Washington University Law Review

Volume 86 | Issue 1

January 2008

KSR: Have Gene Patents Been KO'd? The Non-Obviousness Determination of Patents Claiming Nucleotide Sequences When the Prior Art Has Already Disclosed the Amino Acid Sequence

Kate M. Lesciotto
Washington University School of Law

KSR: HAVE GENE PATENTS BEEN KO'D? THE NON-OBVIOUSNESS DETERMINATION OF PATENTS CLAIMING NUCLEOTIDE SEQUENCES WHEN THE PRIOR ART HAS ALREADY DISCLOSED THE AMINO ACID SEQUENCE

I. INTRODUCTION

As the fields of biotechnology and recombinant DNA have grown, so has the interest in biotechnology patents. One need only look to the financial potential of biotechnology patents to see one reason for this interest. For example, Amgen is the owner of a patent on the human erythropoietin[1] gene, and utilizes this patent to produce a synthetic version of erythropoietin called Epogen.[2] Sales of Epogen reached $2.5 billion in 2005.[3] Although there is no doubt that advances in biotechnology have aided the health and welfare of society, there remain many legal and economic, as well as ethical and moral,[4] concerns regarding the patentability of biotechnology inventions.

In theory, the basic patent requirements apply in the same manner to biotechnology inventions as to any other invention. However, many commentators believe that the Federal Circuit[5] has applied these requirements differently to different technologies, particularly

1. Erythropoeitin is a protein which plays a role in red blood cell production and can be used in the treatment of anemia. Amgen, Inc. v. Chugai Pharm. Co., No. 87-2617-Y, 1989 U.S. Dist. LEXIS 16110, at *1 (D. Mass. Dec. 11, 1989), *aff'd in part*, 927 F.2d 1200 (Fed. Cir. 1991).

2. Andrew Pollack, *Kidney Dialysis Center Deal With Amgen Blocks Roche*, N.Y. TIMES, Oct. 20, 2006, at C4. *See also* Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1203–04 (Fed. Cir. 1991) (describing two patents claiming a method of preparing erythropoietin and the DNA sequence encoding the gene for erythropoietin).

3. Pollack, *supra* note 2, at C4.

4. *See generally* OLIVER MILLS, BIOTECHNOLOGICAL INVENTIONS: MORAL RESTRAINTS AND PATENT LAW (2005); DAVID B. RESNIK, OWNING THE GENOME: A MORAL ANALYSIS OF DNA PATENTING (2004) (discussing the moral arguments against certain biotechnology and DNA related patents). For a discussion of the moral and ethical arguments against the patenting of transgenic animals, see Carrie F. Walter, Note, *Beyond the Harvard Mouse: Current Patent Practice and the Necessity of Clear Guidelines in Biotechnology Patent Law*, 73 IND. L.J. 1025, 1040–45 (1998).

5. The United States Court of Appeals for the Federal Circuit represents the merger of the Court of Claims and the Court of Customs and Patent Appeals. David J. Meador, *Origin of the Federal Circuit: A Personal Account*, 41 AM. U.L. REV. 581, 592 (1992). The new court had jurisdiction over cases previously heard by the two merged courts. *Id*. The Federal Circuit, officially created in 1982, also has jurisdiction over appeals from patent cases originally brought in federal district court. Sean M. McEldowney, Comment, *The "Essential Relationship" Spectrum: A Framework for Addressing Choice of Procedural Law in the Federal Circuit*, 153 U. PA. L. REV. 1639, 1642 (2005).

biotechnology.[6] One of the most currently contentious areas of patent law is the non-obviousness requirement. This requirement ensures that patents will only be awarded to those inventors who contribute subject matter that would not have been obvious to a person of ordinary skill in the inventor's art or industry. Some believe that the Federal Circuit has in fact "bent over backwards" to find biotechnology patents non-obvious.[7]

One area of biotechnology that particularly concerns many commentators is gene patents, or patents attempting to claim a DNA or nucleotide sequence.[8] Current law does not allow the patenting of naturally occurring genes; however, a patent can be granted for an isolated and purified version of a gene.[9] Approximately twenty percent of human

6. *See* Dan L. Burk & Mark A. Lemley, *Biotechnology's Uncertainty Principle*, 54 CASE W. RES. L. REV. 691, 691 (2004) [hereinafter Burk & Lemley, *Biotechnology's Uncertainty Principle*] ("Thus, as a practical matter, it appears that, although patent law is technology-neutral in theory, it is technology-specific in application."); *see also* Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 BERKELEY TECH. L.J. 1155, 1156–57 (2002) [hereinafter Burk & Lemley, *Is Patent Law Technology-Specific?*] (discussing how the Federal Circuit's perception of the level of unpredictability in biotechnology does not accurately reflect current standings and results in a relaxed obviousness standard and more stringent enablement and written description requirements); Janice M. Mueller, *The Evolving Application of the Written Description Requirement to Biotechnological Inventions*, 13 BERKELEY TECH. L.J. 613, 633 (1998) (arguing that the Federal Circuit created a "super-enablement" standard for biotechnological inventions by requiring that the original, rather than the presented or amended, claims meet the written description standard and by holding that the written description requirement for DNA claims cannot be satisfied without disclosure of the specific nucleotide sequence); Margaret Sampson, Comment, *The Evolution of the Enablement and Written Description Requirements Under 35 U.S.C. § 112 in the Area of Biotechnology*, 15 BERKELEY TECH. L.J. 1233, 1240, 1253–54 (2000) (arguing that while generally an inventor may rely on the patent application filing date as a constructive reduction to practice, the Federal Circuit has prevented this in biotechnology and has required a more stringent written description requirement due to the unpredictability of the field hypothetically preventing conception of the invention).

7. Burk & Lemley, *Is Patent Law Technology-Specific?*, *supra* note 6, at 1156. The requirement of non-obviousness is codified in 35 U.S.C. § 103. An inventor may not obtain a patent if the invention would be obvious at the time of the invention to a person of ordinary skill in the art to which the invention pertains. *See infra* Part II.B.1; *see also* Sara Dastgheib-Vinarov, Comment, *A Higher Non-obviousness Standard for Gene Patents: Protecting Biomedical Research from the Big Chill*, 4 MARQ. INTELL. PROP. L. REV. 143, 165 (2000) (pointing out that the number of biotechnology patents issued between 1990 and 1998 quadrupled while the total number of patents issued during that time only increased by sixty percent and proposing that this disparity is caused by a more relaxed non-obviousness standard applied to the biotechnology industry). *But see* Christopher A. Cotropia, *Nonobviousness and the Federal Circuit: An Empirical Analysis of Recent Case Law*, 82 NOTRE DAME L. REV. 911, 914 (2007) (concluding after an empirical study of Federal Circuit non-obviousness cases that the non-obviousness requirement has not been relaxed in recent years and may actually be more stringently applied by the United States Patent and Trademark Office ("USPTO")).

8. *See generally* 37 C.F.R. § 1.821(a) (2005) ("Nucleotide and/or amino acid sequences . . . are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides.").

9. A patent applicant cannot claim that which is naturally occurring, such as a gene in its natural form. However, an applicant can claim a purified and isolated form of the gene or the protein which it creates. *See* Varu Chilakamarri, *Structural Nonobviousness: How Inventiveness is Lost in the*

genes are already the subjects of United States patents.[10] Of particular concern are those patents attempting to claim a gene encoding a protein when the amino acid sequence of that protein has already been disclosed in the prior art.[11] The nature of the genetic code—the predictable relationship between DNA and amino acids[12]—fuels the argument that if the amino acid sequence is known, the underlying DNA sequence would be obvious to a person of ordinary skill in the field of biotechnology.[13] Amino acids are the building blocks of proteins. For each individual amino acid, there are a limited number of DNA sequences that encode for that specific amino acid. Therefore, when a protein has a known amino acid sequence, the underlying gene can only have a limited number of possible DNA sequences. Thus, some would argue that the underlying DNA sequence is obvious and therefore unpatentable.

Conversely, there is legitimate concern that withdrawing patent protection for such DNA sequences due to obviousness would lead to a chilling effect on related biotechnology research efforts.[14] However, these concerns must be viewed in light of the goals of patent law. The merits of encouraging biotechnological research should not trump patent law's axiomatic prerogative to offer protection only to non-obvious contributions.[15]

Discovery, VA. J.L. & TECH. Vol. 10, No. 7, ¶ 3 (Summer 2005), *available at* http://www.vjolt.net/vol10/issue3/v10i3_a7-Chilakamarri.pdf (providing the example that adrenaline in an isolated form is patentable because it is not found in nature in this state). For a discussion of inventions versus discoveries and how the non-obviousness requirement is applied to each, see generally *id.*

10. Stefan Lovgren, *One-Fifth of Human Genes Have Been Patented, Study Reveals*, NATIONAL GEOGRAPHIC NEWS, Oct. 13, 2005, http://news.nationalgeographic.com/news/pf/22064243.html.

11. Prior art refers to "[k]nowledge that is publicly known, used by others, or available on the date of invention to a person of ordinary skill in an art, including what would be obvious from that knowledge." BLACK'S LAW DICTIONARY 119 (8th ed. 2004). Prior art can include things such as previous patents, scientific journal articles, or academic theses.

12. *See infra* Part II.A.

13. Under patent law, protection is unavailable for obvious inventions. *See infra* note 77.

14. *See* Brief of Biotechnology Industry Organization as Amicus Curiae in Support of Respondents, KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007) (No. 04-1350), 2006 WL 2983166, at *2 (arguing that if new biotechnology patents will be vulnerable to obviousness rejections under a new standard, future research and innovation would be hampered by a reduction in investments). *But see* Dastgheib-Vinarov, *supra* note 7, at 144–45 (discussing a chilling effect on the biotechnological industry resulting from the public's potential boycott of donating genetic samples for research and the "bureaucratic red tape" which could result if the Federal Circuit does not strengthen the non-obviousness standard); Anna Bartow Laakmann, *Restoring the Genetic Commons: A "Common Sense" Approach to Biotechnology Patents in the Wake of* KSR v. Teleflex, 14 MICH. TELECOMM. & TECH. L. REV. 43, 45 (2007) ("Despite general consensus that patents are necessary to the vitality of the biopharmaceutical industry, there are substantial concerns that gene patents slow the pace of scientific advancement and deter commercial development of basic genomics research.").

