs for possibly infringing use of the patents in genetic testing.⁷⁴ That fact sufficed for the judge to rule that the plaintiffs had the standing to bring the suit.⁷⁵

The central arguments of the plaintiffs against the patent eligibility of the composition claims to isolated DNA was that the claimed genes are both "products of nature" and "manifestations of laws of nature" for which patents may not be obtained.⁷⁶ Although the Supreme Court has stated that

An isolated DNA selected from the group consisting of: (a) a DNA having the nucleotide sequence set forth in SEQ ID NO: 1 having T at nucleotide position 4056; (b) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having an extra C at nucleotide position 5385; (c) a DNA having the nucleotide sequence set forth in SEQ ID NO: 1 having G at nucleotide position 5443; and (d) a DNA having the nucleotide sequence set forth in SEQ ID NO: 1 having 11 base pairs at nucleotide positions 189-199 deleted.

Id.

70. *Id.* at 212.

71. See *infra* Part III.D. for a discussion of the challenge to the method claims.

72. See, e.g., Richard Gold & Julia Carbone, *Myriad Genetics: In the Eye of the Policy Storm*, 12 GENETICS IN MED. S39, S43-45 (2010) (criticizing Myriad for its failure to account for policy concerns in healthcare during its commercialization); Jon F. Merz, *Disease Gene Patents: Overcoming Unethical Constraints on Clinical Laboratory Medicine*, 45 CLINICAL CHEM. 324, 326 (1999) (discussing how different patent companies have secured licenses for various genetic testing, including tests for Alzheimer's, HFE and BRCA1 and BRCA2); Jordan Paradise, *European Opposition to Exclusive Control Over Predictive Breast Cancer Testing and the Inherent Implications for U.S. Patent Law and Public Policy: A Case Study of the Myriad Genetics' BRCA Patent Controversy*, 59 FOOD & DRUG L.J. 133, 136-37 (2004) (noting that Myriad was exploiting the patent to block all research investigations of BRCA1); Bryn Williams-Jones, *History of A Gene Patent: Tracing the Development and Application of Commercial BRCA Testing*, 10 HEALTH L. J. 123, 132-33 (2002) (discussing the consensus that it was necessary to prevent exclusive control of the patent process by companies like Myriad).

73. See Gold & Carbone, *supra* note 72, at S41-42 (describing how Myriad attempted to stop BRCA testing at competing laboratories after obtaining its patents).

74. *AMP*, 702 F. Supp. 2d at 204-05 (S.D.N.Y. 2010).

75. *Id.* at 205-06 (describing the actions the defendants have taken to assert their exclusive right to BRCA1/2 genetic testing including personal communications, cease and desist letters, licensing offers, and litigation).

76. *Id.* at 184.

“laws of nature, natural phenomena, and abstract ideas” are not patentable,⁷⁷ the initial legal question for the case was whether the purified and isolated DNA was in fact a product of nature and not patentable.⁷⁸ The cases considering this question to date center on what level of human intervention makes a product not natural, and court opinions diverge on when a product is significantly altered from its natural state to legitimize eligibility. The Supreme Court has contended little with this question, with only several cases that investigate the patentability of natural products or inquire as to the kind of inventive application that justifies patenting.⁷⁹

In *American Fruit Growers, Inc. v. Brogdex Co.*,⁸⁰ directed to an invention of a chemically-treated orange, the Supreme Court decided that the addition of borax to the rind of an orange to increase its longevity did not confer a patentable distinction, when compared to an unadulterated orange, to create an article of manufacture, stating “[a]ddition of [the] borax to the rind of [the] natural fruit does not produce from the raw material an article for use which possesses a new or distinctive form, quality, or property.”⁸¹ The Court did not consider improved longevity to be to be a new property, nor did it consider it to be so useful as to support patentability.⁸² It also did not regard the treated orange as possessing any new function as a result of the treatment.⁸³ Later, in *Funk Bros. Seed Co. v. Kalo Inoculant Co.*,⁸⁴ an inventor claimed to have created a novel mixture of bacterial species with no inhibition of function and argued that this accomplishment was not expected and reflected his own inventive contribution.⁸⁵ The Court disagreed, noting that “[h]e who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end.”⁸⁶ The inventor’s focus on the natural non-inhibition actually worked to deny a patent: “[t]he qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of

77. *Diamond v. Diehr*, 450 U.S. 175, 185 (1981).

78. *AMP*, 702 F. Supp. 2d at 222–32 (S.D.N.Y. 2010).

79. *See, e.g.*, *Diamond v. Chakrabarty*, 447 U.S. 303 (1980); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948); *Am. Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1 (1931).

80. 283 U.S. 1 (1931).

81. *Id.* at 11.

82. *Id.* at 11–12.

83. *Id.* at 12.

84. 333 U.S. 127 (1948).

85. *Id.* at 130.

86. *Id.*

knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none.”⁸⁷ The Court’s decision also described the inventor’s work as the “discovery of some of the handiwork of nature.”⁸⁸

In the landmark case of *Diamond v. Chakrabarty*,⁸⁹ where a bacterium was genetically engineered to contain additional genes encoding proteins useful in the degradation of oil spills, the Court confronted a sharper distinction between the natural and the invented, describing the bacterium as a “human-made, genetically engineered bacterium [that] is capable of breaking down multiple components of crude oil”⁹⁰ a property “which is possessed by no naturally occurring bacteria.”⁹¹ The bacterium was compared to the invention in *Funk*: “Here, by contrast, the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature’s handiwork, but his own; accordingly it is patentable subject matter under § 101.”⁹² The Court identified a deceptively simple binary choice for product claims in the life sciences, noting that “the relevant distinction was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions.”⁹³

If the product of nature doctrine requires the exclusion of unaltered, natural products from the patent system, the next question for gene eligibility is factual: is a gene a product of nature or a manifestation of the laws of nature? In *AMP*, the plaintiffs argued that a gene is a product of nature, which is not patentable.⁹⁴ The defendants argued, in contrast, that the isolation and purification of a DNA molecule constitutes an alteration from the natural state, and as such, the DNA is no longer the natural product.⁹⁵ Although the weight of the Supreme Court decisions forbids the patenting of naturally-derived products, proponents of patenting genes and other biomolecules base their arguments on lower court cases. The case most frequently cited for establishing that purification can form the basis for converting a natural product to an inventive form is *Parke-Davis v.*

87. *Id.*

88. *Id.* at 131.

