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A Post-*KSR* Consideration of Gene Patents: The "Obvious to Try" Standard Limits the Patentability of Genes

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A POST-*KSR* CONSIDERATION OF GENE PATENTS: THE "OBVIOUS TO TRY" STANDARD LIMITS THE PATENTABILITY OF GENES

> The information encoded in your DNA determines your unique biological characteristics, such as sex, eye color, age, and Social Security number.
>
> Dave Barry[1]

> I have a hunch that the unknown sequences of DNA will decode into copyright notices and patent protections.
>
> Donald E. Knuth[2]

I. INTRODUCTION

There are approximately 20,000 patents involving genes.[3] For example, "[n]ine patents have been applied for on the genes which determine your eyeball, 40 on those for your heart, and no fewer than 152 on a single grain of rice."[4] However, scholars and practitioners often question the scope and validity of gene patents on the grounds that genes are so essential for any being and so important to basic research that it is unethical to grant a private monopoly on them and that gene patents may hinder important research.[5]

These arguments against gene patents generally aim to overturn court precedent or to advocate new legislation.[6] This Note aims to reevaluate the validity and the scope of gene patents under a decision by the United States Supreme Court in 2007—*KSR Int'l Co. v. Teleflex Inc*.[7]

In *KSR*, the Court analyzed the tests for an important requirement for

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1. Thinkexist.com, http://thinkexist.com/search/searchquotation.asp?search=dna&q=author%3A%22Dave+Barry%22 (last visited Dec. 2, 2009). Dave Barry is a famous humorist.

2. HitXP: Biology Quotes Zone, http://www.hitxp.com/quotes/bio.htm (last visited Dec. 2, 2009). Donald E. Knuth is a famous computer scientist at Stanford University. He authored the seminal multivolume work, THE ART OF COMPUTER PROGRAMMING. He is regarded as the father of the analysis of algorithms.

3. Andrew W. Torrance, *After the Gene Rush*, BIO-IT WORLD, Nov. 2002, at 80.

4. Editorial, *Leader: Whose Life is it Anyway?: The Knowledge Economy Should Be for All*, GUARDIAN (Manchester, U.K.), Nov. 15, 2000, at 23, http://www.guardian.co.uk/science/2000/nov/15/genetics.guardianleaders.

5. *See infra* Part III.C.

6. *See infra* Part III.C.

7. KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398 (2007).

patentability—the nonobviousness requirement.[8] This decision effectively encourages challenges to patent validity based on nonobviousness; cases that raised a nonobviousness challenge nearly doubled in 2008, compared to the number of the cases from the three previous years.[9] Furthermore, *KSR* seems to make it harder for a patent to survive a nonobviousness challenge; in cases that raised a nonobviousness challenge, 30% fewer patentees prevailed in 2008, compared to those that prevailed over the three previous years.[10] This Note focuses on the effect of the *KSR* decision on a specific class of patents: gene patents.

In Part II, this Note outlines the criteria by which an invention qualifies for patent protection. Part III presents the current rationales for granting gene patents and summarizes arguments and efforts to limit or ban such patents. Part IV reviews the tests for the nonobviousness requirement as reiterated in the *KSR* decision and further illustrated in several post-*KSR* cases. Based on an analysis of these cases, this Note argues that the "obvious to try" standard revived by the Court in *KSR* challenges some basic rationales of gene patenting and that the adoption of this standard by lower courts suggests a reconsideration in the judicial branch of gene patentability. Finally, in Part V, this Note proposes that, as a result of *KSR*, the United States Patent and Trademark Office (USPTO) should modify its standard for granting patents on genes. This Note lays out the criteria by which only Deoxyribonucleic acid (DNA) molecules that are discovered by a new strategy, assigned a new function, or modified by a new method would be patentable. These criteria comport with the Court's *KSR* decision and promote basic research.

II. USPTO GRANTS PATENT PROTECTION ON NEW AND USEFUL INVENTIONS

The patent system of the United States is based on the Patent Act.[11] Congress enacted the Patent Act "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to . . . Inventors the exclusive Right to their respective . . . Discoveries."[12] Under the Patent Act, the USPTO examines applications from inventors and renders a decision as to patentability primarily pursuant to sections 101–103.[13]

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8. *Id.* For more on patentability requirements, see *infra* Part II.

9. John T. Aquino, *Biotech, Pharma Patents Said Less Affected than Others by High Court's Decision in* KSR, 76 Pat. Trademark & Copyright J. (BNA) 429 (July 25, 2008). This report claims that the impact of *KSR* on biotech patents will not be as noticeable as the impact on other areas because biotech is generally regarded as less predictable. *Id.*

10. *Id.*

11. Patent Act, 35 U.S.C. §§ 1–376 (2006).

12. U.S. CONST. art. I, § 8, cl. 8.

13. Patent Act §§ 101–103. Congress enacted the first Patent Act in 1790, and two major

Section 101 of the Patent Act lists types of inventions that are patentable (i.e., are patentable subject matter), including any "process, machine, manufacture, or composition of matter, or any . . . improvement thereof."[14] The Court has interpreted this requirement to exclude "[t]he laws of nature, physical phenomena, and abstract ideas."[15] Nevertheless, the scope of patentable subject matter is quite broad, encompassing "anything under the sun that is made by man."[16]

Section 101 also requires that a patentable invention be new.[17] This requirement is further defined in section 102, stipulating that a new invention is not anticipated by prior art, i.e., someone has not already made the same invention,[18] and section 103, stipulating that a new invention as a whole should not have been obvious to a person with ordinary skill in the art at the time of the invention.[19] Section 103 thus contains a nonobviousness requirement.

Section 103's nonobviousness requirement makes instinctive sense: a subject matter that would have been obvious is not inventive enough to justify a grant of a monopoly. However, courts have struggled with how to draw the line between what is obvious and what is not because, in hindsight, inventions may seem more obvious than they were at the time when the invention took place. Not until more than a decade after the adoption of section 103 did the Court lay out the general test for nonobviousness. In the seminal case *Graham v. John Deere Co. of Kansas City*, the Court developed the *Graham*

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revisions took place in 1870 and 1952. JANICE M. MUELLER, AN INTRODUCTION TO PATENT LAW 30, 30–31 (2d ed. 2006). The current Patent Act is very similar to the 1952 version, which has been codified at 35 U.S.C. §§ 101–103. *Id.*

14. The full text of section 101 of the Patent Act reads: "101. Inventions patentable. Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent thereof, subject to the conditions and requirements of this title." *Id.*

15. Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) (citing Parker v. Flook, 437 U.S. 584 (1978); Gottschalk v. Benson, 409 U.S. 63, 67 (1972)).