15. Another concern supporting the argument for raising the obviousness standard is the filing of so-called irresponsible gene patents. Dastgheib-Vinarov, *supra* note 7, at 169. These are patents

At present, the Federal Circuit's generous extension of patent protection to biotechnology inventions, such as genes and nucleotide sequences, stands on tenuous footing with the principles of American patent law—that only non-obvious inventions should be protected. This tension invokes the need for a new approach to biotechnology patents that promotes the progress of science while adhering to the traditional limits of the law. Although a legislative approach may sound appealing, in reality such an approach would be inadequate.[16] As a field, biotechnology is advancing and changing too rapidly for a legislative amendment to be flexible enough to adequately address the issues of obviousness in biotechnology patents.[17]

However, the United States Supreme Court's recent decision in *KSR v. Teleflex*[18] presents one potential solution.[19] In *KSR*, the Court altered how the applicable tests for obviousness, the *Graham* factors and the teaching-suggestion-motivation test,[20] interact.[21] Instead of strictly requiring some type of teaching, suggestion, or motivation to find an invention obvious, the Court referred to this test as merely a "helpful insight" into the *Graham* factors.[22]

While the patent at issue in *KSR* was unrelated to biotechnology, the law subjects patents from every technology to the same obviousness requirement.[23] Thus, application of the principles announced in *KSR* to biotechnology could provide an opening for the Federal Circuit to redefine its approach to patents for DNA sequences when the amino acid sequence

---

claiming hundreds of partial DNA sequences without the patent applicant knowing any associated functions. *Id.*

16. Such an approach was suggested in February 2007 by Congressmen Xavier Becerra and Dave Weldon. Laakmann, *supra* note 14, at 45 (citing H.R. 977, 110th Cong. § 2 (2007)). The Congressmen "introduced the Genomic Research and Accessibility Act, which would amend the U.S. Patent Code to prohibit patents for 'a nucleotide sequence, or its functions and correlations, or the naturally occurring products it specifies.'" *Id.*

17. *See also* Arti K. Rai, *Intellectual Property Rights in Biotechnology: Addressing New Technology*, 34 WAKE FOREST L. REV. 827, 841–42 (1999) (listing several problems with a legislative approach to dealing with the non-obviousness standard, including the influence of special interest groups on the political process, burdensome administrative costs, and the potential inability to deal with future developments in the biotechnology field).

18. KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007). *See infra* Part III.A.

19. However, some commentators believe that *KSR* leaves "the law of obviousness . . . in a state of uncertainty and flux." Harold C. Wegner, *Chemical and Biotechnology Obviousness in a State of Flux*, 26 BIOTECH. L. REP. 437, 437 (2008).

20. *See infra* Part II.B.2.

21. *KSR*, 127 S. Ct. at 1739–43.

22. *Id.* at 1741. *See infra* text accompanying note 192.

23. 35 U.S.C. § 103 (2000).

of the protein is known.[24] The Federal Circuit's current case law follows the principle that even where the prior art discloses the full amino acid sequence of a protein, the DNA sequence of the underlying gene is non-obvious and therefore patentable.[25] Given the continual progress of biotechnology and the increased understanding of genetics, the Federal Circuit's approach to patents claiming DNA sequences is no longer viable. *KSR* called for a more common sense and flexible approach to the non-obvious determination.

I will argue that *KSR*'s new approach should result in bringing the non-obvious determination for biotechnology inventions in line with the current expertise in the field. This can be achieved by finding that patents claiming the nucleotide sequence of a gene when the full amino acid sequence of the protein encoded by the gene has already been disclosed are obvious over the prior art. Part II of this Note provides a brief overview of modern DNA technology, discusses the requirement of non-obviousness in patent law and the appropriate test, and describes two controlling applications of the appropriate test in the Federal Circuit. Part III reviews *KSR v. Teleflex* and studies how the Supreme Court applied the non-obviousness test therein. Part III also discusses how *KSR* has been applied by the Federal Circuit. Finally, Part IV argues that *KSR* demands a reversal of how the Federal Circuit has previously applied the non-obviousness requirement to gene patents claiming a DNA sequence when the amino acid sequence of the protein encoded by the gene is already known. Ultimately, I conclude that the application of *KSR* to such patents should lead to a determination of obviousness when the full amino acid sequence has been disclosed in the prior art.

II. THE PATENTING OF DNA

A. Overview of DNA and Gene Patents

Biotechnology has grown by leaps and bounds in recent decades. Previously unthinkable genetically-modified organisms and genes are now the commonplace content of patent applications. Understanding how the Federal Circuit has treated biotechnology patents in relation to the

24. For a globally based discussion of obviousness in relation to nucleic acid molecules, see Amy Nelson, *Obviousness or Inventive Step as Applied to Nucleic Acid Molecules: A Global Perspective*, 6 N.C.J.L. & TECH. 1 (2004).

25. *See infra* Part II.C.

requirement of non-obviousness requires a brief overview of the structure of DNA and the relationship between DNA, amino acids, and proteins.

DNA, or deoxyribonucleic acid, contains an organism's genetic information.[26] Four different nucleotides link together to form strands of DNA, and two strands of DNA combine to form a stable double helix.[27] The four possible nucleotides in DNA are adenine (A), guanine (G), cytosine (C), and thymine (T).[28] When two strands of DNA form a double helix, each nucleotide on one strand forms a bond with a specific nucleotide on the complementary strand.[29] Adenine and thymine will usually form a bond, as will guanine and cytosine.[30] This is called base pairing. For example, if one strand of DNA contains the nucleotide sequence of AATGCA, the complementary strand that will bind to this portion of the DNA will contain the predictable sequence of TTACGT.

The term *gene* refers to a section of DNA base pairs that encodes a protein.[31] The process of creating a protein from the DNA of a gene involves transcription and translation.[32] Transcription refers to the process of making a copy of the gene portion of the template DNA strand.[33] This copy is usually made up of mRNA, or messenger ribonucleic acid.[34] Translation refers to the process conducted by the cellular mechanism called the ribosome[35] which involves assembling amino acids into a protein according to the mRNA's copy of the gene portion of the template DNA.[36]

Each sequence of three nucleotides in the RNA or DNA acts as a code for an amino acid to be added to the protein being formed at the ribosome.[37] With four possible nucleotides, there are sixty-four possible

26. KENNETH J. BURCHFIEL, BIOTECHNOLOGY AND THE FEDERAL CIRCUIT 18 (1995). Additional background information on molecular biology can be found in *In re O'Farrell*, 853 F.2d 894, 895–99 (Fed. Cir. 1988) and BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL Part II (3d ed. 1994).

27. BURCHFIEL, *supra* note 26, at 18.

28. *Id.*

29. ALBERTS, *supra* note 26, at 99.

30. *Id.* Adenine and thymine, as well as guanine and cytosine, are referred to as complimentary base pairs due to this relationship. *Id.* This relationship is due in part to the number of bonds which form between the two nucleotides during the formation of the double helix. *Id.*

31. BURCHFIEL, *supra* note 26, at 18. It is estimated that the human genome consists of three billion nucleotide base pairs with as many as 100,000 possible genes. *Id.*

32. *Id.*

33. *Id.*

34. *Id.* at 18–19.

35. A ribosome is an organelle contained within cells which link up with the messenger RNA and synthesize the protein. ALBERTS, *supra* note 26, at G-20.

36. BURCHFIEL, *supra* note 26, at 19.

37. *Id*.

sets of three-nucleotide sequences, which are called codons;[38] however, there are only twenty different amino acids.[39] This results in what is known as the degeneracy of the genetic code.[40] Some amino acids can only be encoded for by one possible codon, called unique codons, while other amino acids can be encoded for by up to six different codons.[41] It is important to note that while a single amino acid can result from several different codons, no single codon can result in more than one amino acid. To put this into a concrete example, while the amino acid alanine results from any of the codons GCU, GCC, GCA, or GCG, any of these codons in a strand of mRNA will only result in alanine being added to the building protein.

During translation, the ribosome reads the mRNA sequences and begins building a protein by linking amino acids together.[42] The ribosome moves along the mRNA, reading each codon in sequence and adding the appropriate amino acid, translating the genetic code.[43] Once the entire strand of mRNA has been read and translated into amino acids, a protein has been created.[44]

Recombinant DNA techniques have been used to create micro-organisms that produce useful proteins.[45] For example, once the DNA sequence of a human gene is known, it can be inserted into the DNA of a bacterium.[46] Since all organisms follow the same genetic code, the bacterium will be able to transcribe the human DNA sequence and produce a human protein.[47]

Biotechnology can also be used to isolate specific genes.[48] While there are several different methods for isolating a gene, I will briefly describe one such method. The first step in isolating a human gene is to break down

---

38. The term *codon* simply refers to any triplet of nucleotides. ALBERTS, *supra* note 26, at 106.

39. BURCHFIEL, *supra* note 26, at 19.

40. *In re* Bell, 991 F.2d 781, 783 n.5 (Fed. Cir. 1993). Additionally, there are three possible codons which do not encode an amino acid, but rather act to signal the end of a gene. These are known as the *stop codons*. BURCHFIEL, *supra* note 26, at 19. The beginning of a gene is always signaled by one codon, which encodes the amino acid methionine. *Id*.

41. *In re Bell*, 991 F.2d at 783 n.5.

42. BURCHFIEL, *supra* note 26, at 19.

43. *Id*.

44. *Id.*

45. *In re* O'Farrell, 853 F.2d 894, 898 (Fed. Cir. 1988). One example of a useful protein is insulin. *Id.*

46. BURCHFIEL, *supra* note 26, at 19. *See also O'Farrell*, 853 F.2d at 898 (reviewing the process of transformation, when a bacterium integrates foreign genetic material into its own DNA).