89. 447 U.S. 303 (1980).

90. *Id.*

91. *Id.*

92. *Id.* at 310.

93. *Id.* at 313.

94. 702 F. Supp. 2d at 184 (2010).

95. *Id.* at 224.

Mulford (Parke-Davis).⁹⁶ The defendants further argued that the processing of the DNA molecule rendered it usable, echoing the arguments that were advanced in favor of patenting purified adrenaline in *Parke-Davis*.⁹⁷

The judge first established that products of nature are not patentable, with a review of the relevant cases.⁹⁸ Turning to *Parke-Davis*,⁹⁹ he noted that although Judge Hand had concluded that purified adrenaline was patentable, citing his finding that it became for every practical purpose a “new thing commercially and therapeutically[.]”¹⁰⁰ the holding centered on a novelty analysis, not an eligibility question.¹⁰¹ As such, it did not provide a basis for a purification argument regarding the eligibility of natural molecules.¹⁰²

The judge turned to a deeper investigation of the DNA molecule proposed for patenting, first looking to its function, or “the unique characteristics of DNA that differentiate it from other chemical compounds,”¹⁰³ citing to expert statements regarding the bifunctional nature of DNA as both molecule and information carrier.¹⁰⁴ The court then noted that “This informational quality is unique among the chemical compounds found in our bodies, and it would be erroneous to view DNA as ‘no different’ than other chemicals previously the subject of patents.”¹⁰⁵

In analyzing what the informational component of DNA accomplishes, the judge noted that, “the information encoded by DNA reflects its primary biological function: directing the synthesis of other molecules in the body.”¹⁰⁶ This statement clearly acknowledges the singular attribute of DNA as a template. How does that template work? “DNA, and in particular the ordering of its nucleotides, therefore serves as the physical embodiment of laws of nature—those that define the construction of the human body.”¹⁰⁷ This function remains in the isolated form of the molecule: “The preservation of this defining characteristic of DNA in its native and isolated forms mandates the conclusion that the challenged

96. 189 F. 95 (C.C.S.D.N.Y. 1911) (holding that the purified adrenaline was patentable).

97. 189 F. at 103.

98. *AMP*, 702 F. Supp. 2d at 220–32.

99. 189 F. at 95.

100. *Id.* at 103.

101. *AMP*, 702 F. Supp. at 225.

102. *Id.* at 225–26.

103. *Id.* at 228.

104. *Id.*

105. *Id.*

106. *Id.*

107. *Id.*

composition claims are directed to unpatentable products of nature.”¹⁰⁸ In his citation of “the unique characteristics of DNA that differentiate it from other chemical compounds,”¹⁰⁹ the judge highlighted the fact that his method of analysis is explicitly DNA-centric, although anchored in the product of nature doctrine. He locates the identity of DNA along a molecule-function-information-template axis to reach a conclusion that the unaltered and unique template function of DNA survives purification, and the isolated gene therefore remains a product of nature.

The specific patent ineligibility of the genes can be further theorized by understanding the genes as the natural exemplars of the genetic code, which is a law of nature.¹¹⁰ With this characterization of DNA function, the eligibility analysis is extended further along a molecule-function-information-template-law of nature axis, and the inquiry shifts to asking whether patenting preempts a law of nature, a question that is distinct from the product of nature analysis. It has long been established that “manifestations of laws of nature [are] free to all men and reserved exclusively to none.”¹¹¹ At the genome-wide level, the patenting of genes can be viewed as an application of the merger doctrine to understand how the preemption of a law of nature occurs—if the finite set of expressions (the genes) of the underlying law of nature (the genetic code) are subject to private appropriation, then the underlying law of nature has itself been preempted through patenting.¹¹² This theory of the specific patent ineligibility of genes is consonant with the focus of the *AMP*¹¹³ court on the “unique characteristics”¹¹⁴ of DNA, which can be translated to the bifunctional identity of DNA—as molecule and template. While the defendants argued that making the DNA useable is the result of purification,¹¹⁵ and thus worthy of patent recognition, the weight of the opinion is that any exclusive “use” of DNA obtained through patent protection is to be avoided, precisely because its critical template functions require that it remain in the public domain.

108. *Id.* at 229.

109. *Id.* at 228.

110. See Kane, *supra* note 54, at 744, 752 (describing the function of DNA as executing the genetic code and characterizing the genetic code as a law of nature).

111. Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1947).

112. Kane, *supra* note 54, at 754. The merger doctrine from copyright law identifies instances where property rights in all expressions of an underlying idea amount to practical ownership of the idea itself. *Id.*

113. 702 F. Supp. 2d 181 (2010).

114. *Id.* at 228.

115. *Id.* at 230.

In conclusion, the judge accepted the arguments of the plaintiffs that the patenting of genes violates the prohibitions against patenting products of nature or manifestations of the laws of nature, and ruled that the challenged patent claims were invalid.¹¹⁶ The general applicability of the product of nature analysis in the opinion remains to be determined: should the maintenance of native biological function foreclose the eligibility of any natural product, including all biomolecules, or, alternatively, does the singular biological function of DNA create an entitlement to designation as a very special “product of nature?” The analysis is important, because one view will support a generic application of this product of nature analysis in biotechnology, while the other, narrower interpretation of the product of nature analysis highlights the unique and important function of DNA as the basis for its analysis. The judge’s characterization of DNA as the embodiment of a law of nature supports a theory of specific patent ineligibility for DNA, a conclusion that does not extend to other molecules. It is important to note that although the opinion is particularly DNA-centric, it establishes the complex ineligibility of DNA for patenting according to patent law norms, rather than as a statement of genetic exceptionalism. The appeal to the Federal Circuit will now provide the appellate court with its first opportunity to decide an eligibility challenge to gene patents.

Why wasn’t the patent eligibility of a gene litigated until now? There are several reasons, including the disinclination of commercially similar litigants as well as the absence of any formal opposition mechanism in U.S. patent law.¹¹⁷ In the absence of any formal eligibility decision on gene patents from the courts, remedial actions to limit any harm from gene patenting have been proposed. Legislative proposals to exclude genetic-related inventions from patentable subject matter have been made at the federal level, but none have been enacted.¹¹⁸ In another approach, the recent SACGHS report recommended certain liability exclusions that would alleviate the impact of gene patents on research and patient care.¹¹⁹

116. *AMP*, 702 F. Supp. 2d at 232.