16. *Id.* (quoting S. REP. NO. 82-1979, at 5 (1952); H.R. REP. NO. 82-1923, at 6 (1952)).

17. Patent Act § 101.

18. *Id.* § 102.

19. Patent Act § 103(a) was codified in the 1952 Patent Act. This section provides that:

> 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.

factors.[20] Four decades later, the Court brought the spotlight back to the nonobviousness inquiry in *KSR*.[21]

In addition to the novelty requirement, an invention also must be useful to be deemed patentable.[22] A patentable invention needs to have a well-established utility; a well-established utility means a utility that "a person of ordinary skill in the art would immediately appreciate . . . and . . . [one that] is specific, substantial, and credible."[23] The utility requirement is not hard to satisfy; as long as an inventor can assert a "particular practical purpose" and the invention serves this purpose, the requirement is satisfied.[24] To illustrate its utility requirement, the USPTO notes that using "a complex invention as landfill" is not a substantial and specific utility.[25]

The USPTO currently grants patents on a gene as a new composition of matter.[26] A naturally occurring gene is new and patentable if it is isolated from its natural state, i.e., as a purified DNA molecule.[27] Opponents of gene patents often contend that genes are not patentable subject matter because genes are the secret of life and because naturally occurring genes, i.e., genes that have not been modified by man, are not new.[28] These arguments have not been successful. Although this Note concedes that natural genes can be new compositions of matter under section 101, it proposes that they generally are not patentable because they fail the nonobviousness requirement under section 103.

III. GENE PATENTING UNDER ATTACK

Genes are chemical compositions that carry the information of life.[29] Before diving into the controversy surrounding gene patenting, it is helpful to first review some basic biochemistry. And, because this Note proposes to incorporate the degree of technical difficulties in obtaining a gene sequence into the nonobviousness test, some background information relating to the current state of molecular biotechnology is also included.

Id. § 103(a).

20. 383 U.S. 1 (1966). Part IV of this Note will further discuss the *Graham* factors.

21. KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398 (2007).

22. Patent Act § 101.

23. USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092, 1098 (Jan. 5, 2001).

24. *Id.*

25. *Id.*

26. *See, e.g.*, *id*. at 1093.

27. See *infra* Part III.A for the biochemistry of a gene and detailed rationales upon which genes are patented.

28. *See infra* Part III.C.

29. Laurie L. Hill, *The Race to Patent the Genome: Free Riders, Hold Ups, and the Future of Medical Breakthroughs*, 11 TEX. INTELL. PROP. L.J. 221, 223–24 (2003).

A. Basic Biochemistry: Genes and DNA

A gene is a piece of Deoxyribonucleic acid (DNA) that carries the information for a genetic trait.[30] DNA is a linear polymer consisting of four types of nucleotides, A, T, G, and C, and the sequence of these nucleotides records the genetic information of a cell.[31] Because of the specific matching relationship between these nucleotides, A to T and G to C, a DNA molecule strand can be used as a template to synthesize a complementary DNA strand.[32] This near-perfect self-replication of DNA molecules ensures that genetic information passes on.[33]

The self-replicating DNA molecules in a cell are used as templates in the synthesis of various protein molecules, i.e., a gene is expressed.[34] A gene consists of coding sequences in which every three consecutive nucleotides form a strain of codons.[35] Different codons, i.e., different combinations of tri-nucleotides, dictate specific amino acids, which are the building blocks of a protein molecule.[36] A gene also consists of non-coding sequences, in which elements regulating the expression profile of the gene often reside.[37]

Living organisms are the result of proper gene expression, and the maintenance and evolution of species depend on the replication of DNA.[38] The importance of promoting gene research is obvious. Scientists can easily simulate DNA replication in a test tube, i.e., *in vitro*,[39] as long as they know parts of the sequence.[40] Due to the correspondence between codons and amino acids, when the sequence of a gene is known, scientists can predict the sequence of the protein that the gene encodes.[41] However, due to codon redundancy, scientists cannot determine the exact sequence of a DNA

30. BURTON E. TROPP, MOLECULAR BIOLOGY: GENES TO PROTEINS 12 (3d ed. 2008).

31. *Id.* at 6. This textbook is a good source for basic background knowledge on biology and rudimentary molecular genetics.

32. *Id.* at 21–22. DNA molecules exist in cells as matching double strands. *Id.* Although both strands get replicated to make identical double-stranded molecules, only one strand stores genetic information and participates in transcription. *Id.*

33. *Id.* at 23.

34. *Id.* Different proteins are expressed at different times and in different locations, which results in the complicated machinery we call life. *Id.*

35. *Id.* at 23.

36. *See, e.g.*, a genetic codon table. *Id.* at 907.

37. For example, a small nucleotides motif, the TATA box, is not transcribed but is required for the basal expression of the gene downstream of this motif in eukaryotic cells. *Id.* at 671–72.

38. *See id.* at 23.

39. Latin for "within the glass," referring to an experiment in a test tube.

40. TROPP, *supra* note 30, at 162–63. To simulate DNA replication, scientists need to synthesize a short stretch of nucleotides that matches to a strand of DNA as a primer. *Id.* The sequence following this stretch can then be synthesized by adding matching nucleotides after the primer. *Id.*

41. *See, e.g.*, *id.* for a genetic codon table.

molecule based on the sequence of the protein.[42]

Researchers do not stop at understanding and simulating the natural behavior of a DNA molecule; instead, scientists can manipulate the expression of genes in a variety of ways. Scientists may replace the regulatory sequence of a gene to express the gene at a time or at a location deviated from its endogenous temporal and spatial profile.[43] Alternatively, scientists may modify the coding sequence of a gene to change the gene's protein product and its function in a cell.[44] Some modifications are routine. For example, the coding sequence of gene X can be fused with the regulatory sequence of gene Y, and the gene chimera will express protein X where protein Y naturally exists. If gene X and gene Y are from different species, this modification will enable the expression of a foreign gene in species Y.

Furthermore, scientists often predict the function of a newly discovered DNA sequence based on its homology to other DNA sequences for which functions are known.[45] Homology in molecular evolution theory means a shared ancestry, and related species share genes that are highly similar in their sequences.[46] In research, if an unknown DNA molecule consists of sequence motifs that are similar to some genes with known functions, then the DNA molecule is presumed to share homology with, and perform functions similar to that of, these known genes. Nowadays, with the fast-growing sequence databases, newly discovered sequences often can be assigned to putative functions after a free, quick Internet search.[47]

B. Justification and Rationales to Patent Genes

1. Modified Genes Are Patentable as a Composition of Matter Under *Chakrabarty*

In 1980, the United States Supreme Court's decision in *Diamond v.*

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42. A given amino acid can be the product of several different codons (termed "codon redundancy"). For example, six different codons all can encode the amino acid Arginine. *Id.*

43. For a gruesome example, see the fruit fly that has legs growing out of its eyes due to the expression of genes at the wrong spot. NEIL A. CAMPBELL ET AL., BIOLOGY 371 (8th ed. 2008).

