

2009

Biotechnology Obviousness in the Post-Genomic Era: KSR v. Teleflex and In re Kubin

Rebecca Hays

Follow this and additional works at: <https://scholarship.law.umn.edu/mjlst>

Recommended Citation

Rebecca Hays, *Biotechnology Obviousness in the Post-Genomic Era: KSR v. Teleflex and In re Kubin*, 10 MINN. J.L. SCI. & TECH. 801 (2009).

Available at: <https://scholarship.law.umn.edu/mjlst/vol10/iss2/13>

Note

Biotechnology Obviousness in the Post-Genomic Era: *KSR v. Teleflex* and *In re Kubin*

*Rebecca Hays**

In its landmark decision *KSR International Co. v. Teleflex*, the Supreme Court announced new standards for obviousness determination in patent examination.¹ *KSR* is the Court's first substantive change to the obviousness standards originally set forth in *Graham v. John Deere Co.* over four decades ago.² In *KSR*, the Court expanded the scope of the *Graham* analysis and criticized the long-standing teaching-suggestion-motivation (TSM) test employed by the Federal Circuit to implement the holding of *Graham*.³ The Court held that while TSM is not inconsistent with *Graham* per se, it has been so rigidly applied by the Federal Circuit as to "be inconsistent with [the governing statute] and our precedents."⁴ Under *KSR*, a proper TSM inquiry is not limited to prior art in an inventor's particular field of endeavor or even analogous fields, and may consider whether the invention in question was "obvious to try" to a person of ordinary skill in the art,⁵ a standard that had

© 2009 Rebecca Hays.

* J.D. Candidate, University of Minnesota Law School. Ph.D. Genetics & Molecular Biology, Northwestern University 1999. B.S. Biology, University of Minnesota 1993. Dr. Hays held a National Institutes of Health Postdoctoral Fellowship at Washington University School of Medicine 2000-2003, and served on the faculty of the University of Kansas, Department of Molecular Biosciences 2003-2007. She has researched, lectured, and published in the areas of genetics and developmental biology.

1. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007).
2. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 17-18 (1966).
3. TSM was first articulated by the Court of Customs and Patent Appeals (CCPA) in *Application of Bergel*, 292 F.2d 955, 956-57 (C.C.P.A. 1961). The CCPA (1910-1982), is the predecessor to the Court of Appeals for the Federal Circuit (CAFC, Fed. Cir.)(1983-present).
4. *KSR Int'l*, 550 U.S. at 428.
5. *Id.* at 420.

been explicitly rejected by the Federal Circuit.⁶

In *Ex parte Kubin*,⁷ the Board of Patent Appeals and Interferences (Board) made its first attempt to implement the holding of *KSR* in the context of a biotechnology patent. In that case, the Board affirmed the rejection of claims to nucleic acid sequences encoding the human NAIL protein.⁸ The claims were held obvious because the methods employed to isolate the sequences were known in the prior art and because the protein was known to exist in some form.⁹ Notably, however, the actual sequences claimed in *Kubin* were not disclosed by the prior art.¹⁰

The Board held the *Kubin* rejections permissible under the new standards of *KSR*, in direct opposition to a Federal Circuit case that has set the standard for biotechnology obviousness for over a decade, *In re Deuel*.¹¹ The Board cited language in *KSR* critical of the holding of *Deuel*, which it interpreted as overruling the decision.¹²

In a much-anticipated decision, the Federal Circuit affirmed the Board's rejection of the *Kubin* claims unreservedly.¹³ The court held in *In re Kubin* that because the methods employed by the claimants were well-known in the art, they enjoyed a reasonable expectation of success that rendered the end product obvious and unpatentable.¹⁴ This holding unequivocally overturns some aspects of *Deuel* and dramatically alters the patentability landscape of modern biotechnology.

This Note addresses the current state of obviousness determination in modern biotechnology and the potential impact of *KSR* on the biotechnology industry as seen in *In re*

6. See, e.g., *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995).

7. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) 1410 (B.P.A.I. 2007).

8. **N**atural killer cell **a**ctivation-**i**nducing **l**igand. See Marek Z. Kubin et al., *Molecular Cloning and Biological Characterization of NK Cell Activation-Inducing Ligand, a Counterstructure for CD48*, 29 EUR. J. IMMUNOLOGY 3466 (1999).

9. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) at 1414.

10. *Id.* at 1412-13.

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

12. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) at 1414.

13. *In re Kubin*, No. 2008-1184, 2009 WL 877646 at *1 (Fed. Cir. Apr. 3, 2009).

14. *Id.* at *9-10.

Kubin. Section I discusses the evolution of obviousness doctrine, key Federal Circuit precedents relating to innovations in biotechnology, and the holdings of *KSR*, *Ex parte Kubin*, and *In re Kubin*. Section II discusses functional considerations in biotechnology obviousness and the relevance of *KSR* to the industry as a whole. It addresses the sophisticated level of ordinary skill in the so-called Post-Genomic Era,¹⁵ and describes ways in which generic obviousness standards, such as those articulated in *KSR*, are fundamentally incompatible with realities of biology. The Note concludes by advocating for industry-tolerant obviousness standards that promote the public interest in biotechnology research while setting reasonable standards for patentability.

I. OBVIOUSNESS THEN AND NOW

A. EVOLUTION OF MODERN OBVIOUSNESS STANDARDS: *HOTCHKISS, GRAHAM, KSR*

The statutory requirement for nonobviousness of a novel invention is set forth in 35 U.S.C. § 103, which bars the grant of a patent where the differences between the invention 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.”¹⁶ Enacted in 1952,¹⁷ § 103 is a codification of the judicial doctrine of nonobviousness first articulated by the Supreme Court in *Hotchkiss v. Greenwood*.¹⁸ In that case, the Court held that irrespective of the requirements for novelty and utility,¹⁹ the standard for

15. Life science researchers coined the term *post-genomic* in the late-1990s in reference to the advanced state of modern genetics. Initially, the term referred specifically to the completion of genome sequencing for several genetic model organisms. In the last several years the term has taken on a broader meaning, referring generally to the high level of sophistication of modern life science research and the vast resources available to researchers. See generally Sydney Brenner, *Genomics: The End of the Beginning*, 287 SCIENCE 2173 (2000); Gerald M. Rubin et al., *Comparative Genomics of the Eukaryotes*, 287 SCIENCE 2204 (2000).

16. United States Patent Act, 35 U.S.C. § 103(a) (2006).

17. *Id.*

18. *Hotchkiss v. Greenwood*, 52 U.S. 248, 265–67 (1850).

19. Utility and novelty standards are set forth in 35 U.S.C. §§ 101–102. Section 101 provides for the grant of a patent to “[w]hoever invents or discovers any new and useful process, machine, manufacture, or

patentability of an invention is ingenuity and not ordinary skill.²⁰

The general holding of *Hotchkiss* supports sound public policy considerations. Enforcing a minimal standard for nonobviousness prevents inventors from obtaining rights to products already in the public domain by adding trivial modifications.²¹ It also ensures that the exclusive rights conferred to the patent holder are proportional to the public benefit gained by the inventor's contribution to the public store of knowledge—a classic *quid pro quo*.²² The *ingenuity of invention* standard of *Hotchkiss* proved an inadequate measure, however, as it was too ambiguous and difficult to apply uniformly. As the Court later reflected, “[t]he truth is the word [invention] cannot be defined in such manner as to afford any substantial aid in determining whether a particular device involves an exercise of the inventive faculty or not.”²³ The Court recognized that the *Hotchkiss* standard was sufficiently vague to spur “a large variety of opinions as to its meaning both in the Patent Office, in the courts, and at the bar.”²⁴ Indeed, the Court itself struggled to devise a reasonable

composition of matter, or any new and useful improvement thereof” 35 U.S.C. § 101 (2006). Section 102 sets forth extensive guidelines for determination of the novelty of an invention relative to the prior art. § 102.

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

[U]nless more ingenuity and skill in applying the old method . . . were required . . . 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.

Id. (holding invalid a patent substituting the use of porcelain or clay for wood or metal in the manufacture of doorknobs).

21. See, e.g., *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 6 (1966) (“Moreover, Congress may not authorize the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials already available.”); see also *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146 (1989) (quoting the above passage from *Graham*).

22. See, e.g., *United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 186–87 (1933), *amended by* 289 U.S. 706 (1933) (“[The inventor] may keep his invention secret and reap its fruits indefinitely. In consideration of its disclosure and the consequent benefit to the community, the patent is granted.”).

23. *Graham*, 383 U.S. at 11 (alteration in original) (quoting *McClain v. Ortmayer*, 141 U.S. 419, 427 (1891)).

24. *Id.* at 12.

standard for obviousness after *Hotchkiss*, at one time adopting the controversial and highly subjective test that inventions not created in a “flash of genius” do not meet the requirements for patentability.²⁵

Following Congressional enactment of § 103 mandating an objective standard for nonobviousness,²⁶ the Court fashioned the modern test of *Graham v. John Deere Co. of Kansas City*, issued more than a century after *Hotchkiss*.²⁷ Under *Graham*, obviousness would be determined through characterization of 1) the scope and content of the prior art, 2) the differences between the prior art and the claims, and 3) the ordinary level of skill in the pertinent art.²⁸ The Court also identified secondary considerations that may suggest nonobviousness, including commercial success, long-felt, unresolved needs, and the failure of others in the same endeavor.²⁹ These considerations would be particularly helpful, the Court felt, in avoiding the pitfalls of hindsight bias—“the temptation to read into the prior art the teachings of the invention in issue”³⁰—which had arisen in other post-*Hotchkiss* cases.³¹

The Court recognized that irrespective of its formal pronouncements in *Graham*, uniform application of the nonobviousness test would require further development of the doctrine in the lower courts.³² In fact, the Court of Customs

25. *Cuno Eng'g Corp. v. Automatic Devices Corp.*, 314 U.S. 84, 91 (1941), *amended by* 314 U.S. 587 (1942) (“That is to say the new device, however useful it may be, must reveal the flash of creative genius not merely the skill of the calling. If it fails, it has not established its right to a private grant on the public domain.”). The “flash of genius” standard was overturned by § 103, which states that “[p]atentability shall not be negated by the manner in which the invention was made.” 35 U.S.C. § 103(a) (2006).