117. See generally Kane, *supra* note 10, at 557.

118. A recent example is the Genomic Research and Accessibility Act, H.R. 977, 110th Cong. § 2 (2007). This bill would have added a new Section 106 to the patent statute: “Notwithstanding any other provision of law, no patent may be obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies.” In addition to singling out genetic products, the addition of the correlations may have excluded any patent claims to methods for the relevant genetic testing which exploit any identified mutations as the basis for identifying clinical risk.

119. Perhaps not surprisingly, after concluding that patents are less necessary than often thought, and yet pose less obstacles than frequently claimed, the SACGHS report does not call for a fundamental realignment of patentable subject matter to exclude gene patenting. In contrast, the

Ironically, however, *AMP* emerges in a climate where some empirical knowledge has emerged regarding how gene patenting impacts the genetic testing field, with credible evidence supporting the conclusion that gene patents have not caused widespread underdevelopment of genetic science.¹²⁰ However, the Myriad patent management practices have continued to draw distinct attention as some of the most pernicious, with recent comparative data emerging to illustrate a negative effect from the patents on the breast cancer genetic testing field, in comparison with the development of other similarly situated cancer-related genetic tests.¹²¹ Moreover, some of the plaintiffs in *AMP* were targets of enforcement actions from Myriad for their activities related to providing genetic testing for patients.¹²² As a result, litigation over patent ineligibility remains an obvious pressure point in the efforts to expand the use of the BRCA1 and BRCA2 genes for use in genetic testing and research. Beyond the specific eligibility analysis of genes, *AMP* is also an opportunity for the courts to further clarify how the product of nature/law of nature doctrines apply to the modern patenting of molecules produced from biotechnology.

III. METHOD CLAIMS AND LAWS OF NATURE: APPLIED USES OR PREEMPTIVE EFFECT?

A. Background of the Problem

The evaluation of method claims relevant to genetic testing fits into wider controversies over the patenting of methods in business, software, and general human activities. A central observation in the current analytic picture for the eligibility of method claims in genetic testing is that the recent analytic tests that have dominated eligibility decisions were developed by the Federal Circuit from cases investigating the patent eligibility of business methods. The era began with *State Street v. Signature*,¹²³ which presented a patent claim to a software-implemented

SACGHS opted to call for “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.” SACGHS Report, *supra* note 25, at 4. In addition, the report calls for “an exemption from patent infringement liability for those who use patent-protected genes in the pursuit of research.” *Id.* This is a moderate proposal, in that it effectively nullifies the impact of some gene patents for some purposes, while not recommending a wholesale elimination of such patents through a formal subject matter exclusion.

120. See *supra* notes 25 and 33 and accompanying text.

121. See Cook-Deegan et al., *supra* note 34, at S29 (documenting that Myriad’s patents may be responsible for a chilling effect on further development of genetic tests for the BRCA1 and BRCA2 genes).

122. *Id.* at 204–06.

123. *State St. Bank & Trust Co. v. Signature Fin. Grp., Inc.*, 149 F.3d 1368 (Fed. Cir. 1998).

method for financial accounting.¹²⁴ While arguably a typical software case, the Federal Circuit struggled again with the possible patenting of an algorithm or mathematical formula, the lingering controversy that accounted for decades of wrangling over software patent eligibility.¹²⁵ The court offered a new standard that did not require a proposed invention to fit into a category of 35 U.S.C. § 101; instead, an invention that achieved a “useful, concrete and tangible result” (UCT) would be eligible.¹²⁶ Over the decade since that decision, patent applicants relied on the UCT test articulated in that case to advance many inventions that lacked obvious tangibility, but which, arguably, could achieve a useful result.¹²⁷ The UCT test survived for nearly a decade, although on shaky ground, as illustrated by Justice Breyer’s comment in 2006 that, “[T]his Court has never made such a statement and, if taken literally, the statement would cover instances where this Court has held the contrary.”¹²⁸

A redesigned analytic framework emerged from the Federal Circuit during *In re Bilski (Bilski)*,¹²⁹ the first business method patent case to be heard later by the Supreme Court.¹³⁰ At issue was a claim to a method of commodity trading that was untethered to software implementation; arguably, a pure business method patent.¹³¹ Underneath the eligibility

124. *Id.* at 1373.

125. See, e.g., Richard S. Gruner, *Intangible Inventions: Patentable Subject Matter for an Information Age*, 35 LOY. L.A. L. REV. 355, 384–86 (2002) (discussing the patentability of algorithms and mathematical formulas); Pamela Samuelson, *Benson Revisited: The Case Against Patent Protection for Algorithms and Other Computer Program-Related Inventions*, 39 EMORY L.J. 1025, 1025 (1990).

126. *State St.*, 149 F.3d at 1373. This test had also been used to decide the eligibility of a rasterizer that mathematically transforms data in *In re Alappat*, 33 F.3d 1526, 1544 (Fed. Cir. 1994).

127. See, e.g., *AT&T Corp. v. Excel Commc’ns, Inc.* 172 F.3d 1352, 1353, 1357–58, 1361 (Fed. Cir. 1999) (relying on the UCT test to uphold patentability of a method for recording a telephone call recipient’s primary interexchange carrier).

128. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 136 (2006) (Breyer, J., dissenting).

129. *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) (en banc).

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

131. *In re Bilski*, 545 F.3d at 949 (“Claim 1: A method for managing the consumption risk costs of a commodity sold by a commodity provider at a fixed price comprising the steps of: (a) initiating a series of transactions between said commodity provider and consumers of said commodity wherein said consumers purchase said commodity at a fixed rate based upon historical averages, said fixed rate corresponding to a risk position of said consumer; (b) identifying market participants for said commodity having a counter-risk position to said consumers; and (c) initiating a series of transactions between said commodity provider and said market participants at a second fixed rate such that said series of market participant transactions balances the risk position of said series of consumer transactions.”).

question was the tangibility analysis that had plagued software cases, but now particularly plagued the non-software business/human activity method claims that arose in the post-*State Street* decade, and elicited widespread criticism.¹³² *Bilski* provided an opportunity for the Federal Circuit to revisit the *State Street* standard, and it concluded that the UCT test was “inadequate.”¹³³ It framed its inquiry as “whether Applicants are seeking to claim a fundamental principle (such as an abstract idea) or a mental process.”¹³⁴ Having structured the problem, it stated that the Supreme Court had already provided a “definitive test to determine whether a process claim is tailored narrowly enough to encompass only a particular application of a fundamental principle rather than to pre-empt the principle itself.”¹³⁵ The court announced that “the machine-or-transformation (MOT) test outlined by the Supreme Court is the proper test to apply.”¹³⁶ If a machine implementation is readily identifiable, then patentable subject matter is presumed. However, if that is not present, then the presence of a “transformation” in the patent claim will also signify patentable subject matter.¹³⁷ The Federal Circuit had now established that the MOT test would do the work of the preemption analysis, so that the tests could be

132. See John R. Thomas, *The Patenting of the Liberal Professions*, 40 B.C. L. REV. 1139, 1181 (1999) (arguing that patentable subject matter should exclude business methods which “do not comprise technology and should not be within the grasp of the patent system”).