44. *See, e.g.*, *id.* at 344.

45. Many bioinformatics tools are available to predict gene functions based on sequence homology. *See, e.g.*, *id.* at 430.

46. *Id.* at 463.

47. For example, one can input a DNA sequence into the Basic Local Assignment Search Tool (BLAST) search engine provided by the National Center for Biotechnology Information (NCBI), and, within seconds, a map of matched domains will appear. By following the linked description of these domains, a biologist can often predict the function of the input sequence. The BLAST search engine is equipped with 800 complete genomes from thirty-three species, representing mammals, other vertebrates, invertebrates, plants, fungi, and protozoa. BLAST, http://blast.ncbi.nlm.nih.gov/Blast.cgi (last visited Dec. 2, 2009).

Chakrabarty allowed the patenting of a living organism.[48] The Court noted that the patentable subject matter under section 101 of the Patent Act should be broadly construed, and that a living organism could be viewed as a "manufacture, or [a] composition of matter," both being patentable subject matter.[49] The Court stated that "Congress intended statutory subject matter to 'include anything under the sun that is made by man.'"[50] Therefore, the Court concluded that a genetically modified organism is patentable subject matter because it is "a product of human ingenuity," not a "hitherto unknown natural phenomenon."[51] The Court in *Chakrabarty* found the patentability of a living organism depended on whether the living thing was modified by a human, and thus refused to take an ethical stand on the issue.[52] Under this line of logic, although genes are regarded as sacred by many, they are patentable subject matter under section 101 as long as the genes sought to be patented are modified by a researcher.

2. Purified and Isolated DNA Sequences Are Patentable Even If They Exist in Nature

Chakrabarty does not justify the patenting of a naturally occurring gene. The current rationale for patenting a gene with its sequence unmodified is instead based on the 1970 *In re Bergstrom* decision, in which the court held that a purified form of a compound was patentable even though its impure form was known to the public.[53] In this case, the court conceded that "an unknown compound or composition of materials merely discovered from nature is not patentable."[54] However, the court further noted that, because the pure form of the compound did not exist in nature, the pure form of the natural compound was patentable subject matter.[55] The court also pointed out that whether the pure form of the compound possessed the same function as the impure mixture was irrelevant to the inquiry into patentability.[56]

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48. Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980).

49. *Id.* at 308.

50. *Id.* at 309 (quoting S. REP. NO. 82-1979, at 5 (1952); H.R. REP. NO. 82-1923, at 6 (1952)).

51. *Id.*

52. *Id.* at 316–18. The Court in *Chakrabarty* split five to four. *Id.* at 303. Chief Justice Burger delivered the opinion of the Court, in which Justices Stewart, Blackmun, Rehnquist, and Stevens joined. *Id*. Justice Brennan filed a dissenting opinion, in which Justices White, Marshall, and Powell joined. *Id*.

53. *In re* Bergstrom, 427 F.2d 1394, 1401–02 (C.C.P.A. 1970).

54. *Id.* at 1401.

55. *Id.*

56. *Id.* at 1402.

3. Computer-Predicted Utility Based on Homology to Known Proteins Is a Utility that Satisfies Section 101

Following *Bergstrom*, inventors may apply for gene patents for which they have not developed a practical function; scientists can merely assert a gene's natural function in a cell as its utility in a gene patent.[57] In practice, a gene patent application satisfies the utility requirement if the sequence of the gene is homologous to another gene whose function has been characterized.[58] Homology is often presumed from sequence similarities between the current invention and the prior art genes.[59] However, this sequence similarity creates a prima facie case of obviousness.[60]

4. The Federal Circuit[61] Held in 1995 that a DNA of Which the Protein Product Is Homologous to a Known Protein Is Not Obvious

A prima facie case of nonobviousness based on sequence similarities is not difficult to rebut.[62] For example, in *In re Deuel*, Thomas F. Deuel and his collaborators (collectively Deuel) tried to patent some sequences encoding the protein HBGF at a time when the sequence of neither the protein HBGF nor the gene encoding HBGF was known.[63] Deuel followed an established protocol based on the Maniatis reference to obtain the DNA sequence that encodes HBGF.[64] However, an article by Bohlen had previously disclosed a protein, HBBM, that shares a sequence similarity with an HBGF protein.[65] The USPTO rejected the patent for being obvious under the combination of the Bohlen reference and the Maniatis reference.[66]

The Federal Circuit reversed.[67] First, the court held that the Bohlen reference did not disclose the structure of a DNA molecule but that of a

57. *See id.*

58. USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092, 1092–99 (Jan. 5, 2001).

59. *In re* Deuel, 51 F.3d 1552, 1558 (Fed. Cir. 1995).

60. *Id.*

61. The United States Court of Appeals for the Federal Circuit (the Federal Circuit) is the special venue that deals with patent cases. It was formed in 1982 by the merger of the United States Court of Customs and Patent Appeals and the appellate division of the United States Court of Claims. United States Court of Appeals for the Federal Circuit, http://www.cafc.uscourts.gov/about.html (last visited Dec. 2, 2009).

62. Many DNA sequences that are homologous to known genes have been patented. The claims underlying the *Deuel* case are examples.

63. *Deuel*, 51 F.3d at 1554–55.

64. *Id.* at 1555. "Maniatis describes a method of isolating DNAs or cDNAs by screening a DNA or cDNA library with a gene probe." *Id.* at 1556.

65. *Id.* Peter Bohlen was named as inventor of European Patent Application No. 0326075, published August 2, 1989. *Id.* at 1556 n.3.

66. *Id.* at 1555–56.

67. The court reversed the U.S. Patent and Trademark Office Board of Patent Appeals and Interferences' decision. *Id.* at 1559.

protein molecule.[68] Due to codon redundancy, the DNA sequence encoding HBGF was not obvious upon the release of the protein sequence of HBBM.[69] The court also criticized the USPTO's reliance on the Maniatis reference because the claim was directed at a composition, not a method.[70] The court reasoned that "the existence of a general method of isolating . . . DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs."[71]

Under the USPTO's generous examination standards, many genes are patented. Between 1970 and 1979, only 123 DNA-based patents were granted.[72] The number increased to 16,057 between 1990 and 1999.[73] Since 2000, about 3,000 to 4,000 DNA-based patents have been granted each year.[74] Despite the growing number of gene patents, the opposition to gene patenting remains strong.[75]

C. Ethical and Practical Concerns About Patenting Genes and Unsuccessful Attempts to Abolish or Limit Gene Patents

1. Ethical Concerns and a Recent Legislative Effort in Eliminating Gene Patents

Opponents of gene patents claim that genes should not be patentable subject matter because "the sequence of the human genome is at the core of what it means to be human and no person should be able to own/control something so basic."[76] However, the USPTO and the federal courts adhere to the statutory requirements of patentability and refuse to take an ethical stand on the issue.[77] Because of this reluctance in the executive and judicial branches, these opponents continue to lobby for a complete legislative ban on gene patents.