47. BURCHFIEL, *supra* note 26, at 19.

48. BRUCE ALBERTS ET AL., ESSENTIAL CELL BIOLOGY 327 (1998).

the entire human genome into smaller pieces.[49] Mechanical shearing, or enzymes known as restriction endonucleases, are used to create small DNA fragments from the entire genome.[50] This collection of DNA pieces representing the genome is known as a DNA library.[51] The next step in finding the specific gene being sought requires a DNA probe.[52] A probe is created once a portion of the protein has been sequenced, providing a short amino acid sequence.[53] Using the genetic code, a DNA probe is created, containing the DNA sequence encoding that amino acid sequence.[54] The DNA probe can then be introduced to the DNA library, where it will hybridize, or bond, with the DNA fragment containing that sequence.[55] Once this location is known, the surrounding DNA can be isolated and sequenced to produce the full DNA sequence encoding the protein in question.[56]

Current estimates place the number of genes in the human genome at approximately 20,000–25,000.[57] Once genes have been identified and isolated, they can be patented.[58] While the patentability of genes was questioned originally, the United States Patent and Trademark Office issued official guidelines in 2001 which laid those questions to rest.[59] The Guidelines stated affirmatively that genes were patentable subject matter, so long as the invention satisfied the requirements of the Patent Act.[60] The Patent and Trademark Office stated that "an inventor's discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it."[61] Since things cannot be patented in a form that occurs in nature, the additional steps of isolating and purifying the gene aid the invention in overcoming an initial hurdle to

49. *Id.*
50. *Id.* at 327–28.
51. *Id.* at 328.
52. *Id.*
53. *Id.*
54. *Id.* at 328–29.
55. *Id.* at 329.
56. *Id.*
57. Malcolm Ritter, *Scientists rein in estimate on human genome*, USA TODAY, Oct. 20, 2004, *available at* http://www.usatoday.com/tech/science/genetics/2004-10-20-fewer-genes-needed_x.htm. By comparison, one species of roundworm has approximately 19,500 genes and a flowering plant has approximately 27,000. *Id.*
58. *See supra* note 9.
59. Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).
60. *See infra* notes 70–71 and accompanying text.
61. Utility Examination Guidelines, 66 Fed. Reg. at 1093.

patentability.[62] However, disclosure of only an isolated and purified nucleotide sequence is not sufficient to obtain a patent.[63] The inventor must disclose a "specific, substantial, and credible utility for the claimed isolated and purified gene" in order to be awarded a patent.[64] Both the sequence and the potential use of the sequence must be disclosed.

A recent study found that approximately twenty percent of all human genes were claimed in U.S. patents as of 2005.[65] Gene patents can prove to be invaluable in developing diagnostic tests, researching genetic therapy techniques, and numerous other applications. While the possibility of obtaining a patent acts as a powerful incentive in genetic research, the award of a gene patent can create problems for future researchers. For example, a patent claiming a gene can effectively block downstream research on applications of that gene.[66] This is the precise situation occurring with two breast cancer genes.[67] Myriad Genetics holds patents on *BRCA1* and *BRCA2*.[68] These patents have allowed Myriad to prevent the use of these genes in research and in developing new tests for diagnosing breast cancer based on the presence of the genes.[69]

---

62. *Id*. The Guidelines specifically provide:

> 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.

Id.

63. *Id.*

64. *Id.*

65. Lovgren, *supra* note 10.

66. Natasha N. Aljalian, *The Role of Patent Scope in Biopharmaceutical Patents*, 11 B.U. J. SCI. & TECH. L. 1, 50 (2005). For a more thorough discussion of the potential problems of downstream research when there is a broad grant of upstream gene patents, see generally Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698 (1998) and Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 BERKELEY TECH. L.J. 813 (2001).

67. Aljalian, *supra* note 66, at 53.

68. *Id.*

69. *Id.* at 53–54. Myriad does offer a diagnostic test based on the two patented BRCA genes, but charges up to $3,000 for the test. *Myriad Genetic Launches Direct-to-Consumer Advertising of Breast Cancer Gene Test in Northeastern Cities*, MEDICAL NEWS TODAY, Sept. 13, 2007, http://www.medicalnewstoday.com/articles/82147.php. Additionally, Myriad requires that all such diagnostic testing occur at Myriad facilities. May Mowzoon, Comment, *Access Versus Incentive: Balancing Policies in Genetic Patents*, 35 ARIZ. ST. L.J. 1077, 1093 (2003). This situation brings up many of the moral issues in the debate about biotechnology patents which are beyond the scope of this Note.

B. Non-obviousness Requirement of Patent Law

1. Origination and Codification of 35 U.S.C. § 103

In order to be awarded patent protection, the patent examiner must believe that the invention is useful, new, and non-obvious.[70] While the general patentability requirement of utility was included in the Constitution[71] and both utility and novelty were included in the Patent Act of 1793,[72] it was not until 1952[73] that Congress added the requirement of non-obviousness.[74] The idea of requiring an invention to be non-obvious originated in *Hotchkiss v. Greenwood*.[75] There, the Supreme Court stated:

> [F]or unless more ingenuity and skill in applying [the claimed improvement invention] than were possessed by an ordinary mechanic acquainted with the business, there was an absence of that degree of skill and ingenuity which constitute essential elements of every invention. In other words, the improvement is the work of the skilful mechanic, not that of the inventor.[76]

Although this idea remained consistently within the case law, it was not codified until the 1952 Patent Act when Congress added § 103, entitled "Conditions for patentability; non-obvious subject matter."[77] The Supreme

---

70. *See* 35 U.S.C § 101 (2000) (containing the new and useful requirements); 35 U.S.C. § 103 (2000) (containing the non-obvious requirement).

71. *See* U.S. CONST. art. I, § 8 ("To promote the Progress of Science and *useful* Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries;") (emphasis added); *see also* Steven P. Smith & Kurt R. Van Thomme, *Bridge Over Troubled Water: The Supreme Court's New Patent Obviousness Standard in* KSR *Should Be Readily Apparent and Benefit the Public*, 17 ALB. L.J. SCI. & TECH. 127, 148 (2007) (discussing the Constitutional policy of promoting the useful arts behind the patent clause).

72. Act of Feb. 21, 1793, ch. 11, 1 Stat. 318, *repealed by* Act of July 4, 1836, ch. 357, § 21 5 Stat. 117, 125.

73. Act of July 19, 1952, ch. 950, 66 Stat. 792 (codified as amended at 35 U.S.C. §§ 1-351 (2000)).

74. *See also* Graham v. John Deere Co., 383 U.S. 1, 11 (1966) (discussing the history of the non-obviousness requirement).

75. Hotchkiss v. Greenwood, 52 U.S. 248, 267 (1850); *see also Graham*, 383 U.S. at 11 (discussing the history of *Hotchkiss* and the origin of the non-obviousness requirement).

76. *Hotchkiss*, 52 U.S. at 267.

77. 35 U.S.C. § 103. Section 103 provides:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Court first addressed the application of the non-obviousness requirement in *Graham v. John Deere Co.*[78] and set forth a four-prong test of obviousness.[79] When analyzing obviousness, the court inquires into (1) the scope and content of the prior art; (2) the differences between the prior art and the claimed invention; (3) the level of ordinary skill in the relevant art;[80] and (4) secondary considerations such as commercial success, long-felt but unsolved needs, and failure of others.[81] The *Graham* factors have continued to play an important role in how courts determine obviousness.[82]

2. Teaching, Suggestion, Motivation Test

In addition to utilizing the *Graham* factors, the Federal Circuit applies a two-part test when making a determination of obviousness: (1) there must be some teaching, suggestion, or motivation ("TSM") to combine the prior art to arrive at the claimed invention; and (2) there must have been a

---

35 U.S.C. § 103(a) (2000). Section 103(b) relates to the non-obviousness of biotechnological processes. 35 U.S.C. §103(b) (2000). *See also Graham*, 383 U.S. at 14–15 ("An invention which has been made, and which is new in the sense that the same thing has not been made before, may still not be patentable if the difference between the new thing and what was known before is not considered sufficiently great to warrant a patent.") (quoting S. REP. NO. 1979, at 6 (1952)).

78. 383 U.S. 1.

79. *Id.* at 17–18.

80. *Id.* at 17. Determining this level of skill requires imagining a hypothetical person having ordinary skill in the art, also known as a "PHOSITA." DONALD S. CHISUM ET AL., PRINCIPLES OF PATENT LAW 621 (2004).

81. *Graham*, 383 U.S. at 18. *See also* Brief of Biotechnology Industry Organization as Amicus Curiae in Support of Respondents, *supra* note 14, at 27 (discussing the *Graham* factors and explaining the secondary considerations).

> [C]ommercial success of an invention . . . suggests it was nonobvious or else someone would have developed it earlier as an obvious means of further profit from the prior art. A long felt unsolved need in an area similarly suggests that an invention that comes along to meet the need was nonobvious or else others would have long ago developed it. And, the failure of others, of course, serves as a strong objective indication that an invention was not obvious or else others would not have met failure when they tried to develop it.

Id. In *Graham*, the Court noted that there would be inevitable difficulties in applying the test, but only difficulties similar in magnitude to those already faced by courts. *Graham*, 383 U.S. at 18. The Court recognized that the varying factual contexts would not be easily amenable to a uniform decision on obviousness. *Id.* However, the Court also emphasized the primary role of the USPTO, and not the courts, in making the initial determination of obviousness. *Id.* At the time of the decision, the Court believed that the new obviousness test would "expedite disposition" within the USPTO and "bring about a closer concurrence between administrative and judicial precedent." *Id.* at 18–19. *Contra* Brief of Intellectual Property Law Professors as Amici Curiae in Support of Petitioner at *4, KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007), No. 04-1350, 2006 WL 2452369 (arguing that the Federal Circuit's approach of requiring such a factual inquiry of obviousness impairs the USPTO's ability to utilize the expertise of the patent examiners in determining obviousness).

