

**RESTORING THE GENETIC COMMONS:
A “COMMON SENSE” APPROACH TO
BIOTECHNOLOGY PATENTS IN THE
WAKE OF *KSR V. TELEFLEX***

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INTRODUCTION

The proper scope of patent protection for biotechnology discoveries has been the source of longstanding debate among legal scholars, research scientists, and industry executives. The debate can be traced back to the 1980 *Diamond v. Chakrabarty* decision, in which the Supreme Court held that a bacterium genetically modified to dissolve crude oil

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was a patentable invention.¹ The Court noted Congress's intention to allow the patenting of "anything under the sun that is made by man"² and concluded that non-naturally occurring, living things produced by human ingenuity are patentable.³ Shortly after the *Chakrabarty* decision, the Patent and Trademark Office (PTO) "began issuing patents on human genes and gene fragments, transgenic bacteria that express human genes, and human cell lines that express DNA sequences producing pharmacologically important proteins."⁴

In the 1990s, the commencement of the Human Genome Project, and the subsequent flood of patent filings claiming DNA sequences, fueled the controversy over the patenting of biological discoveries.⁵ The National Institutes of Health (NIH) received sharp criticism from the medical research community after filing two patent applications for over 2000 partial gene sequences identified by one of the Human Genome Project researchers, Dr. Craig Venter.⁶ Critics argued that patents over partial gene sequences would distort the conduct of basic biomedical research and ultimately impede commercial development.⁷ The NIH responded to the criticism by reversing its gene patenting policy and electing not to pursue patents for gene sequences.⁸ Participants in the Human Genome Project, as well as members of the pharmaceutical industry and certain DNA chip⁹ makers acted to render raw sequence data unpatentable by implementing strategies to release genome data into the

1. *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

2. *Id.* at 309 (quoting S. REP. NO. 1979, 82d Cong. 2d Sess., 5 (1952); H. REP. NO. 1923, 82d Cong. 2d Sess., 6 (1952)).

3. *Id.* at 309–10.

4. Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303, 319 (2002).

5. For background information on the Human Genome Project, see Human Genome Project Information, http://www.orl.gov/sci/techresources/Human_Genome/home.shtml (last visited Sept. 25, 2007).

6. See Bernadine Healy, *On Gene Patenting*, 327 NEW ENG. J. MED. 664, 664 (1992).

7. See, e.g., Christopher J. Harnett, *The Human Genome Project and the Downside of Federal Technology Transfer*, 5 RISK 151, 153–54 (1994).

8. Christopher Anderson, *NIH Drops Bid for Gene Patents*, 263 SCIENCE 909 (1994).

9. Also known as microarrays, DNA chips are produced by immobilizing thousands of short oligonucleotide sequences on a substrate. When a solution containing an unknown sample of DNA molecules is washed against the DNA chip, the microarray probes (isolated, purified, single-stranded DNA molecules) are able to hybridize specifically with DNA molecules in the sample that contain their reverse-complementary sequences. See Roger Ekins & Frederick W. Chu, *Microarrays: Their Origins and Applications*, 17 TRENDS IN BIOTECHNOLOGY 217 (1999); Bob Sinclair, *Everything's Great When It Sits on a Chip: A Bright Future for DNA Arrays*, THE SCIENTIST, May 24, 1999, at 18.

public domain.¹⁰ Such initiatives spurred the PTO to revise its utility guidelines in 2001 to require “specific, substantial, and credible utility” in order to satisfy section 101 of the U.S. Patent Code,¹¹ thus excluding from patentability DNA sequences of unknown function.¹²

The debate over biotechnology patents continues to simmer today. In February 2007, Congressmen Xavier Becerra and Dave Weldon introduced the Genomic Research and Accessibility Act, which would amend the U.S. Patent Code to prohibit patents for “a nucleotide sequence, or its functions and correlations, or the naturally occurring products it specifies.”¹³ The bill may have been prompted in part by best-selling author Michael Crichton’s invective against gene patents in a recent novel¹⁴ and a related editorial in the *New York Times* which began: “YOU, or someone you love, may die because of a gene patent that should never have been granted in the first place.”¹⁵