133. *In re Bilski*, 545 F.3d at 959–60.

134. *Id.* at 952.

135. *Id.* at 954. The preemption analysis is central to the exclusion of natural principles, laws and phenomena, as it identifies those scenarios where essential knowledge has been removed from the public domain. The *Bilski* Court identified a nexus between the preemption analysis and the machine or transformation test:

A claimed process involving a fundamental principle that uses a particular machine or apparatus would not pre-empt uses of the principle that do not also use the specified machine or apparatus in the manner claimed. And a claimed process that transforms a particular article to a specified different state or thing by applying a fundamental principle would not pre-empt the use of the principle to transform any other article, to transform the same article but in a manner not covered by the claim, or to do anything other than transform the specified article.

Id.

136. *Id.* at 960. The Court explained that “[a] claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.” *Id.* at 954. The machine-or-transformation test has two further aspects: “the use of a specific machine or transformation of an article must impose meaningful limits on the claim’s scope to impart patent-eligibility,” and “the involvement of the machine or transformation in the claimed process must not merely be insignificant extra-solution activity.” *Id.* at 961–62 (citations omitted).

137. *Id.* at 961.

viewed as congruent.¹³⁸ However, in her dissent, Judge Newman pointed out that an invention which is evaluated as a possible abstract idea is not necessarily testing the boundaries of patenting fundamental ideas; Bilski's invention was "not a fundamental principle or an abstract idea; it is not a mental process or a law of nature."¹³⁹ She criticized the court for its interconversion of eligibility tests: "The court then concludes that because Bilski's Claim 1 fails the machine-or-transformation test it *ipso facto* preempts a 'fundamental principle' and is thereby barred from the patent system under Section 101: an illogical leap that displays the flaws in the court's analysis."¹⁴⁰ The interconversion of eligibility tests that occurred in the cases deciding the patenting of business methods is potentially problematic in cases that more clearly contest any patenting of fundamental knowledge which could violate the prohibition on patenting laws of nature and natural phenomena; such cases are likely to arise from the life sciences.¹⁴¹

The centrality of the MOT test to the eligibility of patent method claims was revisited by the Supreme Court in *Bilski v. Kappos*.¹⁴² The Court declared that the MOT test was not the "sole test" for deciding whether method claims constitute patentable subject matter.¹⁴³ Nearly two years passed between the Federal Circuit's declaration that the MOT test was mandatory and the Supreme Court's review which relaxed this requirement. The eligibility of life science patent method claims containing scientific correlations was contested during those years, and the resulting decisions occurred against this unstable analytic background, as will be discussed in Parts III.C., *infra* (*Prometheus v. Mayo*)¹⁴⁴ and III.D., *infra* (*AMP*).¹⁴⁵ As a result, these opinions reflect the analytic framework that was dominant at the time, regardless of the fact that the framework originally arose from business method patent cases.

138. *See id.* at 963 (stating that "the prevention of pre-emption of fundamental principles" was the basis for the machine-or-transformation test).

139. *Id.* at 995 (Newman, J., dissenting).

140. *Id.* at 996 (Newman, J., dissenting).

141. *See infra* Parts III.B.,D.

142. 130 S. Ct. 3218 (2010).

143. *Id.* at 3227.

144. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336 (Fed. Cir. 2009).

145. *AMP v. USPTO*, 702 F. Supp. 2d 181 (2010).

B. Bimolecular Relationship with Clinical Implications: LabCorp v. Metabolite

In *Laboratory Corporation of America Holdings v. Metabolite Laboratories, Inc.*,¹⁴⁶ (*LabCorp*) the patent at issue claimed a method for detecting a vitamin deficiency by utilizing the quantitative relationship between the levels of the amino acid homocysteine and several B vitamins.¹⁴⁷ There is an inverse relationship between the homocysteine and vitamin B levels, and that observation can be exploited to assess the clinical condition of the patient.¹⁴⁸

The defendant had not raised a formal invalidity challenge to the patent claims for lack of patentable subject matter in the trial court, although, in the petition for certiorari filed by the petitioner *LabCorp* in the Supreme Court, the question of whether “a method patent . . . can validly claim a monopoly over a basic scientific relationship” was advanced.¹⁴⁹ While there is no specific reference to 35 U.S.C. § 101, the petitioners stated that “scientific facts and laws of nature are outside the scope of patentable inventions.”¹⁵⁰ The fact that patentable subject matter had not formally been raised in the lower court complicated the suitability of this particular case for a significant ruling on this doctrine. While considering the petition for review, the Supreme Court invited the Solicitor General to file a brief in the case, and directed attention to a newly posed question that directly invoked its trilogy of exclusions from patentable subject matter: “Is the patent invalid because one cannot patent ‘laws of nature, natural phenomena, and abstract ideas?’”¹⁵¹ In this unusual procedural scenario, the Supreme Court initiated a more formal review of patentable subject

146. 548 U.S. 124 (2006) (per curiam).

147. *Id.* at 128. Claim 13 is as follows: “A method for detecting a deficiency of cobalamin or folate in warm-blooded animals comprising the steps of: assaying a body fluid for an elevated level of total homocysteine; and correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate.” *Id.*

148. *LabCorp*, 548 U.S. at 128.

149. Brief for Petitioner at i, *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124 (2006) (No. 04-607), 2004 WL 2505526, available at http://patentlaw.typepad.com/patent/files/labcorp_Petition_for_certiorari.pdf. Question 3 stated:

Whether a method patent setting forth an indefinite, undescribed, and non-enabling step directing a party simply to ‘correlat[e]’ test results can validly claim a monopoly over a basic scientific relationship used in medical treatment such that any doctor necessarily infringes the patent merely by thinking about the relationship after looking at a test result.

Id.

150. *Id.* at 18.