82. *See* Smith & Van Thomme, *supra* note 71, at 158–92 (reviewing the jurisprudence regarding the *Graham* factors and their application).

reasonable expectation of success in combining the prior art.[83] TSM comes into play in evaluating the first *Graham* factor: the scope and content of the prior art.[84] An evaluation of the prior art considers "[w]hat the prior art teaches, whether it teaches away from the claimed invention, and whether it motivates a combination of teachings from different references."[85] Simply finding each individual element of the claimed invention in the prior art is not sufficient on its own to invalidate the claimed invention.[86] TSM requires the additional step of providing an articulated reason for combining the individual elements found in the prior art in a way to arrive at the claimed invention.[87] Regardless of whether the teaching, suggestion, or motivation to combine those individual elements is found explicitly or implicitly in the prior art, the patent examiner still must show a specific rationale for making the combination.[88] Additionally, there must be a reasonable expectation of success that combining the prior art references will result in the claimed invention.[89]

A review of two cases decided in the last ten years demonstrates the possible extremes of the TSM test. In 1999, the Federal Circuit reviewed the obviousness of a patent for the now popular-plastic garbage bags decorated with a Halloween pumpkin face in *In re Dembiczak*.[90] The court reviewed several pieces of prior art, including two design patents for a bag with a pumpkin face,[91] a book for teaching children to make a "paper bag

83. Dystar Textilfarben GMBH & Co. v. C.H. Patrick Co., 464 F.3d 1356, 1360 (Fed. Cir. 2006) (citing Brown & Williamson Tobacco Corp. v. Phillip Morris, Inc., 229 F.3d 1120, 1124 (Fed. Cir. 2000)). *But see* Brief of Intellectual Property Law Professors as Amici Curiae in Support of Petitioner, *supra* note 81, at 9–10 (pointing out that the TSM test does not originate from either Section 103 specifically or anywhere else in the Patent Act and arguing that if the Supreme Court had utilized TSM in *Graham*, an opposite result may have occurred).

84. *Dystar*, 464 F.3d at 1363. TSM does not supplant any part of the *Graham* factors, but is intended to act as a guide in evaluating the four factors. *KSR*, 127 S. Ct. at 1741.

85. *Dystar*. 464 F.3d at 1363 (quoting *In re* Fulton, 391 F.3d 1195, 1199–1200 (Fed. Cir. 2004)).

86. *In re* Kotzab, 217 F.3d 1365, 1370 (Fed. Cir. 2000) (citing *In re* Rouffet, 149 F.3d 1350, 1357 (Fed. Cir. 1998)).

87. *Id.* This requirement remains regardless of whether the elements of the claimed invention are found in a single piece of prior art or throughout several prior art references. *Id.*

88. *Id.* at 1371 ("[P]articular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed."). *Cf.* Steven J. Lee & Jeffrey M. Butler, *Teaching, Suggestion and Motivation:* KSR v. Teleflex *and the Chemical Arts*, 17 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 915, 922 (2007) (arguing that this stringent requirement of the TSM test acts as a shield for patents which have already been issued and also lowers the patentability requirement for new patent applications).

89. *Dystar*, 464 F.3d at 1360. *See also In re* O'Farrell, 853 F.2d 894, 903-4 (Fed. Cir. 1988) (pointing out that this second prong of TSM does not require an *absolute* prediction of success in creating the claimed invention, just a reasonable expectation of success).

90. *In re* Dembiczak, 175 F.3d 994, 996 (Fed. Cir. 1999), *abrogated by In re* Gartside, 203 F.3d 1305 (Fed. Cir. 2000).

91. *Id.* at 997. These design patents, also owned by the patent applicants in this case, presented

pumpkin" by decorating the bag to make it look like a pumpkin and stuffing it with newspapers, and common plastic garbage bags.[92] The Board had affirmed the patent examiner's rejection based on obviousness over the prior art.[93] The court began its analysis by reviewing the *Graham* factors and emphasizing the danger of falling into a hindsight bias in the obviousness determination.[94] According to the court, the best way to defend against a hindsight-driven obviousness analysis is a "*rigorous* application of the requirement for a showing of the teaching or motivation to combine prior art references."[95] The court cited a laundry list of cases supporting this proposition.[96] The court continued to say that TSM could be found in the prior art, the knowledge of a PHOSITA,[97] or the nature of the problem being solved by the claimed invention.[98] Notwithstanding a seemingly expansive view of TSM, the court again emphasized the requirement of a clear and particular showing of "actual evidence."[99] Despite the simple nature of the invention and the numerous prior art references, the lack of "particular findings" was, in the court's opinion, fatal to the Board's finding of obviousness.[100] Although the Board found each limitation present in the patent claims in the prior art references, the

---

an issue of obviousness-type double patenting. *Id*. at 998. While such issues are beyond the scope of this Note, it is important to point out that the Federal Circuit dealt with the double patenting issue separately, ultimately reversing the original rejection on this ground. *Id.* at 1003.

92. *Id.* at 997.

93. *Id.* at 997–98.

94. *Id.* at 998–99. Hindsight bias describes the tendency of a patent examiner or a judge, when reviewing an invention for obviousness, to look at the invention and the prior art from the current perspective rather than the perspective at the time the invention was created. The court emphasized the importance and difficulty of preventing hindsight bias, stating that the obviousness determination "requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field." *Id.* at 999. See Gregory Mandel, *Patently Non-Obvious II: Experimental Study on the Hindsight Issue Before the Supreme Court in* KSR v. Teleflex, 9 YALE J.L. & TECH. 1 (2006) for discussion of a study on how well the Federal Circuit's teaching-suggestion-motivation test eliminates hindsight bias.

95. *Dembiczak*, 175 F.3d at 999 (emphasis added). *See also* Brief of Biotechnology Industry Organization as Amicus Curiae in Support of Respondents, *supra* note 14, at 18 (arguing that the Federal Circuit's requirement of "specific proof" of TSM is "essential to the predictability of patentability" and at the same time remains "flexible" since the proof of TSM does not need to be expressly written in a prior art reference).

96. *Dembiczak*, 175 F.3d at 999 (citing C.R. Bard, Inc. v. M3 Sys., Inc., 157 F.3d 1340, 1352 (Fed. Cir. 1998), *In re* Rouffet 149 F.3d 1350, 1359 (Fed. Cir. 1998), *In re* Fritch, 972 F.2d 1260, 1265 (Fed. Cir. 1992), *In re* Fine, 837 F.2d 1071, 1075 (Fed. Cir. 1988), and Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297 (Fed. Cir. 1985)).

97. A PHOSITA is a hypothetical person having ordinary skill in the art. *See supra* note 80.

98. *Dembiczak*, 175 F.3d at 999.

99. *Id*.

100. *Id.* at 1000.

Board failed to make specific findings as to where TSM to combine the references was actually found.[101] The Federal Circuit ultimately reversed the Board's obviousness rejection.[102]

On the other side of the spectrum is the Federal Circuit's application of TSM in *DyStar Textilfarben GMBH & Co. v. C.H. Patrick Co.*[103] At issue was DyStar's patented process for dying textiles.[104] Throughout its opinion, the Federal Circuit refuted the characterization of TSM as strict.[105] The court additionally stated that while TSM is generally discussed in relation to the scope and content of the prior art (the first *Graham* factor), TSM is also linked to the level of skill in the art (the third *Graham* factor).[106] When the level of skill of a person having ordinary skill in the art is low, a more substantial showing of some TSM to combine the prior art is required.[107] When the level of skill is higher, a lesser showing is required.[108] The court first had to determine whether the appropriate level of skill was a dyer who had no knowledge of chemistry

101. *Id.* The court stated, "this reference-by-reference, limitation-by-limitation analysis fails to demonstrate how the [prior art] references teach or suggest their combination with the conventional trash or lawn bags to yield the claimed invention." *Id.*

102. *Id.* at 1003.

103. 464 F.3d 1356 (Fed. Cir. 2006). One significant aspect of this decision was the fact that it was handed down after certiorari was granted in *KSR*. This indicated that the Federal Circuit's decision in *Dystar* was written with an eye toward how the Supreme Court would review recent applications of TSM. *See* Clara R. Cottrell, Note, *The Supreme Court Brings a Sea Change With* KSR International Co. v. Teleflex, Inc., 42 WAKE FOREST L. REV. 595, 614 (2007) (pointing out that the Federal Circuit's stance in *Dystar* was a shot at "damage control" over the court's previous applications of TSM).

104. *Dystar*, 464 F.3d at 1358.

105. *See id.* at 1361 ("In contrast to the characterization of some commentators, the suggestion test is not a rigid categorical rule."); *id.* at 1365 ("[Prior cases] correctly applie[d] the suggestion test and by no means require[d] an explicit teaching to combine to be found in a particular prior art reference."); *id.* at 1367 ("It is difficult to see how our suggestion test could be seen as rigid and categorical given the myriad cases over several decades in which panels of this court have applied the suggestion test flexibly."); *id.* at 1367 ("Our suggestion test is actually quite flexible and not only permits, but *requires* consideration of common knowledge and common sense."); *id.* at 1368 ("Because the desire to enhance commercial opportunities by improving a product or process is universal—and even common-sensical—we have held that there exists in these situations a motivation to combine prior art references even absent any hint of suggestion in the references themselves."). The court appeared to back as far away as possible from its previous requirement of a specific showing of some suggestion to combine prior art references by stating that when improving a product or process, "the proper question is whether the ordinary artisan possesses knowledge and skills rendering him *capable* of combining the prior art references." *Id.* at 1368. *But see* Cottrell, *supra* note 103, at 616 ("The Federal Circuit stated that '[c]ommon knowledge and common sense,' even if assumed to derive from the [USPTO's] expertise, do not substitute for evidence of a 'specific hint or suggestion' to combine prior art.") (quoting *In re* Lee, 277 F.3d 1338, 1344–45 (Fed. Cir. 2002)).

106. *Dystar*, 464 F.3d at 1370.