Despite general consensus that patents are necessary to the vitality of the biopharmaceutical industry, there are substantial concerns that gene patents slow the pace of scientific advancement and deter commercial development of basic genomics research. The proliferation of intellectual property rights among a number of patentees in the pharmaceutical field has the potential to create a “tragedy of the anticommons.”¹⁶ According to this theory, a large number of narrow patents on upstream discoveries impede innovation by stripping the public domain of basic research information and increasing the costs associated with research and development (R&D).¹⁷

Recent findings released by the ENCyclopedia of DNA Elements (ENCODE) consortium, which is organized by the National Human Genome Research Institute (NHGRI), part of the NIH, threaten to exacerbate these concerns. These findings refute the longstanding view that the human genome contains vast amounts of “junk DNA that is not

10. Arti K. Rai, *The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, and Access in the Post-Genomics Era*, 2001 U. ILL. L. REV. 173, 194–95 (2001).

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

12. Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 BERKELEY TECH. L.J. 813, 840 (2001).

13. H.R. 977, 110th Cong. § 2 (2007).

14. See Alan Dove, *Stranger Than Fiction*, INTELL. PROP. L. & BUS., April 2007, available at <http://www.law.com> (discussing Crichton’s book, *Next*, whose cast of characters includes a greedy venture capitalist who patents human genes).

15. Michael Crichton, *Patenting Life*, N.Y. TIMES, Feb. 14, 2007, at 6.

16. See Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 698 (1998).

17. See discussion *infra* Part III.B.

biologically active”¹⁸ and challenge the “one gene, one protein” principle upon which the biotechnology industry is built.¹⁹ In fact, the genome is a complex, interwoven network in which genes are just one of many types of DNA sequences that have a functional impact.²⁰ The ENCODE project’s findings emphasize the importance of preserving the genetic commons for the collaborative research that is essential to unraveling the complexities of human genomics.²¹

In this Article, I argue that a new approach to biotechnology patenting is necessary to fully realize the tremendous potential of recent advances in our understanding of the human genome. Part I places the gene patenting debate in context by highlighting the key landmarks that have shaped the biotechnology industry and outlining the products and stakeholders that comprise the industry. Part II describes the current state of the law on biotechnology patents, summarizing the Federal Circuit’s application of the various doctrines that collectively define the patent landscape’s parameters. In this Part, I explain how the Federal Circuit’s jurisprudence is tied to its inaccurate characterization of the “person having ordinary skill in the art” (PHOSITA) of biotechnology. Part III discusses theoretical concerns raised by the Federal Circuit’s jurisprudence regarding biotechnology discoveries and proposals that have been offered to ameliorate these concerns.

18. Geoff Spencer, *New Findings Challenge Established Views on Human Genome: ENCODE Research Consortium Uncovers Surprises Related to Organization and Function of Human Genetic Blueprint*, NIH NEWS, June 13, 2007, <http://www.nih.gov/news/pr/jun2007/nhgri-13.htm>.

19. Denise Caruso, *A Challenge to Gene Theory, a Tougher Look at Biotech*, N.Y. TIMES, July 1, 2007, at 3.

20. The traditional paradigm has been that genes are transcribed to form mRNA, which in turn is translated to form proteins. Recent results from the ENCODE project refute this conventional wisdom by demonstrating that a large number of genes that do not code for protein nonetheless are transcribed into one of several newly discovered types of RNA. One of the most common of these new types of RNA is microRNA, which rather than being translated into protein serves to regulate the activity of protein-encoding genes. Single microRNAs often regulate the levels of hundreds of different proteins. Moreover, some types of regulatory RNA edit other kinds of RNA, leading to a highly dynamic regulatory network in which the output of the cell’s genetic machinery is the result of the complex interplay amongst numerous genetic elements. See *Really New Advances*, THE ECONOMIST, June 14, 2007, http://www.economist.com/displaystory.cfm?story_id=9333471.

21. See Spencer, *supra* note 18 (quoting remarks by Eric D. Green, M.D., Ph.D., director of NHGRI’s Division of Intramural Research:

It would have been impossible to conduct a scientific exploration of this magnitude without the skills and talents of groups representing many different disciplines. Thanks to the ENCODE collaboration, individual researchers around the world now have access to a wealth of new data that they can use to inform and shape research related to the human genome.)