26. *See* *Dann v. Johnston*, 425 U.S. 219, 225–26 (1976) (“[I]t was only in 1952 that Congress, in the interest of ‘uniformity and definiteness,’ articulated the requirement in a statute”) (quoting S. REP. NO. 1979, at 6 (1952); H.R. REP. NO. 1923, at 7 (1952)).

27. *Graham*, 383 U.S. at 3 (invalidating a patent covering a “Clamp for vibrating Shank Plows” as an obvious modification of prior art elements).

28. *Id.* at 17–18.

29. *Id.*

30. *Id.* at 36.

31. *See, e.g., Diamond Rubber Co. v. Consol. Rubber Tire Co.*, 220 U.S. 428, 435 (1911) (“Knowledge after the event is always easy, and problems once solved present no difficulties, indeed, may be represented as never having had any”).

32. *Graham*, 383 U.S. at 18.

This is not to say, however, that there will not be difficulties in

and Patent Appeals (C.C.P.A.) had already devised a method to implement the holding of *Hotchkiss*. The teaching-suggestion-motivation (TSM) standard, first articulated five years before *Graham*,³³ became the cornerstone of obviousness determination in the lower courts. Under the TSM test, an invention is obvious where there is a teaching, suggestion, or motivation in the analogous prior art to make the product in question.³⁴ References are selected for their relevance to the subject matter based on the judgment of a person of ordinary skill in the art, but are not limited to explicit statements.³⁵ Motivation may be implicit in the prior art as a whole, or suggested by the nature of the problem addressed by the invention.³⁶ In the Federal Circuit's view, this test "picks up where the analogous art test leaves off and informs the *Graham* analysis,"³⁷ lending both direction and scope to the inquiry.³⁸

Use of the Federal Circuit's TSM test in the lower courts went largely unchallenged for over four decades. In *KSR International Co. v. Teleflex Inc.*, the Court made its first substantive changes to *Graham*, broadening the scope of the relevant prior art and rejecting the Federal Circuit's TSM application as impermissibly narrow.³⁹

The dispute in *KSR* involved rights to an adjustable automobile pedal featuring electronic sensing devices.⁴⁰ The individual elements of the invention were present in the prior

applying the nonobviousness test. What is obvious is not a question upon which there is likely to be uniformity of thought in every given factual context. The difficulties, however, are comparable to those encountered daily by the courts . . . and should be amenable to a case-by-case development.

Id.

33. *Application of Bergel*, 292 F.2d 955, 956–57 (C.C.P.A. 1961).

34. See, *In re Kahn*, 441 F.3d 977, 986–87 (Fed. Cir. 2006) ("Although our predecessor court was the first to articulate the motivation-suggestion-teaching test, a related test—the the analogous art test—has long been part of the primary *Graham* analysis articulated by the Supreme Court.") (citing *Dann v. Johnston*, 425 U.S. 219, 227–29 (1976)).

35. *Id.* at 987.

36. *Id.* at 987–88.

37. *Alza Corp. v. Mylan Labs.*, 464 F.3d 1286, 1290 (Fed. Cir. 2006) (quoting *Kahn*, 441 F. 3d at 987).

38. See *id.* at 1290–91.

39. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 418–19 (2007).

40. *Id.* at 407–08.

art, but the combination of elements had not been previously disclosed.⁴¹ The Federal Circuit reversed the finding of patent invalidity for failure of the lower court to properly apply the TSM test.⁴² The court recognized that the elements of the invention were known in the industry, but held that the district court failed to identify a motivation in the prior art that would lead a person of ordinary skill in the art to combine the elements.⁴³

In reversing the Federal Circuit's holding, the Supreme Court criticized its application of the TSM test as a "rigid rule that limits the obviousness inquiry."⁴⁴ The Court did not consider the test fundamentally at odds with *Graham*, only the manner in which the Federal Circuit had applied it in this and other cases.⁴⁵ Specifically, the Court held it is error to limit the *Graham* inquiry to the particular problem the inventor is trying to solve or prior art addressing the same issue, stating that, "[u]nder the correct analysis, *any need or problem* known in the field . . . can provide a reason for combining the elements in the manner claimed."⁴⁶ Moreover, courts should not assume that inventors will be guided only by prior art elements directed to the particular problem they are working on, but should regard the person of ordinary skill in the art as having the "ordinary creativity" to assemble even *unrelated* prior art "like pieces of a puzzle."⁴⁷ The Court minimized the Federal

41. *See id.* at 408-09.

42. *Teleflex, Inc. v. KSR Int'l. Co.*, 119 F. App'x 282, 286 (Fed. Cir. 2005), *rev'd*, 550 U.S. 398 (2007).

43. *Id.* at 288.

[The district court invalidated the patent] without making "finding[s] as to the specific understanding or principle within the knowledge of a skilled artisan that would have motivated one with no knowledge of [the] invention to make the combination in the manner claimed." Under our case law, whether based on the nature of the problem to be solved, the express teachings of the prior art, or the knowledge of one of ordinary skill in the art, the district court was required to make specific findings as to whether there was a suggestion or motivation to combine

Id. (second and third alterations in original) (citation omitted) (quoting *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000)).

44. *KSR Int'l*, 550 U.S. at 419.

45. *Id.* ("There is no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis. But when a court transforms the general principle into a rigid rule that limits the obviousness inquiry . . . it errs.").

46. *Id.* at 420 (emphasis added).

47. *Id.* at 420-21.

Circuit's concern that poorly-defined obviousness criteria may give way to hindsight bias,⁴⁸ and called for a "common sense" approach to obviousness determination, including consideration of what may be obvious to try in a given field of endeavor.⁴⁹ As the Court explained:

The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." 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 combination was obvious to try might show that it was obvious under § 103.⁵⁰

Ultimately, the Court called for the Federal Circuit to apply a "flexible" TSM test that considers common knowledge and common sense to assess obviousness in light of prior art.⁵¹

48. *Id.* at 421.

The Court of Appeals, finally, drew the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias. A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning. Rigid preventative rules that deny factfinders recourse to common sense, however, are neither necessary under our case law nor consistent with it.

Id. (internal citation omitted).

49. The Court called for the use of a common sense approach to obviousness determination no fewer than four times throughout the opinion: "Although *common sense* directs one to look with care at a patent application that claims . . . the combination of two known devices . . . it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.* at 418; "[c]ommon sense teaches, however, that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and *common sense*." *Id.* at 420; "[r]igid preventative rules that deny factfinders recourse to *common sense*, however, are neither necessary under our case law nor consistent with it." *Id.* at 421.

50. *Id.* at 421 (internal citation omitted).

51. *Id.* at 421-22. The Court noted that the Federal Circuit had begun to implement a more flexible test prior to the writing of *KSR*. *Id.* (citing *DyStar Textilfarben GmbH & Co Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1367 (Fed. Cir. 2006); *Alza Corp. v. Mylan Labs., Inc.*, 464

The Federal Circuit acknowledged the edict of *KSR* in *Black & Decker, Inc. v. Robert Bosch Tool Corp.*, where it defended the TSM test, holding that “the teaching, suggestion, motivation test remains good law for obviousness, only a rigid application of that test is problematic.”⁵² The court announced a reformulation of the test in *Ortho-McNeil Pharmaceuticals v. Mylan Laboratories*:

The TSM test, flexibly applied, merely assures that the obviousness test proceeds on the basis of evidence—teachings, suggestions (a tellingly broad term), or motivations (an equally broad term)—that arise before the time of invention as the statute requires. As *KSR* requires, those teachings, suggestions, or motivations need not always be written references but may be found within the knowledge and creativity of ordinarily skilled artisans.⁵³

Notwithstanding this change, the court reiterated its view on the pitfalls of hindsight bias, which had been trivialized in *KSR*,⁵⁴ stating that “a flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis.”⁵⁵ The court was also quick to re-tool the *KSR* standard for predictability in obviousness determination. Recall that *KSR* calls for a finding of obviousness where there is a “finite number of identified, predictable solutions.”⁵⁶ The Federal Circuit version limits the *KSR* standard to an “easily traversed, small and finite number of alternatives,”⁵⁷ a standard specifically tailored to accommodate the biotechnology and pharmaceutical industries, which the Federal Circuit has long held to be unpredictable arts.⁵⁸

The impact of *KSR* on biotechnology patents depends largely on whether it is interpreted as overruling *In re Deuel*, a key Federal Circuit decision that centered on the inter-

F.3d 1286, 1291 (Fed. Cir. 2006)).

52. *Black & Decker, Inc. v. Robert Bosch Tool Corp.*, 260 F. App'x 284, 290 (Fed. Cir. 2008).

53. *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1365 (Fed. Cir. 2008).

54. See *supra* note 49 and accompanying text.

55. *Ortho-McNeil*, 520 F.3d at 1364.

56. *KSR Int'l*, 550 U.S. at 421.

57. *Ortho-McNeil*, 520 F.3d at 1364.

58. See, e.g., *Eisai Co. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008) (“To the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these ‘identified, predictable solutions’ may present a difficult hurdle because potential solutions are less likely to be genuinely predictable.”).

relatedness of DNA, RNA, and proteins.⁵⁹ Before discussing the holdings of those cases, a short biology refresher is in order.