107. *Id.*

108. *Id.*

or a dye process designer who would have some knowledge of chemistry.[109] Since the patent was directed to a dyeing process that involved chemical reactions, the higher level of skill of a dye process designer was more appropriate.[110] The court used this higher level of skill to "predetermine whether an implicit suggestion exist[ed]" in the prior art.[111] A dye process designer would be able to draw on his or her chemistry background to combine prior art references without any explicit suggestion to do so.[112] In *Dystar*, the lack of an explicit TSM to combine the prior art references did stop the court from finding that the claimed invention was obvious.[113] The court ultimately held that the claimed invention was simply the work of one skilled in the art, but not the work of an inventor.[114]

C. Current Application of the Non-obviousness Requirement to Gene Patents

1. In re Bell

In re Bell[115] presented the Federal Circuit with the issue of whether a prima facie case of obviousness arises for a gene when prior art references disclosed the amino acid sequence of the corresponding protein and a general method of cloning.[116] The claimed invention was directed to DNA and RNA sequences encoding human insulin-like growth factors.[117] The body of relevant prior art contained two articles which disclosed the amino acid sequence corresponding to the claimed DNA and RNA sequences and a patent which disclosed a method for isolating a gene when at least a portion of the amino acid sequence is known.[118] Rejecting the claims as obvious over the prior art references, the patent examiner reasoned that one of ordinary skill in the art would know how to deduce the nucleic acid sequence once the amino acid sequence was known and therefore the claimed sequences would have been obvious.[119] The Board of Patent

109. *Id.* at 1362.
110. *Id.* at 1362–63.
111. *Id.* at 1370.
112. *Id.* at 1371.
113. *Id.* at 1372.
114. *Id*. at 1371.
115. *In re* Bell, 991 F.2d 781 (Fed. Cir. 1993).
116. *Id.* at 782–83.
117. *Id.* at 782.
118. *Id.* at 783.
119. *Id*.

Appeals and Interferences affirmed the rejection despite the lack of structural similarity between the nucleic acid sequence and the amino acid sequence.[120] Instead, the Board found that the correspondence between the amino acid and nucleic acid sequences found in the genetic code was sufficient to establish a prima facie case of obviousness.[121] The Board cited a lack of evidence "that one skilled in the art, knowing the amino acid sequences of the desired proteins, would not have been able to predictably clone the desired DNA sequences without undue experimentation."[122]

The Federal Circuit reversed the Board's decision on appeal, holding the claimed DNA and RNA sequences to be non-obvious.[123] The court began its analysis by looking for some teaching or suggestion in the prior art which would allow a person of ordinary skill in the art to arrive at the claimed invention.[124] While accepting the proposition of *In re Dillon*[125] that structural similarity[126] between chemical compounds may render a claimed compound obvious, the court declined to analogize this reasoning to the genetic relationship between nucleic acids and amino acids.[127] The court stated that the genetic relationship would only allow one to "hypothesize possible structures" and give one "the potential for obtaining that gene."[128] The genetic code could only direct one to the possible structures due to the degeneracy of the code.[129] Because of the repetition within the genetic code, the amino acid sequence disclosed in the prior art

120. *Id*.
121. *Id*.
122. *Id.* (internal citations omitted).
123. *Id.* at 785.
124. *Id.* at 783. The court stated that "[a] prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art." *Id.* (quoting *In re* Rinehart, 531 F.2d 1048, 1051 (C.C.P.A. 1976)).
125. 919 F.2d 688 (Fed. Cir. 1990). The court held that a prima facie case of obviousness is established by proving structural similarity between the claimed subject matter and the prior art and by showing that the prior art contains some type of motivation to create the claimed subject matter. *Id.* at 692–93.
126. *See generally* Chilakamarri, *supra* note 9, at 21 (discussing the inadequacy of examining structural similarities of discoveries such as DNA sequences as opposed to inventions, since in a discovery the structure is not indicative of what the inventor contributed); Anita Varma & David Abraham, *DNA Is Different: Legal Obviousness and the Balance Between Biotech Inventors and the Market*, 9 HARV. J.L. & TECH. 53, 68–69 (1996) (arguing that the structural similarity test is inappropriate to apply to DNA since minor changes in the structure of DNA can create major changes in function and the structure of DNA is not related to structure of proteins or amino acids); Rai, *supra* note 17, at 835–36 (advocating an analytical approach to DNA obviousness involving a recognition that DNA is primarily "a carrier of *information*" rather than a simple chemical compound).
127. *In re Bell*, 991 F.2d at 784.
128. *Id*.
129. *Id*.

could actually have been encoded for by 10^{36} different nucleotide sequences.[130] Since only a few of the possible nucleotide sequences were being claimed, the prior art would have to contain some kind of suggestion as to which of the possible sequences was actually the human gene in order for the claimed sequences to be obvious.[131]

Additionally, the prior art patent, which taught a method for isolating a gene, appeared to teach away from the method used to isolate the claimed sequences.[132] The reference suggested using a probe based on amino acids encoded by unique codons,[133] and taught away from using a probe without at least four such amino acids, if the total number of nucleotides in the probe exceeded fourteen.[134] In this case, the applicant used a probe without any uniquely encoded amino acids.[135] On these findings, the court held that there was no teaching or suggestion in the prior art to combine the references in a way that would lead to the claimed sequences, and thus, the patent examiner failed to establish obviousness.[136]

---

130. *Id*. *But see* Varma & Abraham, *supra* note 126, at 73 (arguing that 10^{36} was likely not an accurate estimate and that at the time of *Bell* cloning procedures had advanced to the point where handling such high numbers of possibilities was entirely possible); Rai, *supra* note 17, at 836–37 (pointing out that the Federal Circuit did not take into account the fact that practitioners do not simply take the amino acid sequence of a protein and work out the DNA sequence directly, but rather, design a small probe based on a portion of the amino acid sequence). Additionally, Rai points out that the number of possible DNA sequences can be limited by selecting a probe consisting of amino acids coded for by only one or two possible codons and by using "codon catalogs," which provide information on species-specific preferences in codon selection. *Id*.

131. *In re Bell*, 991 F.2d at 784. The court made a point to reserve the possibility of finding a gene obvious when the amino acid sequence of the encoded protein is known, stating that a gene might be obvious if the known amino acid sequence included only amino acids encoded for by a single possible codon. *Id*. The court also explicitly reserved its opinion as to whether a protein might be made obvious by knowledge of full structure of the DNA sequence. *Id.* n.6.

132. *Id.* at 784. *But see* Brian C. Cannon, Note, *Toward a Clear Standard of Obviousness for Biotechnology Patents*, 79 CORNELL L. REV. 735, 762 (1994) (proposing an obviousness analysis for DNA sequence patents focusing on the methods and techniques used rather than on the end product because the novelty is based on discovering and isolating a specific DNA sequence rather than conceiving a utility for that DNA sequence).

133. Unique codons represent the only possible nucleotide triplet for adding a specific amino acid. *See supra* note 41 and accompanying text.

134. *In re Bell*, 991 F.2d at 784. *But see* Varma & Abraham, *supra* note 126, at 74 (indicating the impracticality of selecting only unique codons as only two amino acids, methionine and tryptophan, are coded for by unique codons).

135. *In re Bell*, 991 F.2d at 784. Bell used a probe consisting of twenty-three nucleotides, or eight amino acids. *Id.*

136. *Id.* at 785.

2. In re Deuel

In re Deuel[137] presented the question of whether a prior art reference teaching a method of gene isolation could be combined with another reference disclosing a partial amino acid sequence to establish a case of prima facie obviousness for the DNA and cDNA sequences encoding the partially disclosed amino acid sequence.[138] Whereas the prior art in *Bell* disclosed the full amino acid sequence of the protein, the prior art in *Deuel* only disclosed the first nineteen amino acids.[139]

Deuel claimed isolated and purified DNA and cDNA sequences which encoded heparin-binding growth factors ("HBGFs").[140] The prior art contained a reference which disclosed a group of similar heparin-binding proteins and the first nineteen amino acids of those proteins.[141] These nineteen amino acids were identical to the first nineteen amino acids in the HBGFs.[142] The prior art also contained a reference that disclosed a general technique of isolating a gene using a gene probe.[143] In rejecting the claims, the patent examiner stated that it would have been prima facie obvious to one of ordinary skill to arrive at the claimed sequences given the prior art disclosures of the partial amino acid sequence of similar heparin-binding proteins and a gene isolation technique.[144] The disclosures would make it obvious to use the disclosed partial amino acid sequence to design a probe, allowing a person of ordinary skill to isolate the gene.[145] The Board of Patent Appeals and Interferences affirmed the rejection, noting the routine nature of gene cloning techniques.[146]

---

137. 51 F.3d 1552 (Fed. Cir. 1995).
138. *Id.* at 1557.
139. *Id.* at 1556.
140. *Id.* at 1553–54.
141. *Id.* at 1556.
142. *Id.* at 1156 n.5.
143. *Id.* at 1556.
144. *Id*.
145. *Id. See also Ex parte* Hudson, 18 U.S.P.Q.2d 1322, 1324 (1990) (reviewing an obviousness rejection for patent claiming a nucleotide sequence).

> [O]nce the amino acid sequence of a known useful protein is known, there is motivation for one of ordinary skill in the relevant art to construct a synthetic gene for biosynthesis of that protein. Whether or not the specific biosynthesis involved would have been obvious under 35 U.S.C. § 103 depends on the specific facts in each case, but the critical inquiry is would there have been a reasonable expectation of success in achieving the desired goal, applying only the knowledge evidenced as being part of the prior art.

Id. (citing *In re* O'Farrell, 853 F.2d 894 (Fed. Cir. 1988)).
146. *In re Deuel*, 51 F.3d at 1556–57.