In Part IV, I assert that the Supreme Court's recent decision in *KSR v. Teleflex* should serve as the impetus for the Federal Circuit to abandon its rigid, dogmatic treatment of biotechnology in favor of a flexible approach that will allow the court to align patent doctrine with the current state of the art. The Supreme Court's mandate to insert "common sense" into the obviousness analysis should compel the Federal Circuit to re-examine its depiction of the biotechnology PHOSITA. This may impact the court's application of patent doctrines conceptually linked to the obviousness standard and lead to changes in both the number and scope of biotechnology patents. Such alterations in the patent landscape will have an overall positive effect on the biotechnology industry by alleviating inefficiencies and impediments to scientific and commercial progress engendered by the existing patent regime.

I. BACKGROUND FRAMING THE GENE PATENTING DEBATE

A. *The Bayh-Dole Act*

The Bayh-Dole Act,²² enacted in 1980, encourages small businesses and nonprofit organizations to patent the results of government-sponsored research by allowing them to retain patent ownership, provided they diligently file patent applications and promote commercial development of their inventions.²³ The Bayh-Dole Act also clarifies that federal agencies can apply for and hold patents, and can license their patents to the private sector.²⁴ A 1983 Reagan Memorandum,²⁵ endorsed by Congress in a housekeeping provision to a 1984 change in the law,²⁶ extended the Bayh-Dole Act to large businesses as well.

The Bayh-Dole Act is based on the concept that the rights granted by patent law are necessary, not to provide incentives to invent, but rather to encourage private firms to develop marketable products from inventions arising from federal funds.²⁷ According to this argument, industry would be unwilling to undertake costly and risky commercial development without proprietary rights to the basic research inventions, leaving promising discoveries to languish in government and university archives. This

22. Bayh-Dole Act, 35 U.S.C. §§ 200–11, 301–07 (2000)).

23. Rebecca Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 VA. L. REV. 1663, 1665 (1996).

24. *Id.*

25. Memorandum from Ronald Reagan, President of the United States, to the Heads of Executive Departments and Agencies, Government Patent Policy, Pub. Papers 248 (Feb. 18, 1983), available at <http://www.reagan.utexas.edu/archives/speeches/1983/21883b.htm>.

26. S. REP. NO. 98-662, at 2 (1984), as reprinted in 1984 U.S.C.C.A.N. 5799, 5800.

27. Arti Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77, 96 (1999).

policy contravenes the conventional wisdom that patent protection is necessary to preserve ex ante incentives, despite the net social loss that results ex post.²⁸

The Bayh-Dole Act has sparked the development of a technology transfer industry whereby academic researchers are encouraged to pursue commercialization of their scientific discoveries. Universities routinely file patent applications on DNA sequences, protein products, and disease pathways that are primarily valuable as inputs into further research.²⁹ University technology transfer offices then negotiate with private firms to license the right for the firms to utilize patented discoveries in exchange for fees and royalties. By encouraging the patenting of discoveries that in a previous era might have been freely disseminated, the Bayh-Dole Act pushes some of the gains of innovation upstream, at the expense of firms that develop commercial products.³⁰ The Bayh-Dole Act thus risks retarding product development by impoverishing the public domain of research science that has long been a crucial resource for both academia and industry.³¹

B. *The Federal Circuit*

Created in 1982 to facilitate uniformity in the patent case law, the Court of Appeals for the Federal Circuit has acted to facilitate the patenting of basic biomedical research. Although the court has retained the idea that “products of nature” are not patentable, it has routinely upheld patents on purified and isolated forms of naturally occurring molecules.³² In *Amgen v. Chugai Pharmaceutical Co.*,³³ the Federal Circuit upheld the validity of a patent for the DNA sequence encoding erythropoietin and concluded that genes separated from the chromosomes on which they naturally reside are patentable. Consistent with longstanding case law considering patents on chemicals, this allows patents on isolated and purified molecules if they only exist in nature in an impure state, and

28. Eisenberg, *supra* note 23, at 1666–67.

29. Arti K. Rai and Rebecca S. Eisenberg, *The Public Domain: Bayh-Dole Reform and the Progress of Biomedicine*, 66 *LAW & CONTEMP. PROBS.* 289, 291 (2003).

30. *Id.* at 1712.

31. *Id.* at 1667.