B. A GENETICS PRIMER

The term *genome* refers to an organism's full complement of genetic material.⁶⁰ It is composed of deoxyribonucleic acid

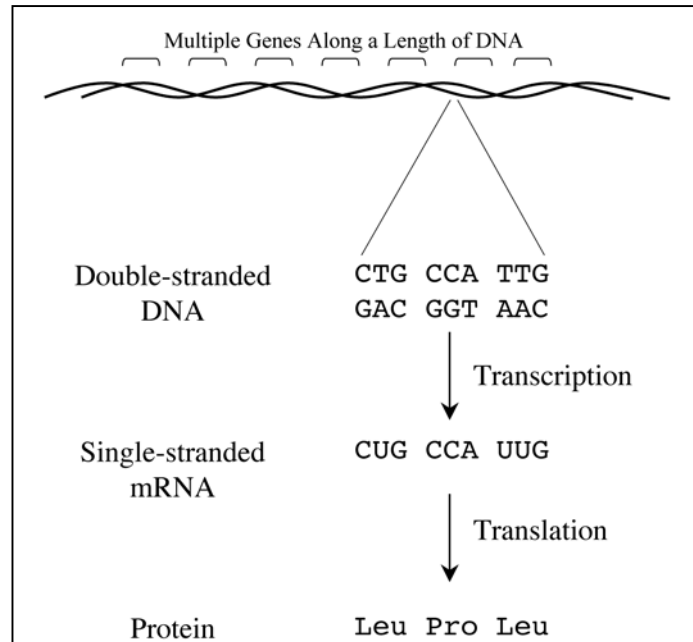


Fig. 1 Schematic diagram of transcription and translation. Double-stranded DNA is transcribed into an mRNA intermediate, which is translated into a polypeptide sequence. Three base-pair codons are separated in this illustration for clarity. Note that the amino acid leucine (Leu) is encoded by two different codons on the level of

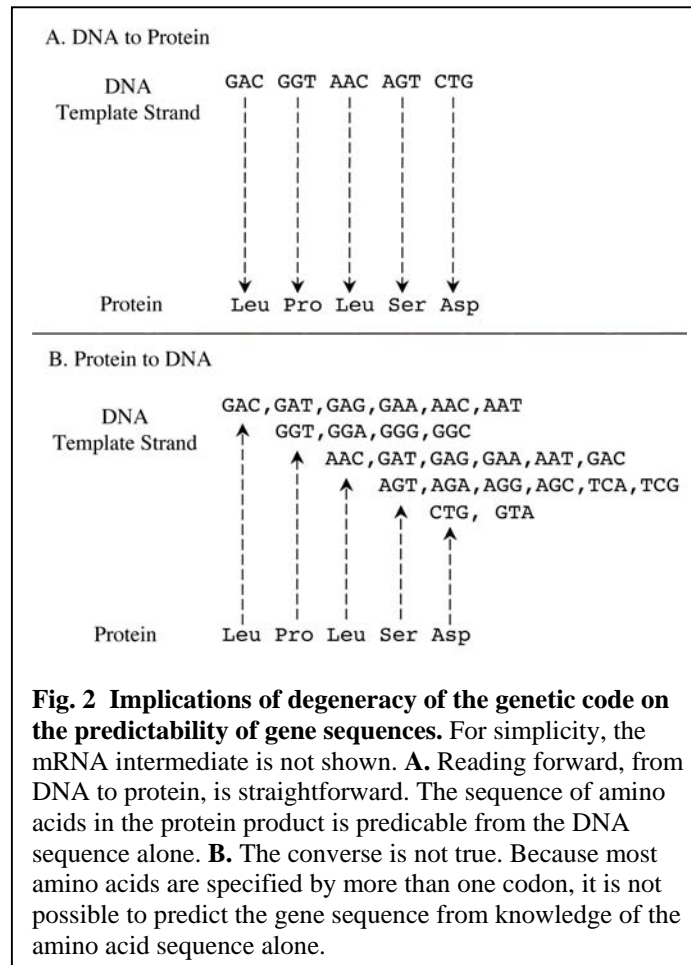
59. *In re Deuel*, 51 F.3d 1352 (Fed. Cir. 1995).
60. See generally ANTHONY GRIFFITHS ET AL., INTRODUCTION TO GENETIC ANALYSIS 298-349 (9th ed. 2008). (providing an undergraduate-level explanation of DNA structure and gene expression); John M. Conley & Robert Makowski, *Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents in the United States—And Perhaps Europe as Well*, 13 INFO. & COMM. TECH. L. 3, 8-11 (2004) (presenting an advanced-level review in the context of a discussion on patentable subject matter); see also, *In re O'Farrell*, 853 F.2d 894, 895-99 (Fed. Cir. 1988) (discussing basic recombinant DNA technology).

(DNA), and is the storehouse of biological information necessary for all aspects of an organism's existence, including embryonic development, growth, maturation, and reproduction. DNA is a linear molecule made up of repeating sub-units called *bases*: adenine (A), cytosine (C), guanine (G), thymine (T). It commonly exists in the form of a double-stranded molecule—a *double helix*—in which two linear DNA molecules twist around each other in a right-handed spiral. The positioning of DNA strands relative to each other is controlled by *complementary base pairing*, which is the result of interactions between bases on opposing strands. The chemical nature of the bases is such that adenine on one strand always pairs with thymine on the other (A-T), and cytosine on one strand always pairs with guanine on the other (C-G). Thus, any given position on a molecule of double-stranded DNA is referred to as a *base-pair* (Fig. 1).

The term *gene* refers to a discrete unit of DNA, and is on the order of 10^3 base pairs in length.⁶¹ Many genes *encode* the proteins that comprise cells and tissues. That is, they carry all of the information—in code—necessary to make the protein product. Proteins are generated through a two-step process called *transcription* and *translation* (Fig. 1). In transcription, DNA serves as a template for the synthesis of ribonucleic acid (RNA), a related but distinct molecule. This particular type of RNA (there are many) is referred to as messenger RNA (mRNA). mRNA is a single stranded molecule also composed of repeating bases, in which thymine is replaced with the related base uracil (U). The order of bases in mRNA is specified by the order of bases on the DNA template strand. Thus, through mRNA synthesis, the code of DNA is *transcribed* into an intermediate molecule. mRNA derives its name from its role in protein synthesis. It literally carries the DNA message from the site of transcription to the site of protein assembly.

In translation, mRNA serves as a template for the assembly of amino acids into a polypeptide or protein. Individual amino acids are specified by nucleic acid sequences three base-pairs in length, called *codons*, present in both the

61. The human genome contains approximately three billion base-pairs of DNA encoding an estimated 20,000-25,000 genes. Human Genome Program, U.S. Dep't of Energy Office of Sci., The Science Behind the Human Genome Project (Mar. 26, 2008), http://www.ornl.gov/sci/techresources/Human_Genome/project/info.shtml.



DNA and mRNA. Together, the processes of transcription and translation are referred to as *gene expression*. Genes are said to be expressed when the DNA is transcribed and the gene product is made. Generally speaking, the cells of a given organism all carry the same complement of DNA—the same genes. However, not all cells express all genes. During development and throughout life, cells assume different fates, with different properties and functions, through *differential gene expression*. For example, liver cells express liver-specific genes, while muscle cells express muscle-specific genes.

One final point about protein translation relates to the specificity of genetic coding for amino acids. As described above, individual amino acids are specified by nucleic acid sequences three base-pairs in length—codons. However, permutation of the four DNA bases generates more codons ($4^3 = 64$ possible three-base-pair sequences) than there are amino acids (20). For this reason, most amino acids are specified by more than one codon. Some are specified by as many as six codons. This is referred to as *degeneracy of the genetic code*, and it is the punch line of this biology primer.

Forward reading of the genetic code—DNA to protein—is straightforward. The mRNA and protein sequences are fully predictable from the DNA sequence alone (Fig. 2A). The converse, however, is categorically untrue. Due to degeneracy of the code, the amino acid sequence of a protein does not give a read of the parent gene sequence. Consider the number of possible codon combinations for the simple peptide shown in Fig. 2B, in which three of the five amino acids are specified by six different codons.⁶² Most proteins are much larger than this example, with a staggering number of potential coding sequences.⁶³

C. FEDERAL CIRCUIT PRECEDENTS: *IN RE BELL* AND *IN RE DEUEL*

Two Federal Circuit decisions in the mid-1990s, *In re Bell*⁶⁴ and *In re Deuel*,⁶⁵ set the standard for obviousness in genetics innovation. In *Bell*, the claims were directed to nucleic acid sequences (both DNA and RNA) encoding human insulin-like growth factors (IGF) I and II.⁶⁶ The Board held the claims

62. Care to try your hand? There are 1728 possible coding sequences for this short peptide.

63. See, for example, *In re Bell*, 991 F.2d 781, 784 (Fed. Cir. 1993), in which the claimant calculated 10^{36} potential coding sequences for insulin-like growth factor, a 79 amino acid protein.

64. *In re Bell*, 991 F.2d at 781.

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

66. *In re Bell*, 991 F.2d at 782 n.3. Claim 25 is representative:

A composition comprising nucleic acid molecules containing a human sequence encoding insulin-like growth factor (hIGF) substantially free of nucleic acid molecules not containing said hIGF sequence, wherein said hIGF sequence is selected from the group consisting of: (a) 5'-GGA CCG . . . wherein U can also be T; (b) 5'-GCU UAC . . . wherein U can also be T; (c) nucleic acid sequences complementary to (a) or (b); and (d) fragments of (a), (b) or (c) that are at least 18 bases in length and which will selectively hybridize to human genomic DNA encoding hIGF.

prima facie obvious over the combined teachings of a U.S. patent to Weissman⁶⁷ and two scientific publications disclosing the amino acid sequences of the growth factors.⁶⁸ The Weissman patent taught the use of nucleic acid probes to isolate genes of interest, wherein the sequence of the probe encodes the relevant protein and is therefore complementary to the relevant mRNA.⁶⁹ The disclosure specified that the probes should be designed using unique codons to circumvent degeneracy of the genetic code, and described use of the method to isolate a gene unrelated to IGF.⁷⁰ The Board reasoned that because of the natural relatedness of proteins and their corresponding genes, knowledge of a protein's amino acid sequence renders the gene sequence obvious.⁷¹ The Board also held that the Weissman patent illustrated that the ordinary artisan would know how to use a protein sequence to isolate the corresponding gene.⁷²

In reversing the Board's rejection of the *Bell* claims, the Federal Circuit emphasized that because of degeneracy of the code, knowledge of a protein sequence does not render a gene sequence obvious, stating:

It may be true that, knowing the structure of the protein, one can use the genetic code to hypothesize possible structures for the corresponding gene and that one thus has the potential for obtaining that gene. However, because of the degeneracy of the genetic code, there are a vast number of nucleotide sequences that might code for a specific protein. In the case of IGF, Bell has argued without contradiction that the [prior art] amino acid sequences could be coded for by more than 10³⁶ different nucleotide sequences, only a few of which are the human sequences that Bell now claims. Therefore, given the nearly infinite number of possibilities suggested by the prior art, and the failure of the cited prior art to suggest which of those possibilities is the human sequence, the claimed sequences would not have

Id. at 782 n.3.