For example, the Genomic Research and Accessibility Act (GRAA) was proposed in the 110th Congress to completely stop granting patents on the

68. *Id.*

69. *Id.*

70. *Id.*

71. *Id*. The court's statement in the *Deuel* decision essentially has been overruled after *KSR*. *See infra* Part IV.D.3.

72. DPD: About the DNA Patent Database, http://dnapatents.georgetown.edu/aboutdpd.htm (last visited Dec. 2, 2009). "The DPD is a core of Duke University's Center for Excellence in ELSI Research . . . ." *Id.*

73. *Id.*

74. *Id.*

75. Hill, *supra* note 29, at 222–23, 241–45.

76. USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

77. *See id.* at 1093–94.

human genome and all nucleotide sequences.[78] The scope of this bill encompasses naturally occurring genes as well as synthetic DNA or RNA molecules. But the GRAA received very little support. After its introduction and referral to subcommittees in early 2007, no movement has been reported, and the Act seems to have been abandoned.[79] Some even found the GRAA "extreme and unprecedented" and noted that "Congress and the courts have . . . refused to enact any subject matter specific limitation on patentable subject matter,"[80] including a ban on controversial issues such as human cloning.

A subject-matter-specific limitation is not likely to succeed in the future either. The only subject-matter limitation that is based on ethical concerns is a USPTO policy to refuse claims encompassing a human being; a policy that does not receive explicit support from either the legislative branch or the judicial branch.[81] There is no indication that the USPTO has considered a similar policy to ban gene patents.[82]

2. Gene Patents Should Not Be Allowed Because They Impede, Rather than Advance, Research and Development

Another group of opponents to gene patents contends that the justification for the patent system fails for gene patents.[83] The patent system grants a time-limited monopoly to an inventor to induce him to disclose his invention to the public. The theory behind this limited monopoly is that the inventor will have an incentive to invest time and resources into developing the invention. Furthermore, the public will receive the benefit of having access to the information regarding the invention. However, opponents of gene patenting assert that a twenty-year term monopoly on genes cannot be justified on either the grounds that the monopoly promotes investment or that it benefits the public.[84]

First, gene patents provide patent owners with more power than that

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78. H.R. 977, 110th Cong. (2007). "Notwithstanding any other provision of law, no patent may be obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies." *Id.*

79. GovTrack.us, http://www.govtrack.us/congress/bill.xpd?bill=h110-977 (last visited on Dec. 2, 2009). Issues regarding the patentability of biological molecules are not mentioned in the latest efforts to reform the Patent Act. S. 515, 111th Cong. (2009); H.R. 1260, 111th Cong. (2009).

80. Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, 76 UMKC L. REV. 295, 296 (2007).

81. U.S. PAT. & TRADEMARK OFFICE, MANUAL OF PATENT EXAMINING PROCEDURE § 2105 (2007).

82. This Note proposes that, in light of the *KSR* decision, the USPTO should adopt a more stringent system for granting patents on genes.

83. Hill, *supra* note 29, at 241.

84. *See id.*

bestowed by other types of patents because gene patents are impossible to design around.[85] When a mechanical device is patented, a person skilled in mechanical engineering may examine the patent and design a device that is different from the one claimed in the patent but achieves a similar purpose.[86] Design-around products are generally encouraged.[87] However, once a gene is patented, all research related to this piece of DNA sequence is suspended until the expiration of the patent. Furthermore, gene patents are often built on knowledge accumulated by publicly funded basic research.[88] Therefore, an imbalance exists between the input and the output of a gene patent owner.

Second, gene researchers generally are not affected by the incentives provided by the patent system.[89] The driving force behind basic scientific research comes from university scientists, who receive mostly public funding for their research and who are often perceived to be motivated by peer recognition rather than economic reward.[90]

However, gene patents are not likely to be limited under this theory because, although Congress enacted the Patent Act to promote progress in science,[91] this purpose is not a statutory requirement of patentability. Also, patent owners rarely file infringement actions against a noncommercial researcher;[92] therefore, whether gene patents will impede basic research is not clear.[93]

In summary, arguments against gene patenting generally assert that genes should be treated differently from other subject matter and new criteria should be adopted for determining the patentability of genes. While the USPTO has issued special guidelines for how a gene patent should be presented, including both a written requirement and a disposition requirement, the USPTO found no statutory basis for treating the patentability of genes differently than other types of patentable subject matter.[94] Opponents of gene patenting argue either that precedent should be overturned or that new legislation should be passed

85. *Id.* at 257.

86. *See id.* at 236.

87. *Id.*

88. *Id.* at 242–46.

89. *Id.* at 243.

90. *Id.*

91. U.S. CONST. art. I, § 8, cl. 8.

92. *See* Amy Yancey & C. Neal Steward Jr., *Are University Researchers at Risk for Patent Infringement?*, 25 NATURE BIOTECHNOLOGY 1225, 1225–28 (2007). Companies producing gene chips, such as Affymetrix, incorporate thousands of gene sequences in their products but have never been sued by a patent owner. *Id.*

93. Many researchers in noncommercial research facilities are not aware of gene patents. Very often, university researchers obtain a free license to work on a patented gene.

94. USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

to limit the patentability of genes.[95] Some even advocate a ban on gene patenting altogether.[96] However, this Note proposes that the Court's decision in *KSR* has already provided a basis for limiting the scope of gene patents on the ground of nonobviousness.