32. See, e.g., *Genentech, Inc. v. Wellcome Found. Ltd.*, 29 F.3d 1555, 1558 (Fed. Cir. 1994) (patent on purified form of tissue plasminogen activator (t-PA), a naturally occurring protein that helps dissolve fibrin clots); *Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991) (patent on a highly purified form of Factor VIII:C, a naturally occurring factor involved in blood clotting).

33. *Amgen v. Chugai Pharmaceutical Co.*, 927 F.2d 1200 (Fed. Cir. 1991), *cert. denied*, 502 U.S. 856 (1991).

thus have been subject to human manipulation.³⁴ PTO examination guidelines reflect the Federal Circuit's position on the patentability of DNA sequences.³⁵

The Federal Circuit has substantially liberalized the patent statute's utility requirement, holding that patent applicants can demonstrate the utility of inventions even if they are far from commercial application. The court has thus retreated from the stringent interpretation of utility espoused by the Supreme Court in *Brenner v. Manson*.³⁶ There, the Supreme Court held that the fact that the claimed invention was being investigated for possible tumor-inhibiting effects in mice did not satisfy the utility standard.³⁷ The Court expressed concern that conferring patent rights in basic research discoveries would create a "monopoly of knowledge" and "confer power to block off whole areas of scientific development, without compensating benefit to the public."³⁸ The Federal Circuit has adopted a markedly different stance since its creation in 1982. For example, if a novel compound demonstrates potential therapeutic activity in vitro, such activity can be sufficient to establish its practical utility.³⁹ The Federal Circuit has also emphasized that usefulness of biopharmaceutical inventions under patent law necessarily includes the expectation of further research and development.⁴⁰

The Federal Circuit's interpretation of the obviousness standard has arguably done the most to facilitate the patenting of upstream biomedical research.⁴¹ The court has repeatedly overturned the PTO's determination that DNA sequences of genes that code for particular proteins are obvious when the amino acid sequence of the protein, as well as a general method of ascertaining the specific DNA sequence through the use of probes, are known.⁴² This position, which has been the subject of widespread criticism from patent scholars,⁴³ serves as a cornerstone of the contemporary biopharmaceutical industry.

34. See, e.g., *Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958) (upholding the patentability of purified Vitamin B-12).

35. As long as they meet the statutory requirements, DNA sequences are eligible for patenting when isolated from their natural state and purified. See *Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

36. *Brenner v. Manson*, 383 U.S. 519 (1966).

37. *Id.* at 529-31.

38. *Id.* at 534.

39. See *Cross v. Iizuka*, 753 F.2d 1040 (Fed. Cir. 1985).

40. See *In re Brana*, 51 F.3d 1560, 1568 (Fed. Cir. 1995).

41. Arti Kauer Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 Nw. U. L. REV. 77, 108 (1999).

42. See, e.g., *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995); *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993).

43. See discussion *infra* Part II.B.

C. Products and Players in the Biotechnology Marketplace

Completed in 2003, the Human Genome Project⁴⁴ has revealed a wealth of information about human DNA which is stored in easily accessible genomic databases. Researchers scour these databases with powerful computers hoping to find and acquire proprietary rights to DNA sequences that may have diagnostic or therapeutic potential.⁴⁵ A few decades ago it might have taken ten years to find a particular gene, but with modern gene maps, a gene can now be found with a fifteen second computer search.⁴⁶ “[S]cientists can use . . . [biological] databases to compare and assign biological functions to particular or characteristic sequences (i.e., motifs) [After sequencing] an unknown DNA, RNA, or protein molecule, researchers can use these databases to identify the unknown molecule and determine its function.”⁴⁷ High-throughput equipment has made sequencing far less laborious, resulting in a large number of patent applications claiming DNA sequences and their associated protein products.⁴⁸

Aided by such resources and techniques, modern day genomics researchers do not face the technological constraints incurred by scientists in the early days of biotechnology. In the 1980s, “researchers . . . were compelled to begin with the known protein and to work backward to the encoding gene.”⁴⁹ Eisenberg notes, “[t]he commercially significant aspect of these discoveries was not the informational value of knowing what the sequence was, but the tangible value of being able to use the DNA molecules in recombinant production facilities to make therapeutic proteins for sale.”⁵⁰ Today the availability of “automated high-throughput sequencing has made it possible for scientists to generate large quantities of raw genomic data.”⁵¹ Such raw genetic sequence information has immediate commercial value as a means for identifying new avenues for product development.⁵²

44. See Human Genome Project, *supra* note 5.

45. Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303, 308 (2002).