67. Method for Cloning Genes, U.S. Patent No. 4,394,443 (filed Dec. 18, 1980) (issued July 19, 1983).

68. *In re Bell*, 991 F.2d at 783; Ernst Rinderknecht and René E. Humbel, *The Amino Acid Sequence of Human Insulin-Like Growth Factor I and Its Structural Homology with Proinsulin*, 253 J. BIOLOGICAL CHEMISTRY 2769 (1978); Ernst Rinderknecht and René E. Humbel, *Primary Structure of Human Insulin-Like Growth Factor II*, 89 FEBS LETTERS 283 (1978).

69. *In re Bell*, 991 F.2d at 783.

70. *Id.*

71. *Id.*

72. *Id.*

been obvious.⁷³

The court explicitly reserved judgment on whether the converse is also true. That is, whether knowledge of a gene sequence renders the corresponding amino acid sequence obvious.⁷⁴ The court also rejected the notion that use of a generally known method to isolate gene sequences renders the sequences themselves obvious.⁷⁵

In *Deuel*, the claims were directed to genomic DNA and cDNA⁷⁶ sequences coding for heparin-binding growth factors isolated from human and bovine placental tissue.⁷⁷ The Board held the claims obvious over the combined teachings of a European patent application by Bohlen⁷⁸ and a molecular biology laboratory manual by Maniatis.⁷⁹ The Bohlen reference

73. *Id.* at 784.

74. *Id.* at 784 n.6 (“We also express no opinion concerning the reverse proposition, that knowledge of the structure of a DNA, e.g., a cDNA, might make a coded protein obvious.”).

75. *Id.* at 785 (“[T]he issue is the obviousness of the *claimed compositions*, not of the *method* by which they are made.”) (citing *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985) (emphasis added)).

76. A cDNA, or complementary DNA, is not a naturally occurring molecule. It is an engineered DNA prepared by reverse-transcribing mRNA isolated from cells or tissue. cDNAs encode for the same products as their corresponding genomic sequences and are used to achieve gene expression outside of its normal context (e.g., in bacteria). See generally J. SAMBROOK ET AL., MOLECULAR CLONING: A LABORATORY MANUAL (3d. ed. 2001) (a comprehensive guide to nucleic acid cloning and expression of cloned genes in vitro).

77. *In re Deuel*, 51 F.3d 1552, 1554 (Fed. Cir. 1995). Claims 4-7 were appealed:

4. A purified and isolated DNA sequence consisting of a sequence encoding human heparin binding growth factor of 168 amino acids having the following amino acid sequence: Met Gln Ala . . . [remainder of 168 amino acid sequence].

5. The purified and isolated cDNA of human heparin-binding growth factor having the following nucleotide sequence: GTCAAAGGCA . . . [remainder of 961 nucleotide sequence].

6. A purified and isolated DNA sequence consisting of a sequence encoding bovine heparin binding growth factor of 168 amino acids having the following amino acid sequence: Met Gln Thr . . . [remainder of 168 amino acid sequence].

7. The purified and isolated cDNA of bovine heparin-binding growth factor having the following nucleotide sequence: GAGTGGAGAG . . . [remainder of 1196 nucleotide sequence].

Id. at 1555 (alterations in original).

78. European Patent No. 89,101,187 (filed Jan. 24, 1989).

79. *In re Deuel*, 51 F.3d at 1557; T. MANIATIS ET AL., MOLECULAR CLONING: A LABORATORY MANUAL 353-61 (1982) (describing a protocol for screening bacteriophage libraries in *Escherichia coli*).

disclosed three protein growth factors known only as heparin-binding mitogens, and reported a partial amino acid sequence for each.⁸⁰ Bohlen taught explicitly that the proteins were brain-specific, and did not teach any details of the corresponding genomic DNA or cDNAs.⁸¹ The Maniatis reference taught general methods for the isolation of gene sequences, including the method used by the inventor.⁸² The Board held that a person of ordinary skill in the art could have designed nucleic acid probes based on the amino acid sequences disclosed in Bohlen, and then used the general methods of Maniatis to isolate the genes in question.⁸³ The Board considered it irrelevant that the Bohlen reference taught away⁸⁴ from the *Deuel* claims by reporting that the proteins were brain-specific, and that the DNA sequences claimed encoded the full-length proteins, not just the portions disclosed by Bohlen.⁸⁵

The Federal Circuit reversed the finding of obviousness, citing its holdings in *Bell*.⁸⁶ The court held that while general aspects of the proteins may have been obvious in light of the Bohlen reference (*e.g.* the general class and function of the proteins), the precise DNA sequences claimed were not obvious and could not have been predicted based on the amino acid sequence due to redundancy of the genetic code.⁸⁷ The court

80. *In re Deuel*, 51 F.3d at 1555–56. Bohlen reported the N-terminal nineteen amino acids of each protein. *Id.* at 1556.

81. *Id.* at 1556.

82. *Id.* at 1555–56. The claimant screened human and bovine cDNA libraries using degenerate DNA probes encoding the N-terminal twenty-five amino acids of the proteins, which he had determined himself from the isolated proteins. *Id.* at 1555.

83. *Id.* at 1557.

84. A reference is said to teach away from an invention when it would discourage a person of skill in the art from pursuing a technology or a particular approach to innovation. *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994).

85. *In re Deuel*, 51 F.3d at 1556–57.

86. *Id.* at 1559.

87. *Id.* at 1558.

[O]ne could not have conceived the [claimed sequences] based on the teachings in the cited prior art because, until the claimed molecules were actually isolated and purified, it would have been highly unlikely for one of ordinary skill in the art to contemplate what was ultimately obtained. What cannot be contemplated or conceived cannot be obvious.

Id.

also reiterated its view that the existence of general methods for gene isolation do not render obvious claimed sequences, even where knowledge of the methods is coupled with knowledge of the protein sequence.⁸⁸ In the words of the court, “obvious to try” has long been held not to constitute obviousness.⁸⁹

D. *EX PARTE KUBIN* AND *IN RE KUBIN*

The pre-*KSR* standard for biotechnology obviousness was grounded in functional aspects of the biology involved. The Federal Circuit appreciated the implications of genetic redundancy, and inventor reliance on proven biochemical methods was not fatal to a claim of non-obviousness.⁹⁰ If *In re Kubin* is any indication, however, *KSR* may have changed all that.⁹¹

The claims in *Kubin* were directed to nucleic acid sequences encoding the human NAIL,⁹² a protein involved in the regulation of immune responses.⁹³ In *Ex parte Kubin*, the Board held the claims obvious⁹⁴ over the combined teachings of a U.S. patent to Valiante,⁹⁵ a molecular biology laboratory manual by Sambrook,⁹⁶ and a scientific publication by Mathew

88. *Id.* at 1559 (“Thus, even if, as the examiner stated, the existence of general cloning techniques, coupled with knowledge of a protein’s structure, might have provided motivation to prepare a cDNA or made it obvious to prepare a cDNA, that does not necessarily make obvious a particular claimed cDNA.”).

89. *Id.* (citing *In re O’Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)).

90. See generally *In re Deuel*, 51 F.3d at 1552; *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993).

91. *In re Kubin*, No. 2008-1184, 2009 WL 877646, at *7-10 (Fed. Cir. Apr. 3, 2009).

92. Claim 73 is representative: “An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide at least 80% identical to amino acids 22-221 of SEQ ID NO:2, wherein the polypeptide binds CD48.” *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) 1410, 1412 (BPAI 2007).

93. See *Kubin et al.*, *supra* note 8.

94. The claimants also appealed the rejection of claims under § 112, ¶ 1, 35 U.S.C. § 112 (2006), for deficiencies in enablement and written description. *Ex parte Kubin*, 83 U.S. P.Q.2d (BNA) at 1415. The Board reversed the examiner’s rejection for lack of enablement and affirmed rejection for insufficient written description. *Id.* at 1417.

95. Human Cytotoxic Lymphocyte Signal Transduction Surface Protein (P38) and Monoclonal Antibodies Thereto, U.S. Patent No. 5,688,690 (filed Sept. 16, 1994) (issued Nov. 18, 1997).

96. J. SAMBROOK ET AL., MOLECULAR CLONING: A LABORATORY MANUAL 2.43-2.84 (2d. ed. 1989). This is the second edition of the Maniatis

that described isolation of the murine (mouse) homologue of NAIL.⁹⁷

The Valiante patent disclosed the existence of a protein present on the surface of natural killer cells⁹⁸ known only as p38, and claimed a monoclonal antibody specific for the protein.⁹⁹ Valiante did not report the amino acid sequence of p38 or the DNA sequences encoding the protein.¹⁰⁰ However, Valiante described a prophetic method to isolate p38 coding sequences using the antibody he had claimed.¹⁰¹ The claimants in *Kubin* used the Valiante method, as well as the Valiante antibody,¹⁰² to isolate the p38 coding sequences, which they then gave the more descriptive name NAIL.¹⁰³

In denying the claims, the Board invoked arguments parallel to those rejected by the Federal Circuit in *Deuel*. It held that the combined teachings of the prior art references rendered it obvious to attempt to clone the NAIL sequences even if the claimed product was not itself previously disclosed, and that the claimants had a reasonable expectation of success.¹⁰⁴ In other words, the general availability of the method employed rendered the product obvious. The Board argued that there were a limited number of methodologies available to isolate the NAIL cDNA and that

[t]he skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. Thus, isolating NAIL cDNA was “the product not of innovation but of ordinary skill and common sense,”

manual. *See supra*, note 79.