151. Invitation to Solicitor General, *LabCorp v. Metabolite*, 543 U.S. 1185 (2005).

matter, despite the lack of any challenge in the lower courts. Ultimately, the Court concluded that it should not decide the issue.¹⁵² This decision by the Court occurred against a backdrop of intense interest in the case, which included the filing of numerous amicus briefs from professional medical organizations and clinical laboratory associations.¹⁵³ The controversy was heightened due to the enforcement strategy of the patent holders, who had alleged contributory infringement on the part of those who simply disseminated the fact of the scientific correlation.¹⁵⁴

Justice Breyer filed a dissent that criticized the court for failing to decide the issue of patentable subject matter, noting that:

*To fail to do so threatens to leave the medical profession subject to the restrictions imposed by this individual patent and others of its kind. Those restrictions may inhibit doctors from using their best medical judgment; they may force doctors to spend unnecessary time and energy to enter into license agreements; they may divert resources from the medical task of health care to the legal task of searching patent files for similar simple correlations.*¹⁵⁵

The dissent then undertook the analysis that the court had avoided. Justice Breyer stated: “There can be little doubt that the correlation between homocysteine and vitamin deficiency set forth in claim 13 is a ‘natural phenomenon.’”¹⁵⁶ He rejected the idea that the scientific relationship was embedded in a specific method claim that implicitly narrowed the scope of the claim and preserved the wider use of the natural phenomenon: “But one can reduce *any* process to a series of steps. The question is what those steps embody. And here, aside from the unpatented test, they embody only the correlation between homocysteine and vitamin deficiency that the researchers uncovered.”¹⁵⁷ Thus, the dissent arrives at a conclusion that Claim 13 effectively monopolizes the scientific correlation between the

152. *LabCorp*, 548 U.S. at 125.

153. *See id.* at 124–25 (describing briefs filed by various laboratories, organizations and individuals); *see also* Supreme Court: LabCorp Briefing Round I, PATENT LAW BLOG (Jan. 5, 2006), http://patentlaw.typepad.com/patent/2006/01/supreme_court_1.html.

154. *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1365 (Fed. Cir. 2004), *cert. denied*, 548 U.S. 124 (2006).

155. *LabCorp*, 548 U.S. at 138 (Breyer, J., dissenting).

156. *Id.* at 135.

157. *Id.* at 137–38.

levels of homocysteine and vitamin B, and preempts the use of a natural phenomenon, which is not allowed.¹⁵⁸

The method claim in *LabCorp* has a generic format as a laboratory assay which determines a primary fact (one biochemical measurement) as a marker for the determination of a secondary fact, which, in this case, is the correlative vitamin level of a patient. More generally, examples of a secondary fact to be determined could be any another molecular measurement, an inference regarding a pharmaceutical regimen, or a diagnostic conclusion. Is the relationship between the primary and secondary facts a scientific correlation which is the result of natural biological phenomena at work? Such claim modeling can be useful to identify other patent method claims which may devolve to nothing more than a natural phenomenon structured as a series of steps in a process. *LabCorp* raised the profile of this kind of method claim in the life sciences, and invited more detailed examination of these claims under the eligibility analysis provided by 35 U.S.C. § 101.¹⁵⁹ It is important to note that the analytic framework for the Breyer dissent was the traditional assessment for the presence of a natural phenomenon, and whether it was preempted by the patent claim; several other analytic options were rejected.¹⁶⁰ Breyer discarded the “useful concrete and tangible result” (UCT) test which was then extant as a result of *State Street*.¹⁶¹ He also rejected an argument, based in earlier process patent jurisprudence, that would evaluate the claim for the presence of a “transformation” that would signal a more conventionally patentable process, in language that would foreshadow the issues later raised by the method claims in *Prometheus v. Mayo* and *AMP*.¹⁶² More generally for the field, the sharp contrast between the formal silence of the Court on the eligibility issue and the spirited dissent from Justice Breyer on the dangers posed by patenting subject matter that belonged in the public domain signaled that this debate would remain unresolved.

158. *See id.* at 135.

159. *See, e.g.,* Cynthia M. Ho, *Lessons From Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*, 23 SANTA CLARA COMPUTER & HIGH TECH. L.J. 463, 464 (2007) (noting that the dismissal of certiorari leaves patent lawyers and institutional bodies waiting for a resolution on the scope of patentable subject matter).

160. *LabCorp*, 548 U.S. at 138 (Breyer, J., dissenting).

161. *Id.* at 136.

162. *Id.* (“Why should it matter if the test results themselves were obtained through an unpatented procedure that involved the transformation of blood?”). *See infra* Part III.C.

C. Metabolic State and Therapeutic Effect: Prometheus v. Mayo

*Prometheus Laboratories Inc. v. Mayo Collaborative Services*¹⁶³ (*Prometheus I*) presented a patent claim to a method of therapeutic optimization that exploited an understanding of drug metabolism to more precisely tailor pharmaceutical dosage.¹⁶⁴ The claim format was a method of treatment claim that relied on an understanding of the pharmacokinetics of the administered drug.¹⁶⁵ Specifically, the method of treatment called for adjusting dosage levels of thiopurine drugs after administration by determining the level of a drug metabolite, 6-TG, which can be toxic at higher levels and undermine any therapeutic response.¹⁶⁶

The invalidity challenge for lack of patentable subject matter centered on the alleged presence of a scientific correlation or natural phenomenon that formed the basis of Claim 1; the correlation was the relationship between the metabolite levels and the toxicity of the pharmaceutical.¹⁶⁷ The district court and the Federal Circuit disagreed about claim construction. The lower court found that “the claims recite the correlations themselves”¹⁶⁸ while the Federal Circuit stated that “the claims are to transformative methods of treatment, not correlations.”¹⁶⁹ These statements flag the very different analytic frameworks applied to the claims by these courts. The district court identified the presence of a natural phenomenon as the defining characteristic of the patent method claim, and concluded that

163. 581 F.3d 1336 (Fed. Cir. 2009).

164. *Id.* at 1340 (“Claim 1 of the ‘623 patent is representative of the independent claims asserted by Prometheus in this case: 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 8×10^8 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 8×10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.”).

165. *See id.* at 1339.

166. *Id.* at 1339–40.

167. *Id.* at 1340–41 (“Mayo contended that the patents impermissibly claim natural phenomena—the correlations between, on the one hand, thiopurine drug metabolite levels and, on the other hand, efficacy and toxicity—and that the claims wholly preempt use of the natural phenomena.”).