46. Malcolm Ritter, *Genetic Map Yields Key Surprises*, ASSOCIATED PRESS, Feb. 12, 2001 (citing J. Craig Venter, President of Celera Corp.).

47. M. Scott McBride, *Bioinformatics and Intellectual Property Protection*, 17 BERKELEY TECH. L.J. 1331, 1337 (2002).

48. Demaine & Fellmeth, *supra* note 45, at 307.

49. James Bradshaw, *Gene Patent Policy: Does Issuing Gene Patents Accord With the Purposes of the U.S. Patent System?*, 37 WILLIAMETTE L. REV. 637, 641 (2001).

50. Rebecca Eisenberg, *Re-Examining The Role of Patents in Appropriating The Value of DNA Sequences*, 49 EMORY L.J. 783, 788 (2000).

51. Bradshaw, *supra* note 49, at 642.

52. *Id.*

Patent protection may cover a broad range of biotechnology inventions, from upstream discoveries useful as research tools to downstream products with immediate clinical applications. Biotechnology “patents may be obtained with claims directed to . . . DNA sequences in purified or isolated form, vectors, vaccines, new or improved organisms, new chemical compositions, kits, methods of treatment, new methods of making or using a new or known compound and research tools.”⁵³ Research tools include clones, cell lines, animal models, receptors and ligands involved in disease pathways, and laboratory techniques.⁵⁴ Various combinations of research tools may be used to identify, develop, produce, and test new diagnostics and therapeutics.

The “traditional dividing line between basic and applied research is blurred” in biotechnology.⁵⁵ Biopharmaceutical companies and academic institutions use the same kinds of tools when performing basic research.⁵⁶ Moreover, researchers within academia and industry often work on similar problems and frequently collaborate with one another.⁵⁷

The biomedical industry is separated into three general sectors: genomics companies, biotechnology companies, and traditional pharmaceutical companies.⁵⁸ Genomics companies concentrate on discovering genes that can be used to develop commercial products.⁵⁹ Indeed, “[s]everal business models exist in the genomics industry: DNA sequencing companies that sell access to sequence information, drug discovery companies, and companies that use genomic data to provide diagnostic tools.”⁶⁰

Companies in the biotechnology and pharmaceutical sectors are distinguishable from one another, but have many similar characteristics. The pharmaceutical sector focuses on the synthesis of chemical compounds, while the biotechnology sector focuses on biological processes

53. Linda R. Judge, *Biotechnology: Highlights of the Science and Law Shaping the Industry*, 20 SANTA CLARA COMPUTER & HIGH TECH. L.J. 79, 85 (2003).

54. Natalie M. Derzko, *In Search of a Compromised Solution to the Problem Arising From Patenting Biomedical Research Tools*, 20 SANTA CLARA COMPUTER & HIGH TECH. L.J. 347, 351 (2004) (citing NAT’L INSTS. OF HEALTH, Report of the National Institutes of Health (NIH) Working Group on Research Tools (June 4, 1998), available at <http://www.nih.gov/news/researchtools/index.htm>).

55. Rebecca Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 177, 195 (1987).

56. Derzko, *supra* note 54, at 351–52.

57. Eisenberg, *supra* note 55.

58. Alexander K. Haas, *The Wellcome Trust’s Disclosures of Gene Sequence Data into the Public Domain & the Potential for Proprietary Rights in the Human Genome*, 16 BERKELEY TECH. L.J. 145, 147 (2001).

59. *Id.* at 150.