97. Porunelloor Mathew et al., *Cloning and Characterization of the 2B4 Gene Encoding a Molecule Associated with Non- MHC-Restricted Killing Mediated by Activated Natural Killer Cells and T Cells*, 151 J. IMMUNOLOGY 5328 (1993). *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) at 1412, 1415.

98. A natural killer cell is a type of lymphocyte (white blood cell) that mediates immune responses. *See generally* Kubin et al., *supra* note 8.

99. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) at 1412.

100. *Id.* at 1412–13.

101. *Id.* at 1412 (“Valiante expressly teaches through a prophetic example how to ‘isolat[e] the cDNA clone by using [mAb] C1.7, screening the protein expression in the cell transfected with the cDNA library and cloning a corresponding cDNA into a plasmid for sequencing.’”) (alterations in original).

102. mAb C1.7 was made commercially available by Valiante following issue of the patent. *Id.* at 1413.

103. *Id.* at 1411–12.

104. *Id.* at 1414–15.

leading us to conclude NAIL cDNA is not patentable as it would have been obvious to isolate it.¹⁰⁵

The Board considered it irrelevant that the Mathew reference taught away from the *Kubin* subject matter by reporting that there is no human homologue of NAIL.¹⁰⁶ Rather, it felt that the Mathew reference merely represented conflicting data in the field and would not deter a skilled artisan from pursuing the teachings of Valiante.¹⁰⁷ In the words of the Board, “one of ordinary skill in the art would have recognized the value of isolating NAIL cDNA, and would have been motivated to apply conventional methodologies, such as those disclosed in Sambrook and utilized in Valiante, to do so.”¹⁰⁸

The Board invoked the language of *KSR* to support its ruling, principally, the Supreme Court’s statement that “obvious to try” is permissible grounds for rejection where there are available “a finite number of identified, predictable solutions” to a problem.¹⁰⁹ Under *KSR*, the Board held, because the protein was already known in *some* form and there existed *some* method to isolate the corresponding gene, the isolated sequence was “the product not of innovation but of ordinary skill and common sense.”¹¹⁰

In this first post-*KSR* ruling on obviousness in genetic innovation, the Board cited *In re Deuel* as being of questionable validity after *KSR*, and called for the Federal Circuit to overrule its precedent.¹¹¹ The Board emphasized its stance in *Ex parte Kubin* by giving it the rare designation *precedential*.¹¹²

The Federal Circuit affirmed rejection of the *Kubin* claims on obviousness grounds and endorsed the Board’s reasoning on the whole.¹¹³ The court held that the inventors’ reliance on

105. *Id.* at 1414.

106. *Id.* at 1414–15.

107. *Id.*

108. *Id.* at 1413.

109. *Id.* at 1414 (quoting *KSR Int’l Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007)).

110. *Id.*

111. *Id.*

112. *Ex parte Kubin* is one of only three BPAI decisions to receive the designation in 2007. U.S. Patent & Trademark Office, BPAI Precedential Opinions, <http://www.uspto.gov/web/offices/dcom/bpai/prec.htm> (last visited Mar. 11, 2009).

113. *In re Kubin*, No. 2008-1184, 2009 WL 877646 at *10 (Fed. Cir. Apr. 3, 2009). The court did not reach the merits of the § 112, ¶ 1

conventional methodology for isolating the NAIL coding sequence, together with a reasonable expectation of success, rendered the claimed product obvious.¹¹⁴ For the court, this was a two-step analysis.

First, the court affirmed the Board's findings that the *Kubin* methods were essentially the same as those in the prior art, and that the prior art references gave the claimants a reasonable expectation of success.¹¹⁵ At least, it would seem that is what the court intended to say. The argument is actually framed in the negative—the *double negative*. In the words of the court,

[o]f note, the record *nowhere suggests* that the [prior art methods], even if slightly different than the technique disclosed in the claimed invention, *would not yield* the same polynucleotide claimed in [*Kubin*]. Stated directly, the record shows repeatedly that Valiante's [method] produces for any person of ordinary skill in this art the claimed polynucleotide.¹¹⁶

This unfortunate construction renders the argument logically precarious, but the court's position is nonetheless clear: the *Kubin* methods are conventional methods well-known in the prior art. The court found especially damning the claimants' own admission that they had used "standard biochemical methods,"¹¹⁷ stating categorically that the claimants, "cannot represent to the public that their claimed gene sequence can be derived and isolated by 'standard biochemical methods' discussed in a well-known manual on cloning techniques, while at the same time discounting the relevance of that very manual to the obviousness of their claims."¹¹⁸

Like the Board, the court was selective in its application of the Mathew reference.¹¹⁹ Recall that Mathew described the

rejection. *Id.* Obviousness is a question of law based on underlying factual determinations. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 17 (1966). The court reviews the Board's factual determinations under the substantial evidence standard and its obviousness determinations without deference. *In re Kubin*, No. 2008-1184, 2009 WL 877646 at *4.

114. *In re Kubin*, No. 2008-1184, 2009 WL 877646 at *10.

115. *Id.* at *4.

116. *Id.* at *5 (emphasis added).

117. *Id.* (quoting U.S. Patent Application No. 09/667, 859 (filed Sept. 20, 2000)).

118. *Id.*

119. *See supra*, note 97.

cloning of the murine 2B4 gene, unknown at the time to be a NAIL homologue, and reported incorrectly that there is no human homologue of the gene.¹²⁰ The court held that while Mathew was valid for its demonstration of the “relative ease of deriving the claimed sequence from the prior art,” it was nonetheless insignificant that the reference taught away from the *Kubin* invention.¹²¹ Rather, the court held that

Mathew’s quasi-agnostic stance toward the existence of a human homologue of the 2B4 gene cannot fairly be seen as dissuading one of ordinary skill in the art from combining Mathew’s teachings with those of Valiante. Rather, Mathew’s disclosure, in light of Valiante’s teachings regarding the p38 protein and its role in NK cell activation, would have aroused a skilled artisan’s curiosity to isolate the gene coding for p38.¹²²

Thus, the court held that there was sufficient evidence in the record to support a finding that the *Kubin* methods were conventional and well-known in the prior art, and that there was no significant disincentive for the inventors to pursue human NAIL isolation.

The second step in the court’s analysis, the heart of the opinion, addressed the status of *In re Deuel* after *KSR*.¹²³ The court began by discussing the aspects of *Deuel* relevant to this case, of which there are three. First, the holding that an amino acid sequence does not render the corresponding DNA sequence obvious per se.¹²⁴ Second, that the method of DNA isolation is not relevant to nonobviousness of the sequence itself,¹²⁵ even where the prior art includes a partial amino acid sequence.¹²⁶ Third, that “obvious to try” is not an appropriate standard for obviousness determination, even where there is a

120. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) 1410, 1414 (B.P.A.I. 2007).

121. *In re Kubin*, No. 2008-1184, 2009 WL 877646 at *5.

122. *Id.* at *6.

123. *See id.* at *6–9.

124. *Id.* at *6 (“[K]nowledge of a protein does not give one a conception of a particular DNA encoding it.”) (quoting *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995)).

125. *Id.* at *7 (“[T]he existence of a general method of isolating cDNA or 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. . . .”) (quoting *In re Deuel*, 51 F.3d at 1559).

126. *Id.* at *6 (“In *Deuel*, this court reversed the Board’s conclusion that a prior art reference teaching a method of gene cloning, together with a reference disclosing a partial amino acid sequence of a protein, rendered DNA molecules encoding the protein obvious.”) (citing *In re Deuel*, 51 F.3d at 1559).

general incentive to undertake the work and general methods by which to proceed are known in the prior art.¹²⁷ Under *Deuel*, the *Kubin* claims are undoubtedly permissible. The outcome of *Kubin* thus turns on whether *Deuel* was overruled by *KSR*, as the Board had held.¹²⁸

The Federal Circuit was emphatic in its position that some aspects of *Deuel* are no longer good law.¹²⁹ The court cites *KSR* as having “unambiguously discredited” the implication of *Deuel* that “the obviousness inquiry cannot consider that the combination of the claim’s constituent elements was ‘obvious to try.’”¹³⁰ The court pointed to the Supreme Court’s criticism of the Federal Circuit’s failure in *Teleflex* to consider whether a particular combination would have been obvious to try,¹³¹ and recited the language of *KSR* establishing that, “the fact that a combination was obvious to try might show that it was obvious under § 103.”¹³²

In perhaps a point of irony, the Federal Circuit explained that in striking down the standard of *Deuel*, the Supreme Court reinvigorated the standard of *In re O’Farrell*, a Federal Circuit decision issued seven years before *Deuel*.¹³³ The court reiterated the view of *O’Farrell* that “obvious to try” is a guideline often misunderstood,¹³⁴ and explained that while it is true that “obvious to try” is formally not the standard of § 103, an invention that is obvious under § 103 *also* would have been obvious to try.¹³⁵ Thus, the critical question is “when is an invention that was obvious to try nevertheless nonobvious?”¹³⁶

The court identified two situations in which “obvious to

127. *Id.* at *7 (“Obvious to try’ has long been held not to constitute obviousness. A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out.”) (quoting *In re Deuel*, 51 F.3d at 1559).

128. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) 1410, 1414 (B.P.A.I. 2007).

129. *In re Kubin*, No. 2008-1184, 2009 WL 877646 at *7-8.

130. *Id.*

131. *Id.* (citing to *Teleflex, Inc. v. KSR Int’l Co.*, 119 F. App’x 282, 289 (Fed. Cir. 2005)).

132. *Id.* at *8 (quoting *KSR Int’l Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007)).

133. *Id.* (citing *In re O’Farrell*, 853 F.2d 894 (Fed. Cir. 1988)).