IV. NONOBVIOUSNESS TESTS: *GRAHAM*, *KSR*, AND POST-*KSR* CASES

A. The Framework for a Nonobviousness Analysis: The Graham *Factors*

Little more than a decade after Congress adopted the statutory requirement of nonobviousness, the Supreme Court in *Graham v. John Deere Co. of Kansas City* laid out a multifactor test to assist in drawing a line between what is or is not obvious.[97] At least one reason why the Court examined the nonobviousness issue was "a notorious difference between the standards applied by the Patent Office [and those applied] by the courts."[98] The Court analyzed the legislative history of section 103 and found that Congress, in enacting section 103, had not intended to lower the bar on patentability but merely intended to bring "uniformity and definiteness" to the issue of what is "new."[99] The Court concluded that this congressional goal could be achieved by conducting a case-by-case inquiry into nonobviousness pursuant to a practical test of patentability, later referred to as the *Graham* factors.[100]

The *Graham* factors provide a step-by-step analysis of nonobviousness according to the statutory language in section 103.[101] The first step of the inquiry is to determine "the scope and content of the prior art [and to ascertain the] differences between the prior art and the claims at issue."[102] The second step is to resolve "the level of ordinary skill in the pertinent art"[103] to determine whether "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."[104] Additionally, the Court noted that factors termed "secondary considerations" might be used "to give light to the circumstances surrounding the origin of the subject matter sought to be patented[,]" including

95. *See supra* Part III.C.1.

96. *See id.*

97. Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 17 (1966).

98. *Id.* at 18.

99. *Id.* at 17. For the requirement that an invention needs to be new to be patentable, see Patent Act § 101.

100. *Graham*, 383 U.S. at 17–18.

101. See *supra* note 19 for the precise language of section 103.

102. *Graham*, 383 U.S. at 17.

103. *Id.*

104. Patent Act § 103(a).

"commercial success, long felt but unsolved needs, failure of others, etc."[105] The Court further explained that secondary considerations were included to "'guard against slipping into use of hindsight'[106] . . . and to resist the temptation to read into the prior art the teachings of the invention in issue."[107]

Essentially, the issue in *Graham* was whether a combination of two known elements could be nonobvious and, thus, patentable.[108] The lower courts found that, although the invention was "a combination of old elements," it was nonobvious and patentable because "nothing in the prior art [suggested the] unique combination of these old features" and because the invention fulfilled "the long-felt need with an economical, efficient, utilitarian apparatus which achieved novel results and immediate commercial success."[109] However, the Supreme Court disagreed and found that the invention "rests upon exceedingly small and quite non-technical mechanical differences in a device which was old in the art."[110] The long-felt need was irrelevant in *Graham* because the reference that rendered the invention obvious had not come out until recently.[111] But the Court did not comment specifically on the absence of a suggestion to combine references.[112]

B. Four Decades: Federal Courts' Efforts to Apply the Graham *Factors*

Federal courts generally have followed *Graham*'s analysis of nonobviousness.[113] Between 1966, when *Graham* was decided, and 2007, when the Court once again picked up the issue of nonobviousness, 978 federal cases involved a determination of nonobviousness,[114] of which at least 688 adopted the *Graham* factors in their analyses.[115] Similarly, of 138 cases in the Court of Appeals for the Federal Circuit (the Federal Circuit) that dealt with

105. *Graham*, 383 U.S. at 17–18.

106. *Id.* at 36 (quoting Monroe Auto Equip. Co. v. Heckethorn Mfg. & Supply Co., 332 F.2d 406, 412 (1964)).

107. *Id.* at 36.

108. *Id.* at 30.

109. *Id.* at 30 (quoting Calmar, Inc. v. Cook Chem. Co., 336 F.2d 110, 113–14 (8th Cir. 1964)).

110. *Id.* at 36.

111. *Id.*

112. Later, the federal courts in applying the *Graham* factors introduced the requirement of a motivation or a suggestion to combine prior art references. *See infra* Part IV.B.

113. The author Shepardized® the *Graham* case on Lexis and restricted the search to Headnote 3 of the *Graham* case for cases that have adopted the *Graham* factors. Before the *KSR* decision, 688 cases utilized the *Graham* factors.

114. The author conducted the searches on http://www.lexisnexis.com/lawschool/research. The time period is from February 21, 1966, to April 30, 2007. The author conducted a search for the term "nonobviousness" in all the cases from federal courts and retrieved 1,041 cases. A refined search for cases from the eleven circuits (district courts and courts of appeals), the D.C. Circuit, and the Federal Circuit yielded 978 cases involving nonobviousness.

115. *See supra* note 113.

nonobviousness, 96 cases adopted the *Graham* factors.[116]

Aside from the *Graham* factors, courts often ask whether there is a suggestion or motivation to combine known elements in prior art references.[117] For example, a Federal Circuit decision in 2005 stated that:

> . . . [S]ection 103 requires some suggestion or motivation in the prior art to make the new combination . . . [and dictates that a] suggestion or motivation to modify prior art teachings may appear in the content of the public prior art, in the nature of the problem addressed by the invention, or even in the knowledge of one of ordinary skill in the art.[118]

The court resorted to expert testimony to determine whether a motivation or suggestion to combine the available prior art references existed for a person with ordinary skill in the art.[119]

In developing this "teaching, suggestion, or motivation" test (the TSM test), federal courts did not add additional requirements to nonobviousness.[120] Rather, the test is a strategy to evaluate the difference between the prior art and the current invention: if something implicitly or explicitly teaches, suggests, or motivates the combination of several prior art references, the difference between the new combination and prior art is not patentable.[121] The courts applied the TSM test because, without evidence of this teaching, suggestion, or motivation, a nonobviousness analysis "simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability. . . ."[122]

This test is apparently a flexible one—a suggestion or motivation can be found beyond the prior art and even in the general knowledge of a person with ordinary skill in the art. However, the application of this test was deemed too rigid when the Supreme Court decided to review the nonobviousness issue again.[123]

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116. The search strategy was similar to those described in *supra* notes 113–15.

117. Princeton Biochemicals, Inc. v. Beckman Coulter, Inc., 411 F.3d 1332, 1338 (Fed. Cir. 2005).

118. *Id.*

119. *Id.*

120. *See Princeton Biochemicals*, 411 F.3d at 1338.

121. *Id.*

122. Teleflex, Inc. v. KSR Int'l Co., 119 Fed. App'x 282, 285 (Fed. Cir. 2005).

123. KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 415–28 (2007).

C. The KSR *Decision: The Return of the* Graham *Factors*

When the Federal Circuit applied the TSM test of nonobviousness, the court held that when two prior art references taught two aspects of an invention but did not specifically address the problem that the patentee had set out to solve, the patentee lacked the motivation to combine the two references and the invention was not obvious.[124] The Supreme Court found that the TSM test, at least as applied by the Federal Circuit, was too rigid and conflicted with the Court's precedents.[125]

Although the Supreme Court acknowledged that the TSM requirement was insightful because "discoveries almost of necessity will be combinations of what, in some sense, is already known,"[126] the Court refused to adopt a rigid and mandatory formula in applying the test; the Court stated that "neither the particular motivation nor the avowed purpose of the patentee controls."[127] Therefore, if the combination of the references was obvious to a person with ordinary skill in the art at the time the invention was made, even though the prior art references failed to specifically teach, suggest, or motivate the invention, the invention would be obvious and nonpatentable.[128]

The impact of *KSR* goes beyond the TSM test. Indeed, the Court did not renounce the TSM test, and this test generally was not rigidly applied in the federal courts.[129] However, because *KSR* was the second case on nonobviousness in four decades, the Court reviewed a series of rationales in finding an invention obvious and brought nonobviousness back to the center stage of a challenge against patent validity.[130] One of the rationales in finding obviousness, the obvious to try standard, provides the basis for the proposed framework in limiting the validity and the scope of gene patents.[131]

*D. Post-*KSR*: The Revived Obvious to Try Standard*

Courts have rejected the obvious to try argument in many cases because "selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings."[132] Courts instead adopted an

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124. *Teleflex*, 119 Fed. App'x at 286.