60. *Id.*

such as recombinant DNA technology.⁶¹ Nonetheless, the biotechnology industry often produces products that are very similar to those produced by traditional pharmaceutical companies.⁶² Moreover the research methodology employed by biotechnology companies is not readily distinguishable from that used by pharmaceutical companies.⁶³ “Although pharmaceutical companies still tend to focus on small molecule drugs, almost all pharmaceutical research is based on genetic and proteomic information. Because this information is often owned by biotechnology companies, pharmaceutical companies now need to work quite closely with biotechnology companies.”⁶⁴ The pharmaceutical sector relies heavily on the research discoveries and product leads provided by biotechnology companies, and twenty-five to forty percent of its sales are reported to come from drugs that originated in the biotechnology sector.⁶⁵

II. THE FEDERAL CIRCUIT’S MISCONCEPTION OF THE BIOTECHNOLOGY PHOSITA

A. Availability and Scope of Biotechnology Patents

In order to qualify for patent protection, an invention must be useful,⁶⁶ novel,⁶⁷ and non-obvious.⁶⁸ The inventor must also satisfy certain disclosure requirements by providing an adequate written description that enables others to make and use the invention and that sets forth the best mode of practicing the invention.⁶⁹ The written description requirement is distinct from the enablement requirement. While the enablement

61. *Id.* at 149.

62. *Id.*; see also *Genentech, Inc. v. Eli Lilly & Co.*, 998 F.2d 931, 935 (Fed. Cir. 1993) (regarding a patent dispute involving two processes for producing human growth hormone).

63. Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 *BERKELEY TECH. L.J.* 813, 816 (2001).

64. *Id.*

65. Iain M. Cockburn, *The Changing Structure of the Pharmaceutical Industry: Drug development under today’s new institutional arrangements could turn out to be faster and better, but not cheaper*, *HEALTH AFF.*, January/February 2004.

66. 35 U.S.C. § 101 (2000).

67. *Id.* § 102.

68. *Id.* § 103; see also *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966) (explaining that

Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. . . . Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized . . .).

69. 35 U.S.C. § 112 para. 1 (2000).

requirement seeks to ascertain whether others in the art will be able to make and use the invention after reading the specification, the written description requirement's purpose is to demonstrate that the patentee had possession of the invention at the time of filing the application.⁷⁰

The non-obvious and disclosure requirements are conceptually linked because each requirement must be considered from the perspective of the PHOSITA.⁷¹ The non-obviousness criterion, developed under common law and codified in the 1952 Patent Act, requires that the claimed invention as a whole was not obvious to one of ordinary skill in the art when the invention was made.⁷² The same language is also used in the first paragraph of section 112 of the statute, which states that the disclosure must enable "any person skilled in the art" to make and use the claimed invention.⁷³ Compliance with the written description requirement also depends on the understanding of a "person skilled in the art."⁷⁴

In addition, the judicially created patent doctrines of claim construction and equivalents incorporate the PHOSITA as a metric.⁷⁵ "Claim construction requires reference to how the PHOSITA would understand the terms in the patent claims."⁷⁶ Equivalence between elements of the claimed invention and an allegedly infringing product are judged from the perspective of one of ordinary skill in the art.⁷⁷ The range of equivalents is bounded by what would have been obvious at the time the patent was filed.⁷⁸

Thus, both the ability of an inventor to obtain a patent on her invention and the extent of protection garnered from a patent stem directly from the Federal Circuit's assessment of the level of skill in the art in that field. The level of skill in the art affects both patent validity and patent scope. With respect to validity, the more skill those in the art have, the harder it is to meet the non-obviousness requirement, and the less needs to be disclosed in a patent application in order to satisfy the enablement and written description requirements.⁷⁹ Regarding patent scope, the court's understanding of the PHOSITA impacts both claim construction

70. Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 BERKELEY TECH. L.J. 1155, 1174 (2002).

71. *Id.* at 1185.

72. *Id.* at 1186 (citing 35 U.S.C. § 103 (2000)).

73. *Id.* (citing 35 U.S.C. § 112 para. 1 (2000)).

74. *Id.* (citing *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988)).

75. *Id.* at 1187.

76. *Id.*

77. *Id.* (citing *Hilton Davis Corp. v. Warner-Jenkinson*, 62 F.3d 1512, 1519 (Fed. Cir. 1995) (en banc), *aff'd in part & rev'd in part on other grounds*, 520 U.S. 17 (1997)).

78. *See Wilson Sporting Goods Co. v. David Geoffrey & Assocs.*, 904 F.2d 677, 684 (Fed. Cir. 1990).