134. *Id.*

135. *Id.* (citing *In re O’Farrell*, 853 F.2d at 903).

136. *Id.* (quoting *In re O’Farrell*, 853 F.2d at 903).

try” does not equate to obviousness under § 103.¹³⁷ First, where “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,” but where there is no guidance from the prior art as to which combinations would be successful.¹³⁸ In other words, a court should not find obviousness where the inventor “merely throws metaphorical darts at a board filled with combinatorial prior art possibilities.”¹³⁹ The court drew support for this in *KSR*’s “finite number of identified, predictable solutions” standard, which it held to be the inverse of the *O’Farrell* exception.¹⁴⁰

The second exception is one in which an inventor explores a new technology or approach to innovation with only general guidance from the prior art.¹⁴¹ The court found support for this in *KSR*’s statement that § 103 bars patent protection unless “the improvement is more than the predictable use of prior art elements according to their established functions.”¹⁴²

Ultimately, the Federal Circuit found that neither of these conditions applied to the *Kubin* invention. The court held that because the prior art disclosed the protein of interest to the appellants, an antibody specific to the protein, and a general method for isolating the protein, the invention was obvious.¹⁴³ Moreover, the court endorsed the Board’s notion that there was in the biotechnology industry a general motivation to pursue the isolation of human NAIL, given the prior art teaching that p38 is “expressed on virtually all human NK cells and thus plays a role in the immune response.”¹⁴⁴ The court declined to “cabin *KSR* to the ‘predictable arts’ (as opposed to the ‘unpredictable art’ of biotechnology),”¹⁴⁵ holding that given the advanced level of skill in the art, the claimants had “every motivation to seek and every reasonable expectation of success

137. *Id.*

138. *Id.* (quoting *In re O’Farrell*, 853 F.2d at 903).

139. *Id.*

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

141. *Id.* (citing *In re O’Farrell*, 853 F.2d at 903).

142. *Id.* (quoting *KSR Int’l*, 550 U.S. at 417).

143. *Id.* at *9.

144. *Id.* (quoting *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) 1410, 1413 (B.P.A.I. 2007)).

145. *Id.* (parentheses in original).

in achieving the sequence of the claimed invention.”¹⁴⁶

In sum, *In re Kubin* overrules two of the three central elements of *Deuel*. The court did *not* hold that a DNA sequence is obvious per se where the protein is known in the prior art. However, it did hold that reliance on conventional methods may preclude patent protection where there is reasonable expectation of success, and that “obvious to try” is a valid consideration even for the unpredictable arts.

II. IMPLICATIONS FOR THE BIOTECHNOLOGY INDUSTRY: OBVIOUSNESS IN THE POST-GENOMIC ERA

A. LOST IN TRANSLATION: *KSR* IS GOOD FOR SOME, BUT NOT ALL

The Federal Circuit’s ruling in *Kubin* is questionable on several levels,¹⁴⁷ and the case serves as a platform for a discussion of the general inadequacies of *KSR*. To start, it is unclear to what extent the holding of *KSR* translates to biotechnology, or any non-mechanical art for that matter. Of course, the Supreme Court did not expressly limit the holding of *KSR* to any particular art. However, all but one of the cases

146. *Id.* at *10.

147. Within days of the decision, a flurry of commentary by biotechnology patent practitioners sharply criticized several aspects of the ruling. See, e.g., Kevin Noonan, *In re Kubin*, PATENT DOCS BIOTECH. & PHARMA. PATENT LAW & NEWS BLOG, Apr. 6, 2009, http://www.patentdocs.org/articles_cases_obviousness/ (criticizing the Federal Circuit’s mishandling of the scientific elements of *In re Kubin*); Donna Young, *Federal Circuit’s Patent Ruling Could Broadly Affect Biotech*, BioWorld Today, Apr. 8, 2009, http://www.bioworld.com/servlet/com.accumedia.web.Dispatcher?next=bioWorldHeadlines_article&forceid=50547 (reporting the views of patent practitioners as to the likely negative impact of *In re Kubin*); Patenly BIOTech, *The Blunders of In re Kubin*, Apr. 8, 2009, <http://patentlybiotech.wordpress.com/2009/04/08/the-blunders-of-in-re-kubin/> (criticizing generally the logic and scope of *In re Kubin*). But see Christopher Holman, *In re Kubin: Federal Circuit Clarifies Obviousness Standard in Context of cDNA Cloning Invention*, HOLMAN’S BIOTECH. IP BLOG, Apr. 6, 2009, <http://holmansbiotechipblog.blogspot.com/2009/04/in-re-kubin-federal-circuit-clarifies.html> (arguing that the implications of *In re Kubin* for the biotechnology industry are not severe because of the unusual facts of the case); David Schwartz, *Fed Circuit Ruling Extends KSR Logic to Biotechnology*, THE TECH TRANSFER BLOG, Apr. 15, 2009, <http://www.technologytransfertactics.com/content/2009/04/15/fed-circuit-ruling-extends-ksr-logic-to-biotechnology/> (presenting a summary of opposing views as to the potential impact of *In re Kubin*).

the Court drew from involved the validity of mechanical patents.

The Court relied principally on three of its precedents to refashion the standard for obviousness determination. *United States v. Adams*, a companion case to *Graham*, addressed the patentability of a non-rechargeable electrical battery.¹⁴⁸ The Court cited to *Adams* for the proposition that when a patent claims a new combination of elements already known in the prior art, “the combination must do more than yield a predictable result.”¹⁴⁹ *Anderson’s-Black Rock, Inc. v. Pavement Salvage Co.* involved an improved road-paving machine.¹⁵⁰ The Court cited to *Anderson’s* for the proposition that to be nonobvious, combination devices must accomplish more than the individual components would do when operated sequentially.¹⁵¹ *Sakraida v. Ag Pro, Inc.* involved a water flush system for the removal of animal debris from the floor of a dairy barn.¹⁵² The Court cited to *Sakraida* for the proposition that a mere rearrangement of prior art elements that gives only predictable results is obvious and unpatentable.¹⁵³ In all three of these cases, the inventions at issue were not only mechanical in nature, they were *combination* devices, as was the patent at issue in *KSR*. Precisely how this paradigm translates to novel biological molecules, such as in *Kubin*, is not at all clear.

The only non-mechanical case cited directly in *KSR* is *In re*

148. *United States v. Adams*, 383 U.S. 39, 40 (1966).

149. *KSR Int’l Co. v. Teleflex, Inc.*, 550 U.S. 398, 416 (2007) (“The Court recognized 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.”) (citing *Adams*, 383 U.S. at 50–51).

150. *Anderson’s-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 58 (1969).

151. *KSR Int’l*, 550 U.S. at 417 (“The device, the Court concluded, did not create some new synergy: The radiant-heat burner functioned just as a burner was expected to function; and the paving machine did the same. The two in combination did no more than they would in separate, sequential operation.”) (citing *Anderson’s*, 396 U.S. at 60–62).

152. *Sakraida v. Ag Pro, Inc.*, 425 U.S. 273, 281–82 (1976).

153. *KSR Int’l*, 550 U.S. at 417 (“[T]he Court derived from the precedents the conclusion that when a patent ‘simply arranges old elements with each performing the same function it had been known to perform’ and yields no more than one would expect from such an arrangement, the combination is obvious.”) (quoting *Sakraida*, 425 U.S. at 282).

Deuel.¹⁵⁴ The Court's pronouncement that a finding of obviousness is appropriate where there exists "a finite number of identified, predictable solutions"¹⁵⁵ is centered on rejection of the *Deuel* holding that "[o]bvious to try' has long been held not to constitute obviousness."¹⁵⁶ In *Ex parte Kubin*, the Board focused on this language and on the opportunity to treat *Deuel* as no longer valid.¹⁵⁷ In doing so, however, the Board handily re-crafted the language of *KSR* to fit the facts of *Kubin*.

In *KSR*, the Court stated that, "[w]hen there is a *design need or market pressure* to solve a problem and there are a finite number of identified, predictable solutions . . . the fact that a combination was obvious to try might show that it was obvious under § 103."¹⁵⁸ However, the Board's version of this holding reads, "[w]hen there is *motivation* to solve a problem and there are a finite number of identified, predictable solutions . . ."¹⁵⁹ Under *KSR*, large-scale market forces such as industry or consumer demands for the correction of design flaws may serve as a predicate for a finding of obviousness.¹⁶⁰ Under the Board's view, it would seem that *any* motivation to solve a problem equates to these large-scale forces. As the Board explained in *Kubin*, "[t]he 'problem' facing those in the art was to isolate NAIL cDNA, and there were a limited number of methodologies available to do so."¹⁶¹ The Board refers to

154. A second biotechnology case, *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286 (Fed. Cir. 2006), was cited in recognition that the Federal Circuit had broadened its application of the TSM test even before the writing of *KSR*, *id.* at 421-22, but did not contribute substantively to the holding of the Court.

155. *Id.* See also *supra* note 50 and accompanying text.

156. *Id.* at 414 (quoting *Teleflex, Inc. v. KSR Int'l. Co.*, 119 F. App'x 282, 289 (Fed. Cir. 2005), *rev'd*, 550 U.S. 398 (quoting *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995)) (alteration in original).

157. At least one USPTO official has acknowledged the agency's dissatisfaction with the holding of *Deuel*, stating that USPTO examiners were "startled that the [Federal Circuit] would have said this was not obvious." Eli Kintisch, *Patent Experts Hope High Court will Clarify What's Obvious*, 314 SCIENCE 1230-31 (2006) (quoting Esther Kepplinger, a supervisor of the biotechnology examiner corps at the time the *Deuel* application was filed).

158. *KSR Int'l*, 550 U.S. at 421 (emphasis added).

159. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) 1410, 1415 (B.P.A.I. 2007) (emphasis added).

160. See *KSR Int'l*, 550 U.S. at 417.

161. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) at 1414.