125. *KSR*, 550 U.S. at 419.

126. *Id.* at 418–19.

127. *Id.* at 419.

128. *Id.* at 419–21.

129. *See, e.g.*, Princeton Biochemicals Inc. v. Beckman Coulter, Inc., 411 F.3d 1332 (Fed. Cir. 2005).

130. *KSR*, 550 U.S. at 419–20.

131. *See infra* Part V.

132. *In re* Dow Chem. Co., 837 F.2d 469, 473 (Fed. Cir. 1988). Until recently, the Federal Circuit clearly denied the obvious to try argument. *See, e.g.*, Abbott Labs. v. Andrx Pharms., Inc., 452 F.3d 1331, 1352 (Fed. Cir. 2006).

inquiry that was similar to the TSM test and examined whether there was "a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure."[133]

The *KSR* Court, however, held that "the fact that a combination was obvious to try might show that it was obvious under § 103" in some instances.[134] Whether an invention is obvious under the obvious to try standard depends on (1) whether "there are a finite number of identified, predictable solutions" for the problem that the invention seeks to resolve, and, thus, "a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp"; and (2) whether the effort "leads to the anticipated success."[135] If the answer is affirmative to both inquiries, the invention "is likely the product not of innovation but of ordinary skill and common sense" and is not patentable.[136]

Courts immediately adopted this revived obvious to try standard in nonobviousness inquiries. The following three cases illustrate how courts find nonobviousness in biotech patents using the revived obvious to try standard.

1. *PharmaStem*: An Invention May Be Obvious If It Merely Proves Something Suggested by Prior Art

Only two months after the *KSR* decision, the Federal Circuit in *PharmaStem* found claims obvious where the scientists did not create anything new but merely proved by experimentation that something suggested in the literature was true.[137] The court further noted that "obviousness 'does not require absolute predictability of success.'"[138]

On the other hand, the court noted that the amount of effort that the inventor needs to put in to succeed might decide whether the invention is obvious.[139] For example, the invention is not obvious if the inventor has "'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.'"[140] Similarly, the invention is not obvious if "the prior art gave only general guidance as to the particular

133. *Dow Chem. Co.*, 837 F.2d at 473.
134. *KSR*, 550 U.S. at 421.
135. *Id.* at 402.
136. *Id.* at 402–03.
137. PharmaStem Therapeutics, Inc. v. Viacell, Inc., 491 F.3d 1342, 1364–65 (Fed. Cir. 2007).
138. *Id.* at 1364 (quoting *In re* O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988)).
139. *Id.*
140. *Id.* (quoting *In re O'Farrell,* 853 F.2d at 903).

form of the claimed invention or how to achieve it," and the inventor must "explore a new technology or general approach that seemed to be a promising field of experimentation."[141]

2. *Board of Trustees v. Roche*: An Invention May Be Obvious Even Though It Does Not Seem to Be Obvious to Try in General

In 2008, a district court utilized the obvious to try standard to invalidate a claim involving a biotech patent.[142] The invention claimed a method of evaluating the effectiveness of anti-HIV therapy through quantifying the amount of HIV RNA by PCR.[143] The relevant prior art references included (1) an article by Holodniy disclosing a method of quantifying the amount of HIV RNA molecules by PCR and suggesting the potential of using HIV RNA as a marker for the amount of HIV virus;[144] and (2) an article by Ho presenting a correlation between the therapeutic effectiveness of a drug and the amount of HIV virus through viral culture.[145]

The court conceded that "although the use of HIV RNA as a surrogate marker was arguably not obvious to try with any reasonable expectation of success, the claims-at-issue may still be obvious" because the focus of a court's nonobviousness inquiry is "to determine the validity of each individual claim, in light of the prior art."[146] The major difference between the claims and Holodniy's article was "the evaluation and correlation steps of the claims," which was obvious in light of Ho's article.[147]

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141. *Id.*

142. Bd. of Trs. v. Roche Molecular Sys., Inc., 563 F. Supp. 2d 1016 (N.D. Cal. 2008).

143. *Id.* at 1021. PCR is a bio-technique in which the presence of a certain DNA molecule is amplified in a test tube through mimicking DNA replication. *See* Kamrin T. MacKnight, *Polymerase Chain Reaction (PCR): The Second Generation of DNA Analysis Methods Takes the Stand*, 20 SANTA CLARA COMPUTER & HIGH TECH. L.J. 95, 108–16 (2003). PCR can be used to relatively quantify the amount of a certain DNA molecule in a bio-sample. *Id.*

144. *Roche*, 563 F. Supp. 2d at 1023 n.2. The method involves two primary steps: in the first step, the HIV RNA molecules are reverse-transcribed into DNA molecules; and, in the second step, these DNA molecules are magnified by PCR. *Id.* at 1024; *see also* Mark Holodniy et al., *Detection and Quantification of Human Immunodeficiency Virus RNA in Patient Serum by Use of the Polymerase Chain Reaction*, 163 J. INFECTIOUS DISEASES 862, 864–65 (1991).

145. *Roche*, 563 F. Supp. at 1027 n.10; *see also* David D. Ho et al., *Quantitation of Human Immunodeficiency Virus Type 1 in the Blood of Infected Persons*, 321 NEW ENG. J. MED. 1621, 1621–25 (1989).

146. *Roche*, 563 F. Supp. at 1044. When this invention was made, several molecules had potential to be used as markers, including the HIV RNA, but the RNA was not particularly promising. *Id.* at 1027.

147. *Id.* at 1044.