168. *Prometheus Labs. v. Mayo Collaborative Servs.*, No. 04cv1200 JAH (RBB), 2008 U.S. Dist. LEXIS 25062, at *18 (S.D. Cal. Mar. 28, 2008). “Because the claims cover the correlations themselves, it follows that the claims ‘wholly pre-empt’ the correlations.” *Id.* at *35.

169. *Prometheus*, 581 F.3d at 1349.

preemption occurred, invalidating the claim.¹⁷⁰ However, in the period between the district court and Federal Circuit decisions in *Prometheus I*, *Bilski*¹⁷¹ was decided by the Federal Circuit, and it established that the MOT test was mandatory for the evaluating the eligibility of method claims.¹⁷² Of course, *Bilski* is not a patent case from the life sciences but a challenge to the patentability of business methods.¹⁷³ The Federal Circuit decision in *Prometheus I* illustrates how an analytic test derived from the business method patent controversies can govern the eligibility analysis of subject matter in the life sciences.¹⁷⁴

In applying the MOT test to the method claim at issue in *Prometheus I*, the Federal Circuit went to great lengths in order to identify where transformations might occur.¹⁷⁵ The court decided that transformations were accomplished by the administration of the drug to the patient and the subsequent act of analyzing the blood of a patient for the levels of 6-TG, thus satisfying the MOT test for eligibility.¹⁷⁶ The Federal Circuit criticized the district court for “failing to recognize that the first two steps of the asserted claims are not merely data-gathering steps.”¹⁷⁷ Numerous amicus briefs filed in the case noted the chilling effect of the method claims on the use of basic scientific facts.¹⁷⁸ However, the Federal Circuit disagreed and stated that the patent claims “do not preempt natural processes; they utilize them in a series of specific steps.”¹⁷⁹ Although the MOT test was the primary framework for considering the eligibility of the method claims, the analysis of the court further defined the method claim as an application, rather than a preemption, of a natural phenomenon.

170. *Prometheus*, 2008 U.S. Dist. LEXIS 25062, at *14.

171. 545 F.3d 943 (Fed. Cir. 2008) (en banc).

172. *Id.* at 959 (noting that the machine-or-transformation test is the applicable test for patent-eligible subject matter). *See also supra* notes 130–44 and accompanying text.

173. *See id.* at 949 (“In essence, the claim is for a method of hedging risk in the field of commodities trading.”).

174. *See Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1350 (Fed. Cir. 2009) (noting that the claimed methods in *Prometheus* satisfy all requirements of *Bilski*’s transformation test for patentability).

175. *Id.* at 1346–47 (discussing the transformation which must occur to determine the levels of 6-TG or 6-MMP).

176. *Id.* at 1347, 1350.

177. *Id.* at 1347.

178. *See e.g.*, Brief of American College of Medical Genetics et al. as Amici Curiae Supporting Respondents at 25–26, *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336 (Fed. Cir. 2009) (No. 2008-1403) (noting negative impacts of patents on scientific facts, including stifling innovation, increasing health care costs, and interference with medical providers in patient care).

179. *Prometheus*, 581 F.3d at 1349.

When *Bilski v. Kappos*¹⁸⁰ reached the Supreme Court, the court eliminated the MOT test as the sole determinant of the patentability of a method claim.¹⁸¹ It stated that the test could be useful, but not be mandatory.¹⁸² The Supreme Court then remanded *Prometheus I* back to the Federal Circuit to reconsider the patentable subject matter analysis in view of the multi-dimensional analysis it now endorsed.¹⁸³ *Prometheus II* has now been reconsidered by the Federal Circuit.¹⁸⁴ The court again concluded that the method claims were patentable subject matter, noting that they “recite a patent-eligible application of naturally occurring correlations”¹⁸⁵ and “do not wholly preempt all uses of the recited correlations.”¹⁸⁶

The method of treatment claim in *Prometheus III* incorporates the use of an uninvited scientific correlation to execute its goal of therapeutic optimization. It has long been established that method of treatment claims are a generally allowable form of patentable subject matter, and that premise works to enhance the eligibility of this particular claim. However, the analysis of this complex patent method claim must contend with a possible distinction in patent law between methods of treatment and underlying biochemical mechanism of effect. Ultimately, that dividing line is actually between the invented and the natural. It must be considered whether all substantial practical applications of the scientific relationship are preempted by the claim—in this case, the fact that 6-TG levels are responsible for drug toxicity. Moreover, the administration of the drugs, while transformative, is not the novel aspect of the method. Therefore, further analytic work must consider how the *Bilski*-inspired focus on transformations may dictate an analytic sequence that under analyzes the central question of preemption: are all substantial practical applications of a scientific correlation now covered by a patent claim? If that question is formally asked at the beginning, and an authoritative answer provided, the answer should then be synthesized with a transformation analysis, if utilized, in order to ensure that the requirement for excluding laws of nature and natural phenomena from the patent system is maintained.

180. 130 S. Ct. 3218 (2010).

181. *Id.* at 3226.

182. *Id.* at 3227 (noting that the machine-or-transformative test is “a useful and important clue” but is not “the sole test for deciding whether an invention is a patent-eligible ‘process’”).

183. *Prometheus*, 581 F.3d 1336 (Fed. Cir. 2009), No. 09-490, *vacated and remanded*, 78 USLW 3254 (U.S. June 29, 2010).

184. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 2010 U.S. App. LEXIS 25956 (Fed. Cir. 2010).

185. *Id.* at *20.

186. *Id.*

D. Genotype and Phenotype: AMP v. USPTO

In *AMP*,¹⁸⁷ the plaintiffs challenged the eligibility of patent claims to methods for determining whether the DNA sequence of an individual revealed any mutation in the BRCA1 or BRCA2 genes that conferred a higher risk for early onset breast and/or ovarian cancers.¹⁸⁸ This patent claim exploits the molecular status of an individual, revealed through the DNA sequence (primary fact), to infer a clinical fact about a patient (secondary fact). It is an example of predictive genetic testing.¹⁸⁹ In the cancer field, the identification of BRCA1 and BRCA2 mutations which explain a genetic tendency for some to develop early-stage breast and/or ovarian cancer has led to the demand for genetic testing for individuals wishing to learn whether they carry mutations in their genes that elevate their susceptibility to the early-onset cancers.¹⁹⁰ The plaintiffs argued that the scientific correlation central to the claim, in the form of a classic genotype/phenotype relationship, was a law of nature, and the method of analysis was simply an abstract idea; in either case, the claim was ineligible for patenting.¹⁹¹

In the *AMP* decision, the judge centered his analysis on the application of the MOT test to the method claims.¹⁹² As referenced in the earlier discussion for *Prometheus I*,¹⁹³ the eligibility standard for the method claims was the MOT test from *Bilski* that was elevated to answer the most pressing question in the business method patent field.¹⁹⁴ The judge found that the claims did not pass the MOT test, as any purported transformation

187. 702 F. Supp. 2d 181 (S.D.N.Y. 2010).