The Federal Circuit reversed the Board's decision, finding the claimed DNA sequences to be non-obvious in light of the prior art.[147] The court again focused on the lack of structural similarity[148] between known chemical compounds and the claimed invention. It discarded the possibility of analogizing the requisite chemical structural similarity to the relationship the genetic code provides between an amino acid and a nucleotide sequence.[149] Degeneracy of the genetic code would prevent a person of ordinary skill in the art from "contemplat[ing]" a specific nucleotide sequence, and "[w]hat cannot be contemplated or conceived cannot be obvious."[150]

The court then addressed the Board's reliance on the routine nature of the gene cloning technique used, stating that prior art knowledge of such a method was "essentially irrelevant" to the determination of obviousness without some suggestion in the prior art of the specific sequences claimed.[151] Knowledge of the general technique and partial knowledge of the protein's amino acid sequence would not necessarily lead a person of ordinary skill in the art to prepare the specific sequence claimed.[152] Although it may have been "obvious to try" to prepare the claimed sequences, the actual sequences themselves were not obvious.[153]

---

147. *Id.* at 1560.

148. *See also* Chilakamarri, *supra* note 9, at 19 (proposing that using a structural analysis for DNA sequence patents could lead to awarding patents to those able to perform the most work and experimentation rather than those who make a novel contribution to the art).

149. *In re Deuel*, 51 F.3d at 1557–58. The court directly stated that "[t]he genetic code relationship between proteins and nucleic acids does not overcome the deficiencies of the cited references." *Id.* at 1558.

150. *Id*. The court noted the possibility of obviousness of a gene where the protein in question was "of sufficiently small size and simplicity" and lacked redundancy of the genetic code. *Id.* at 1559.

151. *Id.*

152. *Id.*

153. *Id*. *See also In re* O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988) (discussing the "impermissible" obvious to try standard).

> The admonition that "obvious to try" is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

Id. (citations omitted).

III. *KSR* AND A NEW OUTLOOK ON THE NON-OBVIOUSNESS DETERMINATION

A. The Supreme Court's Decision in KSR v. Teleflex

In 2007, the Supreme Court issued an opinion on the Federal Circuit's TSM test and the non-obviousness determination in *KSR International Co. v. Teleflex, Inc.*[154] Although the Court did not entirely reject the TSM approach to determining obviousness, the Court did admonish the Federal Circuit for applying TSM too strictly in the *KSR* appeal.[155] The Federal Circuit's decision that the claims were not obvious was reversed, and the case was remanded.[156]

At issue in *KSR* was a single claim of a patent (the "Engelgau patent") for combining an electronic sensor with an adjustable car pedal, allowing the car's internal computer to transmit information regarding the position of the pedal to the throttle.[157] Teleflex was the exclusive licensee of the Engelgau patent and brought suit against KSR alleging patent infringement.[158] In defense, KSR argued that the Engelgau patent was invalid for obviousness.[159]

There were several relevant prior art references. U.S. Patent No. 5,010,782 ("Asano") disclosed a type of pedal that would allow the driver to adjust the pedal's location rather than having to adjust the driver's seat in order to correct the distance between the driver's foot and the pedal.[160]

---

154. KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007). Other recent Supreme Court cases that deal with patent related issues, but are beyond the scope of this Note, include *Microsoft Corp. v. AT&T Corp*., 127 S. Ct. 1746 (2007), *MedImmune, Inc. v. Genentech, Inc*., 127 S. Ct. 764 (2007), *Lab. Corp. of Am. Holdings v. Metabolite Labs.*, 126 S. Ct. 2921 (2006), and *eBay, Inc. v. MercExchange, L.L.C*, 126 S. Ct. 1837 (2006).

155. *KSR*, 127 S. Ct. at 1739.

156. *Id.* at 1746.

157. *Id.* at 1734. Claim 4 of the Engelgau patent reads as follows:

> A vehicle control pedal apparatus comprising: a support adapted to be mounted to a vehicle structure; an adjustable pedal assembly having a pedal arm moveable in force and aft directions with respect to said support; a pivot for pivotally supporting said adjustable pedal assembly with respect to said support and defining a pivot axis; and an electronic control attached to said support for controlling a vehicle system; said apparatus characterized by said electronic control being responsive to said pivot for providing a signal that corresponds to pedal arm position as said pedal arm pivots about said pivot axis between rest and applied positions wherein the position of said pivot remains constant while said pedal arm moves in fore and aft direction with respect to said pivot.

Adjustable Pedal Assembly With Electronic Throttle Control, U.S. Patent No. 6,237,565 col.6 l.17-36 (filed Aug. 22, 2000) (issued May 29, 2001).

158. *KSR*, 127 S. Ct. at 1734.

159. *Id*.

160. *Id*. at 1735.

Asano's pedal design allowed one of the pedal's pivot points to remain fixed.[161] U.S. Patent No. 5,460,061 ("Redding") disclosed a similar adjustable pedal without a fixed pivot point.[162] Additionally, the body of prior art contained references that disclosed electronic pedal sensors.[163] U.S. Patent No. 5,063,811 ("Smith") corrected the problem of wear and tear on an electronic pedal sensor by placing the sensor on a fixed part of a non-adjustable pedal instead of the footpad.[164] Finally, U.S. Patent No. 5,819,593 ("Rixon") disclosed an adjustable pedal with an electronic pedal sensor mounted to the footpad.[165] However, Rixon suffered from the wear and tear problems that Smith was designed to correct for non-adjustable pedals.[166]

The district court held that the Engelgau patent claim at issue would have been obvious to a person of ordinary skill in the art, given the body of knowledge in the relevant prior art.[167] The court proceeded to undertake a step-by-step analysis of obviousness under the four-part *Graham* inquiry.[168] The prior art discussed above[169] was reviewed in determining the scope and content of the prior art, and the level of ordinary skill in the art was ascertained.[170] Next, the court looked to the differences between the prior art and the claimed invention.[171] Emphasizing that the prior art must be considered as a whole and that consideration must be given to what the prior art would suggest to a person of ordinary skill in the art,[172] the court found "little difference" between the prior art and the claim at issue.[173] Specifically, Asano taught the same type of adjustable pedal design as the claim at issue aside from the electronic pedal sensor, which was also fully disclosed in the prior art.[174]

The court did not stop after finding that the elements of the claim at issue were disclosed in the prior art; it proceeded to look for some teaching, suggestion, or motivation in the prior art to combine those

161. *Id*.
162. *Id*.
163. *Id.* at 1735–36.
164. *Id*.
165. *Id.* at 1736.
166. *Id*.
167. Teleflex Inc. v. KSR Int'l Co., 298 F. Supp. 2d 581, 596 (E.D. Mich. 2003) *rev'd*, 127 S. Ct. 1727 (2007).
168. *Id.* at 587.
169. *See supra* notes 160–66 and accompanying text.
170. *Id.* at 587–91.
171. *Id.* at 591–95.
172. *Id.* at 591.
173. *Id.* at 592.
174. *Id.* at 592–93.

disclosures to arrive at the claimed invention.[175] Given the wear and tear problems of the Rixon pedal design, the court found motivation to combine the prior art from both the nature of the problem involved and the express teaching in Smith.[176] While Teleflex did offer evidence of commercial success, it did not offer evidence on any other secondary considerations.[177] Such evidence was insufficient to defeat KSR's evidence of obviousness.[178] Ultimately, the district court held that it would have been obvious to combine Asano with an electronic pedal sensor attached to the fixed pivot point in order to avoid the wear and tear problems of Rixon, and granted KSR's motion for summary judgment.[179]

On appeal, the Federal Circuit, in a nonprecedential opinion, vacated the grant of summary judgment in favor of KSR, stating that the district court erred in not making specific findings of the teaching, suggestion, or motivation in the prior art to combine the references to arrive at the claimed invention.[180] The court provided:

> The reason, suggestion, or motivation to combine [prior art references] may be found explicitly or implicitly: (1) in the prior art references themselves; (2) in the knowledge of those of ordinary skill in the art that certain references, or disclosures in those references, are of special interest or importance in the field; or (3) from the nature of the problem to be solved, "leading inventors to look to references relating to possible solutions to that problem."[181]

Despite the seemingly broad reach of this language, the court went on to require a "rigorous application" of TSM as a guard against the temptation to view the claims in question through hindsight.[182] When the district court found that a person of ordinary skill in the art would have found it obvious to combine Asano with an electronic pedal sensor attached to the fixed pivot point, it erred in not making "specific findings" as to where this motivation to combine came from in the prior art.[183] The district court felt that the combination would have been obvious based on the nature of the problem to be solved, yet the Federal Circuit believed

175. *Id.* at 593.
176. *Id.* at 594.
177. *Id.* at 595–96.
178. *Id.* at 596.
179. *Id*.
180. Teleflex, Inc. v. KSR Int'l Co., 119 F. App'x 282, 290 (Fed. Cir. 2005), *rev'd*, 127 S. Ct. 1727 (2007).
181. *Id.* at 285 (quoting Ruiz v. A.B. Chance, Co. 234 F.3d 654, 665 (Fed. Cir 2000).
182. *Id.*
183. *Id.* at 288.

that the prior art references were directed to solving different problems.[184] A person of ordinary skill would not have found it obvious to combine Asano, which the court said was directed to the "constant ratio problem,"[185] with Smith, which was directed to solving the problem of wear and tear.[186] Additionally, since Smith was not directed to adjustable pedals, the court did not believe that it would adequately address wear and tear in such pedals.[187] Under the Federal Circuit's analysis, summary judgment was inappropriate, and the case was remanded.[188]

The Supreme Court granted certiorari to address how obviousness is determined and how TSM functions as part of that analysis.[189] After reviewing the prior art and the decisions of the district court and the Federal Circuit, the Court began by rejecting the "rigid approach" of the Federal Circuit as inconsistent with the more flexible approach advocated by previous Supreme Court decisions.[190] While there is a requirement for courts to provide reasons for the ultimate conclusion on obviousness, those reasons do not have to include "precise teachings" in the prior art, for the "court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ."[191] The Court stated that TSM was not adverse to the *Graham* framework of obviousness analysis, but also referred to TSM as merely a "helpful insight."[192]

---

184. *Id*.

185. The constant ratio problem refers to the problem of guaranteeing that the same amount of force will be required when pressing on the pedal, regardless of how the pedal is adjusted. The problem was solved by the use of a fixed pivot point on the adjustable pedal. KSR Int'l Co., v. Teleflex Inc., 127 S. Ct. 1727, 1735, 1738 (2007).

186. *Teleflex*, 119 F. App'x at 288–89.