3. *In re Kubin*: A DNA Patent Is Found Obvious Under the Obvious to Try Standard

In 2009, the Federal Circuit applied the revived obvious to try standard and found unpatentably obvious "a claim to a classic biotechnology invention—the isolation and sequencing of a human gene that encodes a particular domain of a protein."[148] The appellant, Kubin, sought to patent some cDNA[149] sequences, and the prior art disclosed the method to obtain homologous cDNA sequences from a different species.[150] The Federal Circuit held that "the claimed invention was reasonably expected in light of the prior art and 'obvious to try'" because "artisans in [the] field . . . had every motivation to seek and every reasonable expectation of success in achieving the sequence of the claimed invention."[151] To reach this holding, the *Kubin* court specifically addressed the earlier *Deuel* decision[152] and stated that "the Supreme Court in *KSR* unambiguously discredited [*Deuel*]."[153]

The *Kubin* court outlined two classes of situations in which an obvious to try combination of prior art references may not render the invention obvious under section 103.[154] First, an obvious to try combination may not be obvious when the inventor "merely throws metaphorical darts at a board filled with combinatorial prior art possibilities . . . ."[155] The *Kubin* court contrasted this situation to the nonobviousness finding described in *KSR* "where a skilled artisan merely pursues 'known options' from a 'finite number of identified, predictable solutions.'"[156] Second, an obvious to try combination may not be obvious "'where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it[, rather than providing a] detailed enabling methodology for practicing the claimed invention' . . . ."[157]

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148. *In re* Kubin, 561 F.3d 1351, 1352 (Fed. Cir. 2009).

149. cDNA is the shorthand for complementary DNA. TROPP, *supra* note 30, at 168. It is a synthetic strand of DNA that complements an RNA strand. *Id.* Because of the instability of an RNA molecule, cDNA is often used in studying RNA. *Id.* cDNA is different from genomic DNA in that it does not contain introns, the non-coding sequences between coding sequences in a gene. *Id.* at 760–61. During transcription, when an RNA molecule is made using a piece of genomic DNA as a template, introns are incised and, thus, the mature RNA molecule contains sequences complementary only to coding sequences. *Id.*

150. *Kubin*, 561 F.3d at 1352–53.

151. *Id.* at 1361.

152. *See In re* Deuel, 51 F.3d 1552 (Fed. Cir. 1995) (discrediting the obvious to try standard and holding that a DNA molecule with known homologs is not obvious, even though it would have been obvious to try to isolate this gene based on its known homologs); *supra* Part III.B.

153. *In re* Kubin, 561 F.3d 1351, 1358 (Fed. Cir. 2009).

154. *Id.* at 1359.

155. *Id.*

156. *Id.* (quoting KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 421 (2007)).

157. *Id.* at 1359–60 (quoting *In re* O'Farrell, 853 F.2d 894, 902–03 (Fed. Cir. 1988)) (emphasis omitted).

Further, the *Kubin* court discredited the idea that the *KSR* decision will have less impact on the biotech field due to the field's unpredictable nature.[158] The court pointed out that, although *KSR* involved predictable arts, as opposed to the unpredictable art of biotechnology, the current invention was obvious due to "the well-known and reliable nature of the cloning and sequencing techniques in the prior art . . . [and] the readily knowable and obtainable structure of an identified protein."[159]

Therefore, pursuant to the obvious to try standard of nonobviousness that was revived by the *KSR* Court and the interpretation of this standard by lower courts, the USPTO should accordingly modify its guidelines for granting patents to genetic material. In Part V, this Note proposes a system whereby genes are patentable only under certain conditions when a gene sequence survives the obvious to try standard, such as when the claim sequence has no counterpart with known functions or when the claimed function of this sequence deviates from what is expected based on the sequence homology.

V. PROPOSED LIMITATIONS ON VALIDITY AND SCOPE OF GENE PATENTS

The revived obvious to try standard and its interpretation by federal courts calls for a reconsideration of the validity and scope of gene patents. This Note suggests a set of criteria for the patentability of genes that incorporates this revived obvious to try standard into a nonobviousness inquiry. This set of criteria at least partially addresses the major concerns about gene patenting.

*A. The Impact of Post-*KSR *Obvious to Try Cases on the Validity and Scope of Gene Patents*

1. *PharmaStem* Limits Patents on Naturally Occurring Genes to Those with New or Unexpected Functions Only

Under *PharmaStem*, a gene with a previously identified homolog may be unpatentable due to a lack of nonobviousness because the previously identified homolog often suggests the existence of this gene with a similar sequence and similar functions.[160]

For example, many plant species have genes belonging to the so-called *APETALA1* (*AP1*) family.[161] Genes from this family share similar sequences,

158. *In re* Kubin, 561 F.3d 1351, 1360 (Fed. Cir. 2009); *cf.* Aquino, *supra* note 9, at 429.

159. *Kubin*, 561 F.3d at 1360.

160. *See* PharmaStem Therapeutics, Inc. v. Viacell, Inc., 491 F.3d 1342, 1364–65 (Fed. Cir. 2007).

161. For a review of the evolution of genes in this family, see, e.g., Amy Litt & Vivian F. Irish, *Duplication and Diversification in the* APETALA1/FRUITFULL *Floral Homeotic Gene Lineage: Implications for the Evolution of Floral Development*, 165 GENETICS 821, 821–33 (2003).

especially in the portions that are important to their functions.[162] The function of these genes, in their respective species, is to make the outer layers of a flower—the sepals and the petals.[163] Manipulations of the expression level of these genes generally will produce plants with a different floral morphology[164] and flowering time.[165]

If there is market pressure to study the reproductive development of a dicot plant, a researcher may be interested in isolating the *AP1* gene of this plant because that gene is likely to play an important role in the floral development of this plant, as has been suggested by previous literature relating to *AP1* genes from other species.[166] There are several standard protocols that the researcher may use to isolate *AP1* genes.[167] The success is not guaranteed, and the researcher may have to adjust the conditions and parameters in the protocols. Nevertheless, in many situations, this discovery process is routine laboratory work.

The discovery of another gene from the *AP1* family in a different species is similar to the situation in *PharmaStem*, in which the scientists simply proved by experimentation that something suggested in the literature was true but nothing new was created.[168] This gene is not patentable under the obvious to try standard in *KSR*[169] unless at least one of two situations occurs.

First, if the newly found member of the family exhibits a new and unexpected function, for example, if the *AP1* gene of this plant displays a function unrelated to other *AP1* genes, its discovery may be nonobvious because the effort does not "lead[] to the anticipated success."[170] Second, if the plant is so unique that the previously established standard protocols cannot produce the desired result and, instead, the researcher has to devote extensive effort to prove the existence and to obtain the sequence of this gene, its discovery may be nonobvious because the inventor's expenditure of effort is relevant in a nonobviousness inquiry.

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162. *Id.*

163. John L. Bowman et al., *Control of Flower Development in* Arabidopsis Thaliana *by* APETALA1 *and Interacting Genes*, 119 DEVELOPMENT 721, 721–43 (1993).