188. *Id.* at 185. Claim 1 of U.S. Patent No. 5,709, 999 is as follows:

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.

Id. at 213.

189. *See supra* note 29.

190. *See* Miki et al., *supra* note 67, at 66 (discussing the connection between BRCA1 and BRCA2 and breast and ovarian cancers).

191. Plaintiffs' Memorandum of Law in Support of Motion for Summary Judgment at 19, *AMP v. USPTO*, 702 F. Supp. 2d 181 (2010) (No. 09 Civ. 4515), available at http://www.aclu.org/files/assets/brca_08262009_memoinsupportof_motionforsummjudge1.pdf.

192. *See AMP*, 702 F. Supp. 2d at 233 (articulating the application of the machine-or-transformation test).

193. *See supra* Part III.C.

194. *See supra* notes 139-44 and accompanying text.

in the claims comparing patient DNA to normal DNA was not essential to the patent claim, and was simply a predicate to obtaining the data.¹⁹⁵ In the rote application of the existing standard which required that any method claim be evaluated according to the MOT test, a more formal analysis of the public domain inspired prohibitions (laws of nature, natural phenomena) did not occur.¹⁹⁶

The application of the MOT test to the genetic testing method claims in *AMP* resulted in a finding that the claims lacked any transformations which would confer patent eligibility. This is a different outcome from the application of the MOT test to the method claims in *Prometheus I/II*. However, the more complex claim in *Prometheus I/II*, as discussed in Part III.C, *supra*, subsumed the use of the scientific correlation within a standard method of treatment claim. That claim structure allowed the courts to focus on the treatment method, and to leverage its potential eligibility in a manner that avoided a detailed examination of whether the scientific correlation became preempted by the patent claim. The genetic testing claim in *AMP* is a more direct presentation of the preemption question, as the claim is essentially reciting the performance of a laboratory assay utilizing the scientific correlation. As a result, the claim analysis by the court identifies the purported transformations as simply incident to the establishment of the genotype/phenotype relationship, and therefore insufficient to support eligibility. While the reasoning in *Prometheus I* is explained by application of the MOT test,¹⁹⁷ the analysis in *AMP* is distracted by the test. In both cases, the life science field was deprived of a fuller analysis of the public domain inspired exclusions of subject matter that could have been performed, where more attention would be given to identifying when a natural phenomenon is presented and when it is preempted. The genetic testing claim in *AMP* is more analogous to the method claim presented in

195. *AMP*, 702 F. Supp. 2d at 236 (noting that “the transformations [. . .] would constitute no more than ‘data gathering step[s]’ [sic] that are not ‘central to the purpose of the claimed process’”).

196. See *id.* at 236–37 (describing the isolation and sequencing of DNA as merely data-gathering steps). See also generally Brian P. Murphy & Daniel P. Murphy, *Bilski’s “Machine-or-Transformation” Test: Uncertain Prognosis for Diagnostic Methods and Personalized Medicine Patents*, 20 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 755, 757–58 (2010) (arguing that the Fundamental Principles Exception is superior to the machine-or-transformation test because it more closely aligns with public policy). The judge did find that Claim 20, directed to a method for assaying a chemotherapeutic compound in a transformed cell, was an attempt “to patent a basic scientific principle.” *AMP*, 702 F. Supp. 2d at 237.

197. See Murphy & Murphy, *supra* note 196, at 774 (“In our view, the mandatory machine-or-transformation test caused the court to strain unnecessarily to try to fit a square peg into a round hole by arguing that the claims are methods of treatment.”).

LabCorp; both are laboratory assays that can result in the exclusive control of the use of an uninvended scientific correlation. As a result, the issues left unresolved by the Supreme Court in *LabCorp* are now resurfacing in the form of the genetic testing claim in *AMP*. The impact of these deliberations will be felt in genetic medicine, but even more broadly, across the wider fields of biochemical testing, where the limits of patent eligibility for the molecular observations from modern biological science remain unclear.

E. Scientific Correlations in the Era of Reductionism

What are the common attributes of the disputed patent method claims in *LabCorp*, *Prometheus I/II* and *AMP*? All of the claims center on identifying a data point (the primary fact), whether the homocysteine levels in *LabCorp*, the metabolite levels in *Prometheus*, or the presence of a DNA mutation in *AMP*.¹⁹⁸ From the status of that observable and measurable data point, one is led to a conclusion regarding the patient's metabolic state, the therapeutic potential of a pharmaceutical, or a patient's genetic susceptibility to cancer (the secondary fact). None of these claims, in their most general form, specifically require the use of a particular test method or device.¹⁹⁹ The absence of these limiting mechanisms more clearly points to the conclusion that the claims must be evaluated for impermissibly claiming natural phenomena. Potentially, any knowledge of the data point/primary fact—whether deliberately procured or assayed or incidentally obtained—will set up the possibility of infringement if the data is interpreted to arrive at a correlative conclusion/secondary fact.

The patent method claims for genetic testing can capture the basic techniques of molecular medicine. Classical genetics advanced the theory of genotype and phenotype—a distinct chemical composition explaining biological manifestations. Modern molecular biology has allowed precise defining of the genotype of an individual down to the level of the genes, the DNA. The much-heralded arrival of genetic testing to offer the genome-level view promises to offer an individual a clinical forecast based on an innate genetic makeup, a personalized therapeutic regimen, or a precise diagnostic assessment. Patent claims which essentially cover the foundational genotype/phenotype relationships that comprise genetic

198. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 128 (2006) (Breyer, J., dissenting); *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1339 (Fed. Cir. 2009); *AMP v. USPTO*, 702 F. Supp. 2d 181, 185 (S.D.N.Y. 2010).