187. *Id*.

188. *Id.* at 290.

189. *KSR*, 127 S. Ct. at 1734–35.

190. *Id.* at 1739.

191. *Id.* at 1741. *Cf.* Brief of Biotechnology Industry Organization as Amicus Curiae in Support of Respondents, *supra* note 14, at 29 ("Requiring the legal determination of obviousness to be based upon concrete facts will ensure that courts measuring the prior art and the expertise of a person with ordinary skill in the art will not take for granted the difficulties of combining well-known divergent elements and methodologies for new uses").

192. *KSR*, 127 S. Ct. at 1741. *See also* Lee & Butler, *supra* note 88, at 929 ("The Supreme Court Justices seemed to emphasize ambiguities in the TSM test throughout the *KSR v. Teleflex* oral arguments. . . ."). The transcripts of the oral arguments demonstrate the Justices feeling that TSM, in its present form, was inadequate in and of itself. *See* Transcript of Oral Argument, *KSR*, 127 S. Ct. 1727, No. 04-1350, 2006 U.S. Trans LEXIS 77. Justice Breyer stated "I've read it about 15 or 20 times now, I just don't understand what is meant by the term 'motivation.'" *Id.* at 9. When Mr. Goldstein, on behalf of Teleflex, said "I think you can't understand what motivation means and what the whole test that the Federal Circuit is employing means—", Justice Scalia interrupted to quip, "You're right about that." *Id.* at 28. As Goldstein continued to attempt to explain the distinction between motivation and teaching and suggestion, he said, "Justice Breyer, you don't understand," to which Justice Breyer admitted, "That's true." *Id.* at 31. Justice Scalia later on went so far as to say, "You say its test is

The Court assigned four crucial errors to the Federal Circuit's reasoning.[193] First, the Federal Circuit erred in limiting courts and examiners to only reviewing the problem that the patentee was trying to solve.[194] Even if the patentee was only concerned with finding a solution to a single problem, the obviousness determination is based not on what was obvious to the patentee, but what would have been obvious to one of ordinary skill in the art.[195] One of ordinary skill in the art would be aware of other problems existing in the field, and these other problems could provide the necessary motivation to combine prior art references.[196]

Second, the Federal Circuit erred in assuming that one of ordinary skill trying to solve a problem in the field would only look to prior art references which address the same problem.[197] The Court stated that "[c]ommon sense teaches . . . that familiar items may have obvious uses beyond their primary purposes" and emphasized that the hypothetical person of ordinary skill in the art must be afforded a level of common sense and creativity.[198]

Third, the Federal Circuit erred in concluding that a claim can never be shown to be obvious when it is shown that the combination of prior art references making up the claim would have been obvious to try.[199] The Court reasoned:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a

---

inclusive. I would say its test is meaningless." *Id.* at 36. Even Chief Justice Roberts agreed, arguing that the test was "worse than meaningless." *Id.* at 40.

193. *KSR*, 127 S. Ct. at 1742.

194. *Id.*

195. *Id*.

196. *Id*.

197. *Id*. *See also* Brief of Intellectual Property Law Professors as Amici Curiae in Support of Petitioner, *supra* note 81, at 12 ("There was apparently no room for the possibility that a person of ordinary skill in the art might find it obvious to apply prior art technology to a problem slightly different from the problem articulated in the prior art references").

198. *KSR*, 127 S. Ct. at 1742. *See also* Brief of Intellectual Property Law Professors as Amici Curiae in Support of Petitioner, *supra* note 81, at 12 ("This approach limits the role of the PHOSITA to that of a sort of reference librarian, who can locate appropriate prior art references but is apparently incapable of applying or recombining them with even a modicum of creativity in light of his or her knowledge and skill.").

199. *KSR*, 127 S. Ct. at 1742.

> combination was obvious to try might show that it was obvious under § 103.[200]

Finally, the Federal Circuit erred by holding that the risk of hindsight bias must be addressed by a strict adherence to finding specific teachings in the prior art which provide motivation to combine.[201] The Court held that such a strict adherence was unnecessary and would in fact lead to a denial of "recourse to common sense."[202] After reviewing these errors, the Court agreed with the district court's initial holding that the claim in question was obvious.[203]

B. The Federal Circuit's Application of KSR

In decisions handed down subsequent to *KSR*, the Federal Circuit has indicated it will now handle the non-obvious determination. Although the Federal Circuit has yet to address the question of obviousness of patents claiming DNA sequences of a protein when the amino acid sequence is known, analysis of its post-*KSR* decisions addressing other technologies is helpful in predicting how the Federal Circuit will handle such a case.

In re Icon Health and Fitness, Inc.[204] addressed the problem of combining prior art references absent an explicit suggestion to make such a combination.[205] The patent at issue claimed a treadmill with a folding base to allow for easier storage.[206] The obviousness rejection was based on two prior art references, with the conflict focused on the folding mechanism.[207] The court paid close attention to the similarity between the problems to be solved by the prior art references and the patent in question.[208] Even without an express suggestion to combine the two references, the court still found a sufficient rationale for the argument that a person having ordinary skill in the art would be motivated to combine

200. *Id*.
201. *Id*.
202. *Id.* at 1742–43. *See also* Brief of Intellectual Property Law Professors as Amici Curiae in Support of Petitioner, *supra* note 81, at 22 (arguing that requiring specific proof of a suggestion in the prior art may be untenable since practitioners are unlikely to publish common knowledge; if it obvious to practitioners in the field to combine prior art references, that information is unlikely to ever be published).
203. *KSR*, 127 S. Ct. at 1743.
204. 496 F.3d 1374 (Fed. Cir. 2007).
205. *Id.* at 1377–78.
206. *Id.* at 1377.
207. *Id.* at 1380–81.
208. *Id.* at 1381.

the references.[209] Although *In re Icon* dealt with technology unrelated to gene patents, it does show that the Federal Circuit is taking seriously the Supreme Court's demand that TSM is to be applied more leniently.[210]

Since *KSR*, the Federal Circuit has had the opportunity to address obviousness in several cases dealing with chemical compound patent claims.[211] In *Takeda Chemical Industries v. Alphapharm*, the patent in question claimed pioglitazone, a chemical compound for the treatment of diabetes.[212] Although the prior art did not disclose pioglitazone, a reference did disclose over one hundred chemical compounds, including compound b, a structurally similar compound to pioglitazone but which would require two modifications to arrive at the claimed compound.[213] Additionally, the prior art reference did not identify compound b as a promising line of interest.[214] The court determined that pioglitazone was not obvious, and provided a helpful insight to their analysis.[215] The court stated that "[r]ather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds, any one of which could have been selected as a lead compound for further investigation."[216] Further, the court pointed to the prior art's teaching away from choosing compound b.[217] This was not the situation, in the Federal Circuit's opinion, that the Supreme Court had envisioned when it stated that a determination of obviousness might flow from a finding that the claimed invention was obvious to try.[218] While the prior art in *Takeda* disclosed a wide array of possible solutions for antidiabetic treatment, the genetic code provides a "predictable solution" when attempting to determine the DNA sequence for a known amino acid sequence. Rather than a wide array of possibilities, only a limited number of DNA sequences would have to be considered.

The Federal Circuit also addressed the obviousness of a chemical compound in *Aventis Pharma Deutschland GMBH v. Lupin, Ltd*.[219] There,

209. *Id*.

210. *See id.* at 1380 ("Indeed, '*any* need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.'") (emphasis added) (quoting *KSR*, 127 S. Ct. at 1742).

211. *See* Takeda Chem. Indus. v. Alphapharm Pty., 492 F.3d 1350 (Fed. Cir. 2007); Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293 (Fed. Cir. 2007).

212. *Takeda*, 492 F.3d at 1353.

213. *Id.* at 1357–58.

214. *Id.* at 1358.

215. *Id.* at 1364.

216. *Id.* at 1359.

217. *Id.*

218. *Id.*

219. 499 F.3d 1293 (Fed. Cir. 2007).

the court made two statements of significant interest. First, the court stated that "it is sufficient to show that the claimed and prior art compounds possess a 'sufficiently close relationship . . . to create an expectation,' in light of the totality of the prior art, that the new compound will have 'similar properties' to the old".[220] If the Federal Circuit insists on treating DNA as a chemical compound in its analysis, it should both recognize the close relationship between DNA and amino acids and how that relationship functions in the creation of a protein. Second, the court commented that "isolation of interesting compounds [from a mixture] is a mainstay of the chemist's art" and should not be regarded as an invention worthy of protection.[221] It will be hard for the Federal Circuit, if it evenly evaluates the level of skill in biotechnology, to state that while it may not be innovation for a chemist to isolate a compound from a mixture, it somehow rises to the level of patent-worthy inventive genius for a biologist or geneticist, already knowing the amino acid sequence, to determine the DNA sequence.

IV. APPLYING *KSR*

Since the Court's *KSR* decision did not set forth a new test for obviousness, the actual effect of the decision is hard to predict. The Court explicitly endorsed using both the *Graham* factors and TSM to determine whether a patent claim is invalid due to obviousness over the prior art.[222] However, the Court firmly reprimanded the Federal Circuit for applying TSM in too strict a fashion.[223] Recent Federal Circuit decisions have demonstrated that the court is taking seriously the instruction that TSM is to be applied more flexibly.[224] While the Federal Circuit has not yet had the opportunity to readdress the obviousness of a DNA sequence patent for a gene where the full amino acid sequence has already been disclosed in the prior art, this issue is likely to reappear in light of *KSR*.[225]

---

220. *Id.* at 1301 (quoting *In re* Dillon, 919 F.2d 688, 692 (Fed. Cir 1990)).

221. *Id.* at 1302.

222. KSR Int'l Co., v. Teleflex Inc., 127 S. Ct. 1727, 1741 (2007).

223. *See supra* notes 190–92 and accompanying text.

224. *See supra* notes 204–21 and accompanying text.