164. *Id.*

165. M. Alejandra Mandel & Martin F. Yanofsky, *A Gene Triggering Flower Formation in* Arabidopsis, 377 NATURE 522, 522–24 (1995).

166. *Id.* at 524.

167. *E.g.*, JOSEPH SAMBROOK ET AL., MOLECULAR CLONING: A LABORATORY MANUAL (2d ed. 1989).

168. PharmaStem Therapeutics, Inc. v. Viacell, Inc., 491 F.3d 1342, 1364–65 (Fed. Cir. 2007).

169. *See* KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 419–21 (2007).

170. *Id.* at 421.

2. *Board of Trustees v. Roche* Limits Patents on Modified Genes to Those with Novel Modifications

The court in *Board of Trustees v. Roche*[171] noted that an obviousness determination is not made in the abstract but is made in light of prior art references. A modified gene may not be obvious when viewed in the abstract for it does not exist in any natural being.[172] However, in light of prior art references relating to the natural sequence of this gene and those relating to the method of modification, the modified gene may be obvious.

For example, a scientist may want to express gene X from species-x in species-y. However, literature-1 teaches that gene A from species-a does not express very well in species-b, unless a certain DNA piece, B, from species-b is incorporated into gene A. Literature-2 discloses that species-b is closely related to species-y, while a is closely related to x. The scientist thus incorporates a piece of DNA from species-y, Y, into gene X and synthesizes a new gene X-Y to express in y. The gene X-Y may not be obvious in the abstract because it did not exist previously, and to add Y onto X may not be obvious if there are several other possible ways to modify gene X for its expression in species-y. Nevertheless, the gene X-Y may be obvious because the only difference between the current invention and literature-1 is the applicability of the method in literature-1 in a different species, and literature-2 makes it obvious to try this modification in a related species and there is a reasonable expectation of success.

Therefore, only genes modified in a way that is novel to a person with ordinary skills in the art should be patentable under *Board of Trustees v. Roche*.

3. *In re Kubin* Demonstrates the Potential for Limiting Gene Patentability Under *KSR*

The *Kubin* decision makes the technical difficulty relevant in a nonobviousness inquiry,[173] which should significantly limit gene patents because today a skilled artisan essentially can create any DNA molecule. Therefore, under *Kubin*, naturally occurring genes with known homologs may not be patentable because the techniques involved in obtaining these genes are routine experiments; further, DNA sequences resulting from modifications of natural genes may not be patentable if the method of modification is routine.

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171. Bd. of Trs. v. Roche Molecular Sys., Inc., 563 F. Supp. 2d 1016 (N.D. Cal. 2008).

172. *Id.*

173. *In re* Kubin, 561 F.3d 1351 (Fed. Cir. 2009). *See supra* Part IV.D.

B. A Set of Criteria for Gene Patentability that Complies with the Revived Obvious to Try Standard

Based on the obvious to try standard revived in *KSR* and its subsequent interpretation by lower courts, this Note proposes a system in which, generally, genes are not patentable. This system deals differently with genes that naturally exist in cells and those that are products of human modifications, and it takes into consideration how much effort an inventor needs to invest to obtain the gene.

For a naturally occurring DNA molecule, if its function as described in the patent application is one that agrees with the prediction based on its sequence homology to a protein with a known function, it is not patentable on the ground of nonobviousness, without regard to the fact that the inventor is the first to purify and isolate this DNA molecule.

On the other hand, if a naturally occurring DNA molecule does not have any identifiable functional domain, or its function as described in the patent application is distinct from the prediction based on its sequence homology to a protein with a known function, it may be nonobvious and thus patentable.

Also, if a naturally occurring DNA molecule is of a species that makes molecular discoveries quite difficult due to the unique characteristics of the species or the mere fact that few studies have been performed on the species, it may be nonobvious and thus patentable.

For a modified DNA molecule, if the modification is based on a technique that is obvious to a person with ordinary skill in the art and the modification leads to an expected change in the function or expression of the gene, it is not patentable. On the other hand, if the modification itself is novel or the modified DNA displays a characteristic that is not predictable, given the current state of the art, it may be nonobvious and thus patentable.

C. This Set of Criteria for Gene Patentability Addresses Major Concerns About Gene Patenting

These proposed gene patentability criteria generally deny patent protection for naturally occurring genes, which addresses at least part of the ethical concerns about gene patenting. The human genome has been fully sequenced, and many human genes have been functionally characterized or assigned putative functions based on sequence homology to known proteins.[174] Strategies for studying human genes are well developed.[175] Therefore, the threshold for a human gene to obtain patent protection under

174. For information on the Human Genome Project, see *Human Genome Project Information*, http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml (last visited Dec. 2, 2009).

175. *See id.*

this system is quite high and unusual. Only when an inventor establishes that a human gene functions in a way that is distinct from the prediction based on sequence homology may this gene be patentable.

These proposed gene patentability criteria balance the interests in encouraging gene discovery and in promoting follow-up research, and they agree with the congressional authority of enacting the Patent Act—to promote the progress of the sciences. Under this system, gene discovery resulting from routine laboratory work will not qualify for patent protection. Exclusive rights in a gene, in this instance, will hinder the follow-up research on a gene's function and its potential benefits to society because such monopoly will restrain the right to study this gene to only the owner of the patent for a term of twenty years. At the same time, the disclosure of the gene's sequence without a function or utility to the public does not provide any clear societal benefit. However, genes that are technically difficult to discover may qualify for patent protection. In this scenario, the exclusive rights are the incentive for the inventor to invest in the discovery and the public disclosure of these new genes will benefit scientists who face similar technical difficulties. These benefits outweigh the limitation that only inventors may further develop the function of the genes. Furthermore, a naturally occurring gene with a novel function, or a gene modified in a novel way, may qualify for patent protection under this system. The public disclosure of a gene with unexpected functions opens possibilities for future research on other genes, while a new way to modify a gene for a novel utility benefits the public because it opens new possibilities in gene research.

VI. CONCLUSION

Gene patenting has always provoked controversy. Opponents of gene patenting seek either to pass a statutory ban on gene patenting on ethical grounds or to limit the scope of gene patents by adding new criteria to patentability. However, these efforts have not proven successful. This Note, instead, argues that the *KSR* decision by the Supreme Court already limits the patentability of genes by its revived obvious to try standard.[176] Therefore, the USPTO should modify its examination guidelines regarding gene patents so that only genes that are nonobvious under a post-*KSR* standard are patentable. The proposed system of gene patentability addresses several major concerns of gene patenting and promotes societal benefits to gene research.

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176. *See* KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398 (2007).

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