NAIL isolation as facing those in the art, but in fact it was the problem facing *these artisans*. The Board attributed the individual motivation of these claimants to the whole of the biotechnology industry in order to find a market pressure and suggest the researchers were essentially passive in deciding whether and how to pursue NAIL isolation. It is more than a little disturbing that the Federal Circuit endorsed this reasoning.¹⁶² This broad interpretation of *KSR* is literally without bounds, as presumably all work is undertaken with some kind of motivation.

The distortion of this aspect of *KSR* speaks to the vagueness of the holding. What is a market pressure? What is a design need? How large a segment of the market must have the need? How must the need be expressed? In *KSR*, need and pressure took the form of a contract for services by a dominant American auto manufacturer,¹⁶³ an easy example. How this translates to other industries is impossible to say without more concrete definitions of these fundamental concepts. Does the fact that many people die each year from cancer create a market pressure to discover new treatments? Under a strict reading of *Kubin*, the answer may be *yes*.

The Federal Circuit's view that the use of known methodologies renders the NAIL cDNA obvious is equally misguided. *KSR* refers to the use of known methodologies only in the context of improvements to mechanical devices, stating:

When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, *if a technique has been used to improve one device*, and a person of ordinary skill in the art would recognize that it would *improve similar devices in the same way*, using the technique is obvious unless its actual application is beyond his or her skill.¹⁶⁴

The Court cites to *Anderson's* and *Sakraida* as illustrative of this holding,¹⁶⁵ which, as described above, related to mechanical combination devices.¹⁶⁶ In both cases, the technique for improvement was the joining of prior art

162. *In re Kubin*, No. 2008-1184, 2009 WL 877646 at *9-10 (Fed. Cir. Apr. 3, 2009).

163. *KSR Int'l*, 550 U.S. at 409-10.

164. *Id.* at 417 (emphasis added).

165. *Id.*

166. *See supra*, notes 150-153 and accompanying text.

elements that previously existed only separately. The *Anderson's* patent combined on one chassis a radiant heat burner, a pavement spreader, and a leveling device.¹⁶⁷ The *Sakraida* patent combined prior art water storage tanks, means for rapid water release, and drains positioned at the low end of a sloped floor to create a system for flushing debris from the floor of a barn.¹⁶⁸ Likewise, the technique in question in *KSR* was to combine known pedal elements that had not been joined in the prior art.¹⁶⁹ None of these scenarios involves the use of existing methods to derive something new, as in *Kubin*.

The obvious-by-methodology argument also conflates two aspects of the *KSR* holding. The first, described immediately above, is that the use of known methods to improve known elements is obvious.¹⁷⁰ The second is that obviousness may be found where there is a finite number of possible solutions.¹⁷¹ The Board split the difference between these statements to find obviousness where there are “a limited number of methodologies available,”¹⁷² and the Federal Circuit endorsed this position without comment. There is an important difference between these views, however. The claims at issue in *KSR* address a design need in the automotive industry where the solution (of which there are a finite number) is the claimed device. By contrast, in *Kubin*, the method (of which there are a limited number) is the *means to obtain* the claimed device. Under *Kubin*, the pedal assembly in *KSR* would be held obvious not because of the design itself, but because there are a limited number of ways to cast the metal used to make the device. This approach runs contrary to the language of § 103, which states that “[p]atentability shall not be negated by the manner in which the invention was made.”¹⁷³ Recall that this language was included to quash the flash of genius standard announced by the Supreme Court in *Cuno*.¹⁷⁴ The very essence

167. *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 58 (1969).

168. *Sakraida v. Ag Pro, Inc.*, 425 U.S. 273, 281–82 (1976).

169. *KSR Int'l*, 550 U.S. at 406.

170. *Id.* at 417; *see also supra* note 164 and accompanying text.

171. *See id.* at 421; *see also supra* note 50, 56, and accompanying text.

172. *Ex parte Kubin*, 83 U.S.P.Q.2d (BNA) 1410, 1414 (B.P.A.I. 2007) (emphasis added).

173. United States Patent Act, 35 U.S.C. § 103(a) (2006).

174. *See supra* note 25.

of this provision is that the focus of an obviousness inquiry should be the product of the inventive effort, not the means employed by the inventor. The Federal Circuit would have inventors disavow proven technologies in favor of re-inventing the wheel, so to speak, in order to withstand an obviousness determination. Not only would this be inefficient and socially wasteful, it may not always be possible to devise novel methods, especially in highly technical fields. In *In re Kubin*, the court made a point of the fact that the claimants cited to the “*very same cloning manual*” as the Valiante reference.¹⁷⁵ What the court failed to appreciate is that both cited to Sambrook/Maniatis because it was the *only* manual of any repute, to which any molecular biologist can attest.

The reasoning of *In re Kubin* illustrates the shortcomings of KSR, which is both too narrowly tailored to translate easily to other disciplines and sufficiently vague on key elements to yield little guidance as to their meaning. On the whole, KSR is unsatisfying as the Supreme Court’s first declaration on the issue in over forty years. A common sense approach is inadequate to address this difficult question of law when applied to biological science. Nonetheless, together *KSR* and *Kubin* raise interesting and difficult questions regarding nonobviousness standards in biotechnology as it exists today. Standards implemented by the Federal Circuit in the industry’s infancy are coming under increased scrutiny and have perhaps been outgrown by advances in the art.

B. LIFE ON PLANET EARTH: THE REALITIES OF BIOTECHNOLOGY

Some scholars have criticized *In re Bell* and *In re Deuel* as overindulgent to the biotechnology industry, arguing that knowledge of a protein sequence is sufficient to render the corresponding gene sequence obvious to a person of skill in the art.¹⁷⁶ However, this criticism fails to consider the relevant

175. *In re Kubin*, No. 2008-1184, 2009 WL 877646 at *9 (Fed. Cir. Apr. 3, 2009) (emphasis in original).

176. See, e.g., Harold C. Wegner, *Chemical and Biotechnology Obviousness in a State of Flux*, 26 BIOTECH. L. REP. 437, 459–60 (2007) (criticizing the Federal Circuit’s approach to biotechnology obviousness and calling for “death to the holding in *Deuel*.”); Harold C. Wegner, *Deuel* Death to “Motivation”: Whither *KSR* and *Kahn* 9 (Apr. 21, 2006), http://www.foley.com/files/tbl_s31Publications/FileUpload137/3349/KSRDeuelDeath.pdf (criticizing the holdings of *Bell* and *Deuel*; referring to the holding of *Deuel* as a “deviant standard for biotechnology”). But see Andrew V. Trask, Note, “*Obvious to Try*”: A Proper Patentability Standard

facts on which an obviousness determination is based for genetic innovation—the *biological facts*.

It is indisputable that DNA and proteins are fundamentally related, and that their interrelatedness is largely stable and reproducible.¹⁷⁷ Were this not true, genetic engineering as it exists today would not be possible. However, as illustrated in Fig. 2, a one-to-one codon-to-amino acid correlation simply does not exist. Some amino acids are specified by as many as six different codons.¹⁷⁸ From an evolutionary standpoint, degeneracy of the genetic code is a good thing, because it allows for small mistakes in codon sequence to occur without altering the corresponding protein sequence, which could have a devastating result for the viability of a cell.¹⁷⁹ From a molecular biologist's standpoint, however, degeneracy is a barrier to predicting gene sequence based solely on protein sequence. For even the smallest of proteins, there are simply too many possible coding sequences to make feasible a trial and error approach.¹⁸⁰ This is precisely why geneticists have developed various other means to clone genes. It is also the reason the Federal Circuit was quick to re-tool *KSR's* "finite number of identified, predictable solutions" standard to one that encompasses an "easily traversed, small and finite number of alternatives."¹⁸¹ True, it is possible to tabulate all the possible gene sequences, one of which is correct. However, it is not possible to predict which is correct based solely on protein sequence. Regardless of the legal implications of *Deuel*, the Federal Circuit got the science right.

From an industry standpoint, the holding of *Deuel* was important because it respected the historical progression of life science research. Scientists had begun to characterize proteins

in the Pharmaceutical Arts?, 76 FORDHAM L. REV. 2625, 2632–36 (2008) (arguing that unpredictability is simply a reality of the biotechnology and pharmaceutical arts and that "obvious to try" is not an appropriate standard for those industries; arguing that *KSR* does not permit courts to deny patents in these arts on the basis that the innovation was obvious to try).

177. See generally GRIFFITHS ET AL., *supra* note 60.

178. *Id.*

179. For example, note the similarity of the codons that specify leucine (leu) shown in Fig. 2. They are: AAT, AAC, GAC, GAT, GAG, GAA, Reading the codons in sequence, only a single base differs one to the next.

180. See *supra* notes 62 and 63 and accompanying text.

181. See *supra* notes 56–58 and accompanying text.

in great detail¹⁸² long before it was known that DNA is the genetic material,¹⁸³ much less how it is that DNA encodes protein products. Until relatively recently, it was the norm for proteins to be characterized in some form and at least partially sequenced before the corresponding gene was cloned, just as a practical matter.¹⁸⁴ If protein sequences were held to render gene sequences obvious, entire fields of genetic research would have been precluded from patent protection by protein chemistry done years (or decades) before recombinant DNA technology even existed.

Nevertheless, one aspect of the *Bell-Deuel* standard may be vulnerable. While the *Bell* court held that protein sequences do not render gene sequences obvious, it explicitly reserved judgment on whether the converse is also true—whether DNA sequences render proteins obvious.¹⁸⁵ At the time, prior to the release of the first completed genomes,¹⁸⁶ so-called forward

182. *E.g.*, Linus Pauling et al., *The Structure of Proteins: Two Hydrogen-bonded Helical Configurations of the Polypeptide Chain*, 37 PROC. NAT'L. ACAD. SCI. 205 (1951); Linus Pauling & Carl Niemann, *The Structure of Proteins*, 61 J. AM. CHEMICAL SOC'Y 1860 (1939); Alfred E. Mirsky & Linus Pauling, *On the Structure of Native, Denatured, and Coagulated Proteins*, 22 PROC. NAT'L. ACAD. SCI. 439 (1936).