225. However, the USPTO has heard an appeal based on an obviousness rejection for a patent claiming a polynuecleotide sequence. *Ex Parte* Kubin, Appeal 2007-0819, 2007 WL 2070495 (Bd. Pat. App. & Interf. May 31, 2007). The Board of Patent Appeals and Interferences stated the issue as "[w]ould Appellants' claimed nucleotide sequence have been obvious to one of ordinary skill in the art, based on [prior art] disclosure of p38 [the same protein that was being claimed] and [prior art] express teachings how to isolate its cDNA by conventional techniques?" *Id.* at *2. While the protein itself was disclosed in the prior art, its sequence was not disclosed, but could easily have been obtained through routine methodologies. *Id.* at *3. Further, the prior art disclosed the mouse version of the

A. Applying KSR *to Gene Patents*

The Supreme Court provided several distinct opportunities for the Federal Circuit to interpret *KSR* in ways which would allow or even require a determination of obviousness for a patent claiming a DNA sequence of a gene when the amino acid sequence of the encoded protein has already been disclosed in the prior art. First, while reviewing *United States v. Adams*,[226] a companion case to *Graham*, the Court stated that "when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result."[227] *Adams* dealt with a patent claim that substituted one known type of battery electrode for another.[228] At the time of *Adams*, biotechnology had not entered the world of patents, yet the principle articulated there can easily be extrapolated and applied to gene patents. If one considers a known amino acid sequence as the structure already known in the art, and the substitution of codons for each amino acid via the genetic code as the substitution of one element for another known in the field, the resulting DNA sequence ought to be regarded as an obvious, predictable result. Due to the degeneracy of the genetic code, the substitution may not be as simple as a one-to-one relationship. However, the principle is the same.

Second, the Court discussed the situation where a problem is identified in a field and has only a certain number of possible solutions.[229] If a person having ordinary skill in the art were to try these possible solutions and come up with nothing more than a foreseeable result, then a thing has not been *invented* so much as it has resulted from the interplay between common sense and ordinary skill in the art.[230] The Court then explicitly provided an opportunity for the "obvious to try" doctrine to have a place in the obviousness determination in those particular circumstances.[231]

---

protein and the mouse version's nucleotide sequence. *Id.* The Board argued that *Deuel* was not controlling due to the factual differences and the significant advances in the field since the *Deuel* decision. *Id.* The Board also noted that *KSR* "cast doubt on the viability of *Deuel* to the extent the Federal Circuit rejected an 'obvious to try' test." *Id.* at *5 (citing *KSR*, 127 S. Ct. 1727). To this end, the Board proposed that it might be more able to utilize an "obvious to try" standard than previously thought. *Id.* at *5.

226. 383 U.S. 39 (1966).

227. *KSR*, 127 S. Ct. at 1740.

228. *Id*.

229. *See supra* note 200 and accompanying text.

230. *KSR*, 127 S. Ct. at 1742.

231. *Id. Contra In re* O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988).

Since the Court's language was broadly worded, the principles flowing from the overall decision can once again easily be applied to gene patents. Guided by the genetic code, one can see how, given a full amino acid sequence for a known protein, there are only a finite number of possible DNA sequences which would code for that specific protein.[232] For each individual amino acid, there are only a certain number of codons that will add that specific amino acid to the growing protein.[233] As the number of possibilities grows, the time required to explore each of those possibilities also grows; however, it is still within the realm of a biotechnology PHOSITA's skill to make the attempt.[234] While it would certainly require a dedicated work ethic, the work of trying these known possibilities is not the type of invention meant to be rewarded by patent protection.[235]

Finally, the Court's opinion is laced with admonitions to apply TSM more flexibly and allow fact-finders to use a PHOSITA's common sense in making the obviousness determination.[236] Biotechnology is one of the fields that many commentators have recognized has been subjected to a much stricter determination of obviousness than other fields.[237] Use of common sense to provide a suggestion or motivation to combine certain prior art references absent an explicit teaching to do so is not necessarily an allowance of hindsight bias.[238] While hindsight bias still must be avoided, courts must allow the hypothetical PHOSITA to resort to common sense in "[fitting] the teachings of multiple [prior art references] together like pieces of a puzzle."[239]

B. Overruling In re Bell

In re Bell still governs the Federal Circuit's treatment of the obviousness of a patent claiming a DNA sequence of a gene was obvious when the amino acid sequence of the protein encoded by that gene had already been disclosed in the prior art.[240] However, the Supreme Court's

---

232. The Federal Circuit has already recognized the possibility of finding patent claims for DNA sequences obvious if the protein is of a sufficiently small size. *See In re* Deuel, 51 F.3d 1552, 1559 (Fed. Cir. 1995); *In re* Bell, 991 F.2d 781, 784 (Fed. Cir. 1993).

233. *See supra* notes 37–41 and accompanying text.

234. See *supra* note 130 for Rai's discussion of the use of codon catalogs.

235. *See KSR*, 127 S. Ct. at 1741 ("Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility.").

236. *See supra* notes 190–203 and accompanying text.

237. *See supra* note 6 and accompanying text.

238. *KSR*, 127 S. Ct. at 1742–43.

239. *Id.* at 1742.

240. *See supra* Part II.C.1.

decision in *KSR* and the principles therein demand the reversal of *Bell*. First, the Court restated the premise that substituting one known element for another which produced a predictable outcome would result in a finding of obviousness.[241] Given the full amino acid sequence already known in *Bell*, the DNA sequence claimed in the patent was merely a substitute. The genetic code provides a reliable and predictable relationship between amino acids and DNA. Each amino acid could easily be substituted by a codon, each codon simply being a set of three nucleotides. Thus, under *KSR*, the DNA sequence of the gene encoding the protein would have been a relatively simple substitution of one element for another known in the field of biotechnology, and therefore, obvious and unpatentable.

Further, *Bell* represents the situation envisioned by the Court when a problem has only a certain number of possible solutions.[242] Each amino acid of the protein encoded for by the gene claimed in *Bell* could only be encoded for by, at most, six different codons. Provided with the genetic code, any biotechnology PHOSITA would have been fully capable of determining the limited number of possible DNA sequences that would result in the amino acid sequence known in *Bell*. This is the type of common sense that the Court demanded be taken into account when making the obviousness determination.[243] Once that limited number of possibilities had been determined, it would have been obvious to try each possibility until arriving at the true DNA sequence.

C. Maintaining In re Deuel

While *KSR* mandates the reversal of *In re Bell*, the Federal Circuit should maintain the holding of *In re Deuel*. Unlike *Bell*, only a partial amino acid sequence had been disclosed in the prior art in *Deuel*.[244] The transition from this partial amino acid sequence to the nucleotide sequence claimed in the patent was not mere substitution. While it may have been feasible to substitute the possible DNA sequences for the known portion of the amino acid sequence, only nineteen amino acids in the sequence had been disclosed.[245] A further inventive step was required to arrive at the full DNA sequence of the gene. Additionally, the known partial amino acid

241. *See supra* text accompanying notes 227–28.
242. *See supra* text accompanying note 229.
243. *See supra* text accompanying note 230.
244. *In re* Deuel, 51 F.3d 1552, 1556 (Fed. Cir. 1995). *See supra* Part II.C.2.
245. *Id.*

sequence did not provide a limited number of possible solutions. It would only be possible to predict the possible DNA sequences for the known amino acid portion of the protein. The claimed DNA sequence contained the gene which encoded for a protein with a sequence of 168 amino acids.[246] There was no feasible way to predict the possible DNA sequence corresponding with the remaining 149 unknown amino acids. The Federal Circuit was correct in holding that a patent claiming a DNA sequence of a gene was warranted when only a partial amino acid sequence of the protein encoded by the gene was known in the prior art.

V. CONCLUSION

The Federal Circuit should overrule *Bell* and hold that a DNA sequence is obvious when the entire amino acid sequence of the protein of interest is known in the prior art. The Supreme Court's decision in *KSR*, advances in the field of biotechnology, and the simple relationship between amino acids and DNA sequences all point to such a conclusion. The structural similarity standard can no longer be applied in a workable fashion to DNA patents.[247] *Deuel*, however, presents a slightly different situation where only a portion of the amino acid sequence was known. In such a case, there is not a predetermined, finite set of potential DNA sequences. A researcher provided only with a partial amino acid sequence must still utilize more than simple common sense in discovering the full DNA sequence. Given the differences between *Bell* and *Deuel*, one can be overruled without affecting the precedent set by the other.[248] The patent system will be strengthened by reaffirming the maxim that only those

246. *Id.* at 1555.

247. *Compare* Natalie A. Lissy, Note, *Patentability of Chemical and Biotechnology Inventions: A Discrepancy in Standards*, 81 WASH. U. L.Q. 1069, 1094–95 (2003) (proposing that the Federal Circuit continue to follow precedent set in chemical compound cases in order to maintain consistency and predictability), *with* Dastgheib-Vinarov, *supra* note 7, at 144 (proposing that the Federal Circuit require gene patent applicants to sequence a complete gene, or enough of the gene to enable one to determine its function and preliminary diagnostic uses).

248. However, not all commentators believe the revision of the Federal Circuit's treatment of DNA patents should stop at *Bell*. *See* Wegner, *supra* note 19, at 459–60 ("It may be expected that in the wake of KSR, there will be a renewed challenge to the viability of the holding of *Deuel*."). Even the Board of Patent Appeals and Interferences asserts that the *Deuel* holding is questionable after *KSR*. *Ex Parte* Kubin, Appeal 2007-0819, at *5, 2007 WL 2070495 (Bd. Pat. App. & Interf. May 31, 2007). One commentator has gone further, believing that *KSR* calls for a change in not only the obviousness test, but also disclosure requirements. Laakmann *supra* note 14, at 72. Laakmann argues that such changes will push biotechnology patents downstream, meaning that patents will be directed to "more direct clinical applications" rather than "basic genomics discoveries." *Id.*

inventions representing a non-obvious advance of the prior art should be awarded patent protection.

Kate M. Lesciotto[*]

---

* B.S. Zoology and Biological Science (2004), Colorado State University; J.D. Candidate (2009), Washington University School of Law. I would like to thank Professor F. Scott Kieff for his helpful comments on this Note.