199. See *LabCorp.*, 548 U.S. at 125 (“The process consists of using any test (whether patented or unpatented) to measure the level in a body fluid of an amino acid called homocysteine [. . .]”); *Prometheus*, 581 F.3d at 1339–40; *AMP*, 702 F. Supp. 2d at 185.

science may impermissibly preempt the use of the most basic genetic knowledge; the future appellate review of *AMP* may provide some authoritative guidance. Following the recent *Prometheus II* decision,²⁰⁰ the question of whether scientific correlations that are tethered to treatment methods—such as the use of genotype/phenotype correlations in personalized therapeutic designs—are fully vetted for possible preemption requires further deliberation.

The recent life science cases in the discussion illustrate several method claim formats that require an analysis for the patenting of natural phenomena: the simple laboratory assay-based method claim (*LabCorp, AMP*) or the more complex method of treatment claim (*Prometheus I/II*). Collectively, they illustrate the modern scope of the reductionism in the life sciences, which characterizes biological reality as the output from molecular interactions. Other upcoming patenting dilemmas in the life sciences arise from method claims that may capture the basic intellectual tasks in standard medical care. *Classen Immunotherapies v. Biogen IDEC*,²⁰¹ a life science case that presents a method claim which captures the relationship between medical treatment and clinical outcomes — tailoring an immunization protocol following the observation of patient responses — does not present a sharp biochemical correlation in the patent claim; however, this method claim format foreshadows the possibility of patenting any professional medical judgment, and is likely to face scrutiny as an abstract idea, as well as a natural phenomenon.²⁰² All of these cases illustrate the challenge for patent law, in that each case presents the possibility of converting basic knowledge into patented subject matter. The evolution of biological science must be synchronized with established eligibility limits from patent law; it is possible that modern life science research actually produces more subject matter that must remain in the public domain than can be captured through patenting.

IV. CONCLUSION

The paradox of patent eligibility as applied to inventions in the genetic sciences is that while this patent law doctrine has received the most critical

200. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 2010 U.S. App. LEXIS 25956 (Fed. Cir. 2010).

201. *Classen Immunotherapies, Inc. v. Biogen IDEC*, 304 Fed. App'x. 866 (Fed. Cir. 2008), No. 08-1509, *vacated and remanded*, 130 S. Ct. 3541 (U.S. June 29, 2010). In 2008, the Federal Circuit decided that the method claims failed the then-governing MOT test. 304 Fed. App'x. 866, at 867.

202. *See supra* note 12.

public attention, it has escaped the formal legal review that has mapped other patent law doctrines to biotechnological inventions.²⁰³ Thus, it is no surprise that the recent set of cases impacting the eligibility of genes and genetic methods has generated intense interest. The patentable subject matter doctrine is charged with policing the domain of unpatentable ideas, which must remain available as the “the basic tools of scientific and technological work”²⁰⁴ so critical to the progress rationale that animates the patent system. The intellectual force of reductionism in the life sciences—deepening the investigation of molecules and relationships that explain biological phenomena—generates direct conflicts with patent law’s exclusion of basic knowledge from patenting.

The life sciences await a definitive and modern interpretation of the product of nature doctrine and its scope, and a contemporaneous analysis of whether and how correlations in the life sciences are regarded as natural phenomena or laws of nature. The resolution of eligibility for genes has implications for the patenting of other biomolecules. The resolution of eligibility of genetic testing methods has implications for the contours of the preemption analysis as applied to subject matter in the life and physical sciences, an issue that will likely emerge in such fields as nanotechnology.

The DNA-centric reasoning of the judge in *AMP*²⁰⁵ might be interpreted to confine the implications of the decision to genes alone. However, the holding also solidifies a more generic understanding of the product of nature doctrine, expressed in other cases, that maintenance of function — without weighing the importance of the function—argues against patentable subject matter. In a DNA-specific view, the unique and complex role of DNA is accorded special analytic weight and DNA is excluded from patenting because of this special character. The sequential analysis for DNA can be diagrammed: molecule-function-information-template-law of nature, a forensic view of DNA that reveals the complex ineligibility of this molecule for patenting, without invoking a simple theory of genetic exceptionalism.

The method claims in genetic testing are essential for capturing the application of genetic status for diagnostic, prognostic and therapeutic purposes in medical care. The legal tests that originated with business method patent cases—the UCT and the MOT tests²⁰⁶—are capable of dictating outcomes that may be directly opposite to the public domain

203. See *supra* notes 35–44 and accompanying text.

204. *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972).

205. 702 F. Supp. 2d 181 (2010).

206. See *supra* notes 126 and 137 and accompanying text (defining the UCT and MOT tests).

protecting analysis of the preemption inquiry. It is possible to imagine examples of inventions that would pass the UCT or MOT tests, but which, viewed through the alternative test of preemption, would not be patentable. Thus, the tests may not be congruent; the relative weight accorded to the transformation analysis or the preemption analysis may be outcome-determinative. The legal standards from the business method patent cases arose to answer the central dilemma for that field—must an invention have a tangible form or be tied to physical processes? These were not the pressing questions from life science patenting. Instead, the central questions for biological patenting involved whether natural processes were being patented, and whether the preemption of basic scientific knowledge occurred. As a result of the fact that some of the important life science patent cases involving method claims have been litigated without directly reaching the public domain questions embedded in the patentable subject matter doctrine, the field awaits more definitive guidelines for how the detailed investigation of biological mechanism can coexist with patent law's prohibition on patenting basic and essential knowledge.

The most pressing questions in patentable subject matter for the life sciences are presented in *AMP*²⁰⁷ and they could be resolved in the appellate courts over the next several years. The courts confront an opportunity to update the set of “basic tools” for genetic science, and to settle these eligibility controversies for the benefit of scientists, medical practitioners, and patients who seek to use isolated genes and genetic correlations in research and medical care. The Supreme Court could decide to hear *AMP*, in recognition of the sensibility it expressed when the Court raised the patentable subject matter issue *sua sponte* in *LabCorp*.²⁰⁸ That does not indicate how the Court might rule. However, one advantage of the full attention of the Supreme Court to the patentable subject matter questions in *AMP* is that it presents both composition and method claims in the genetic sciences.

The patenting of applied research and true invention can coexist alongside the preserve of open and available knowledge, and both will contribute to future developments in genetic science. It should be possible to reconcile the prohibitions on patenting laws of nature, natural phenomena, and abstract ideas with careful patenting practices that advance the application of genetics to medicine.

207. 702 F. Supp. 2d 181 (2010). See discussion *supra* Part II and Part III.D.

208. See *supra* note 151.