183. Alfred D. Hershey & Martha Chase, *Independent Functions of Viral Protein and Nucleic Acid in Growth of Bacteriophage*, 36 J. GEN. PHYSIOLOGY 39 (1952).

184. Consider the history of the characterization of insulin, for example. The protein was physically isolated from cellular extracts in 1921, the amino acid sequence was determined in 1953, and the human gene was sequenced in 1980. Quite literally, the techniques used to sequence the amino acid were not in existence at the time the protein was first identified. Moreover, when the protein was sequenced in 1953, it was not yet widely accepted that DNA is the genetic material. Graeme I. Bell et al., *Sequence of the Human Insulin Gene*, 284 NATURE 26 (1980); Frederick Sanger & E.O.P. Thompson, *The Amino-acid Sequence in the Glycyl Chain of Insulin: 1. The Identification of Lower Peptides from Partial Hydrolysates*, 53 BIOCHEMICAL J. 353 (1953); Frederick Sanger & E.O.P. Thompson, *The Amino-acid Sequence in the Glycyl Chain of Insulin: 2. The Investigation of Peptides from Enzymic Hydrolysates*, 53 BIOCHEMICAL J. 366 (1953); Fredrick G. Banting, Nobel Lecture Delivered at Stockholm on September 15th, 1925: Diabetes and Insulin (Sept. 15, 1925).

185. *In re Bell*, 991 F.2d 781, 785 n.6 (Fed. Cir. 1993); *see also supra* note 74 and accompanying text.

186. The first complete genome sequenced was that of *Haemophilus influenzae*, released in 1995. Robert D. Fleischmann et al., *Whole-Genome Random Sequencing and Assembly of Haemophilus influenzae Rd*, 269 SCIENCE 496 (1995). The first eukaryotic genome to be completed was *Saccharomyces cerevisiae* (yeast), released in 1996. André Goffeau et al., *Life With 6000 Genes*, 274 SCIENCE 546 (1996). The first multicellular

reading of genetic information—DNA to protein—was uncommon. The court could afford to reserve judgment then, but perhaps no longer. Genomic data (partial or complete) are publicly available for hundreds of species, with more on the way.¹⁸⁷ The information is of course invaluable to genetic researchers, but it may be the elephant in the room from the standpoint of patentability of proteins. The reason is that, as illustrated in Figs. 1 and 2, forward reading of genomic sequence is straightforward.¹⁸⁸ Quite literally, anyone with a table of the genetic code could translate coding sequence to protein sequence.¹⁸⁹ It is precisely because DNA, RNA, and proteins have discernable relationships that biotechnology research has progressed as far as it has. This is a central element of modern medicine and is the basis for breakthrough therapies such as recombinant human insulin (an old example) and gene replacement therapy (a new example).¹⁹⁰

On one hand, it is inconsistent to invoke the realities of biology to argue that reverse reading is not obvious, and then avoid the converse reality because it is inconvenient. On the other hand, to hold that forward reading is obvious would radically alter the landscape of biotechnology patenting. Whole classes of biological molecules—mRNAs and proteins—would be removed from the patent arena overnight, and scores of issued patents would be brought into crisis. The public stores of knowledge would also be negatively affected as industry players resort to trade secret practice to protect new developments. Industry analysts also argue that the subjective obviousness analysis of *KSR* will stem the flow of money into

eukaryotic genome completed was that of *Caenorhabditis elegans*, released in 1998. *C. elegans* Sequencing Consortium, *Genome Sequence of the Nematode C. elegans: A Platform for Investigating Biology*, 282 SCIENCE 2012 (1998).

187. Genbank is an annotated collection of all publicly available DNA sequences maintained by the National Institutes of Health. It is available for searching at <http://www.ncbi.nlm.nih.gov/Genbank/>. See Dennis A . Benson, et al., *GenBank*, 36 NUCLEIC ACIDS RES. D25 (2008).

188. See *supra* pp. 810–12.

189. Of course, there are aspects of genomic interpretation that are not so straightforward, such as alternative transcriptional start sites and alternative splicing. For simplicity, these are not considered here.

190. See Gary Walsh, *Biopharmaceutical Benchmarks*, 18 NATURE BIOTECH. 831 (2000).

the industry, something of particular importance to biotechnology because research and development is so costly.¹⁹¹

C. INDUSTRY-TOLERANT OBVIOUSNESS STANDARDS

One thing made clear by *KSR* and *Kubin* is that generic obviousness standards do not translate well to biotechnology. It is implausible to equate biological science with the automotive industry, as artisans in these fields face radically different challenges. An obvious solution would be to address the needs of specific industries directly and separately from those of other industries. As some scholars point out, when the uniform patent system was adopted, inventive efforts in this country were predominantly mechanical in nature, and were far more homogeneous than today.¹⁹² With the emergence of new technologies such as biotechnology, computer hardware and software, electronics, and semiconductors, uniform rules are no longer appropriate or adequate.¹⁹³

Some proponents of industry-tolerant patentability standards argue that courts already enforce differential standards across industries.¹⁹⁴ Burk and Lemley argue that the Federal Circuit has responded to the needs of new technologies by applying the uniform rules in a manner that effectively creates industry-specific standards.¹⁹⁵ Through close case analysis the authors demonstrate, for example, that the Federal Circuit enforces a much stricter written description requirement¹⁹⁶ in biotechnology than in other industries,¹⁹⁷

191. Brief of Biotechnology Industry Organization as Amicus Curiae in Support of Respondents 5–10, *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007) (No. 04-1350).

192. John R. Allison & Mark A. Lemley, *The Growing Complexity of the United States Patent System*, 82 B.U. L. REV. 77, 134–38 (2002).

193. *Id.* at 142–44.

194. See generally Sean B. Seymore, *Heightened Enablement in the Unpredictable Arts*, 56 UCLA L. REV. 127 (2008); Dan L. Burk, *Biotechnology in the Federal Circuit: A Clockwork Lemon*, 46 ARIZ. L. REV. 441 (2004); Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 BERKELEY TECH. L.J. 1155 (2002).

195. See Burk & Lemley, *supra* note 194 at 1183.

196. United States Patent Act, 35 U.S.C. § 112, ¶ 1 (2006).

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set

while permitting a lowered standard for nonobviousness.¹⁹⁸ Conversely, the computer software industry enjoys minimal enablement and best mode requirements,¹⁹⁹ and a more stringent nonobviousness standard.²⁰⁰

Opponents argue that industry-tolerant standards will be administratively burdensome,²⁰¹ and prone to erosion.²⁰² However, it is not clear why an explicit standard would be any more prone to erosion than the ad hoc judicial approach currently in place. If anything, an unambiguous standard should be more resistant than the stop-gap measures of the Federal Circuit. Regarding the administrative burden, the United States Patent and Trademark Office (USPTO) already operates an industry-specific examiner corps.²⁰³ Implementation of industry-tolerant standards could be as straightforward as revising examination guidelines to reflect the new practice. The real burden would be in conducting an initial study of the issue and drafting recommended guidelines. However, there is likely no shortage of biotechnology industry advocates willing to contribute to the process. Critics of the USPTO may argue that the agency struggles to enforce statutory requirements as it is, and that introducing non-uniform standards would only complicate matters further. If anything, however, that argument speaks to the need to reform

forth the best mode contemplated by the inventor of carrying out his invention. *Id.*

197. See Burk & Lemley, *supra* note 194, at 1183 & n.120.

198. *Id.*

199. *Id.* at 1162–63 (citing *N. Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931 (Fed. Cir. 1990)).

200. *Id.* at 1167–68 (citing *Amazon.com v. Barnes & Noble*, 239 F.3d 1343 (Fed. Cir. 2001); *Lockwood v. Am. Airlines*, 107 F.3d 1565 (Fed. Cir. 1997)).

201. Mark D. Janis, *Equilibrium in a Technology-Specific Patent System*, 54 CASE W. RES. L. REV. 743, 744 (2004) (“One threshold question is whether we will even be able to talk about a unitary patent law jurisprudence if [such] proposals are implemented. Might we instead find ourselves confronted with fifty-seven patent law jurisprudences, each specifically tailored to particular technologies?”).

202. *Id.* (“Perhaps the [proposals] should give greater attention to elucidating controls that would guard against the dissolution of [industry-specific standards] and thereby maintain some level of systematic coherence.”).

203. See, e.g., U.S. Pat. & Trademark Off., Patent Examiner Positions, <http://www.uspto.gov/web/offices/pac/exam.htm> (last visited Mar. 16, 2009).

standards. If *Bell*, *Deuel*, and *Kubin* are any indication, it would seem that the problem lies not in the relative complexity of the standard, but in the fact that examiners are required to apply uniform standards to vastly different technologies, and the fit is often poor. The reality is that legal standards for obviousness are rooted in the practical considerations of invention. Practically speaking, it seems obvious that wet batteries, pavement spreaders, and manure flushers—combination mechanical devices—should be viewed through a slightly different lens than novel biological molecules designed to improve our collective health and well-being.

III. CONCLUSION

Biotechnology in the post-genomic era is an exceedingly advanced industry, and is growing more so every year. Genetic innovation is a central component of modern medicine and it is in the public interest to foster industry advances wherever possible. Adequate patent protection is an important counterbalance to the enormous risk and expense of biotechnological undertakings, but current obviousness standards are poised to fail the industry.

The Supreme Court's reformulation of obviousness determination in *KSR* is inadequate to address the needs of varied modern industries, the highly technical arts in particular. While the Court purported to set forth a generic standard, broadly applicable to the patentable arts, it crafted a standard that is too narrow and too vague to be of use generally. A strict reading of *KSR* would revoke patent protection for innovations that are standard in the biotechnology industry, as illustrated by the Board's mechanical application of *KSR* in *Ex parte Kubin*.

Obviousness standards that tolerate the realities of biotechnology research are necessary to foster continued investment in the industry and the dissemination of research data to the public. Standards that parallel the Federal Circuit's pre-*KSR* biotechnology jurisprudence would promote the public interest in advancing high-level research while maintaining reasonable standards for patentability.