79. Burk & Lemley, *supra* note 70, at 1156.

and the extent to which a patentee may obtain patent protection beyond the literal scope of the claims under the doctrine of equivalents.⁸⁰

The Federal Circuit has interpreted the disclosure requirements rigorously in the context of biotechnology. In *Fiers v. Revel*, the Federal Circuit held that the patentee's disclosure did not contain an adequate written description, largely because it failed to disclose the actual sequence of the claimed DNA molecule at issue.⁸¹ Although the patent application disclosed methods for isolating a fragment of the claimed DNA sequence and for isolating its corresponding mRNA, the court stated: "A bare reference to a DNA with a statement that it can be obtained by reverse transcription is not a description; it does not indicate that Revel was in possession of the DNA."⁸² Rather, conception of a DNA molecule "requires conception of its structure, name, formula, or chemical or physical properties."⁸³ A similar conclusion was reached in a subsequent case, *Regents of the University of California v. Eli Lilly*.⁸⁴ Relying on the *Fiers* opinion, the court concluded: "Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the DNA itself."⁸⁵

The Federal Circuit's interpretation of the written description requirement as requiring precise sequence data has bearing on a patent applicant's ability to claim an entire genus, or family, of molecules.⁸⁶ In *Eli Lilly*, the court rejected an applicant's attempt to patent mammalian or vertebrate insulin, holding that the disclosure of the cDNA sequence encoding rat insulin was insufficient to describe the broad class of cDNAs coding for mammalian or vertebrate insulin.⁸⁷ The court cited previous chemical cases to support its conclusion that the patentee need not show every member of a claimed genus in the written description, but is required to show a "representative" sample of cDNAs that illustrate the common structural features of a "substantial" portion of the genus.⁸⁸ A similarly broad claim was rejected in *Amgen v. Chugai Pharmaceutical Co.* for failing the enablement requirement rather than the written description requirement.⁸⁹ The Federal Circuit held that the patentee's claims to nucleic acid sequences coding for erythropoietin and

80. *Id.*

81. *Fiers v. Revel*, 984 F.2d 1164, 1170–71 (Fed. Cir. 1993).

82. *Id.* at 1170–71.

83. *Id.* at 1169.

84. *Regents of the Univ. of Cal. v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997).

85. *Id.* at 1567.

86. Burk and Lemley, *supra* note 70, at 1176.

87. *Regents of the Univ. of Cal.*, 119 F.3d at 1567.

88. *Id.* at 1569.

89. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212–14 (Fed. Cir. 1991).

for other proteins with the same biological function were not enabled because the myriad DNA sequences covered by the claims could not be made and used on the basis of a few examples.⁹⁰ “Thus, claims to a functionally defined set of genes or proteins, unlimited by the . . . specific nucleotide or amino acid sequences disclosed, are invalid.”⁹¹

In an effort to reconcile the *Eli Lilly* decision with the Federal Circuit’s previous holdings, the PTO, in 2001, issued examination guidelines stating that “the written description for a claimed genus may be satisfied through sufficient description of a representative number of species by . . . disclosure of relevant, identifying characteristics . . . sufficient to show that the applicant was in possession of the claimed genus”⁹² The guidelines do not require the identifying characteristics to take the form of a structural formula, rather description of one or more physical and/or chemical properties, or “by functional characteristics coupled with a known or disclosed correlation between function and structure” may be acceptable.⁹³ In *Enzo Biochem, Inc. v. Gen-Probe Inc.*,⁹⁴ the Federal Circuit expressed approval for the PTO guidelines regarding the written description requirement and reaffirmed the principle established in *Eli Lilly* that genetic information must be described by reference to a particular, known structure.⁹⁵

The Federal Circuit’s application of the obviousness test mirrors the conceptual framework set forth in its analysis of the disclosure requirements. Just as disclosure of a specific structure is required to uphold the validity of a claim to a biological molecule, delineation of a specific structure is also required in the prior art in order to render an invention obvious. In *In re Bell*, the Federal Circuit held that a gene is not prima facie obvious even though the amino acid sequence of the protein encoded by the gene is disclosed in the prior art and a method is disclosed for isolating a gene for which at least a partial amino acid sequence of the encoded protein is known.⁹⁶ The court reasoned that, due to the redundancy of the genetic code, numerous possible DNA sequences were suggested by the amino acid sequence of the protein and thus the amino

90. *Id.* at 1212–14.

91. Antony L. Ryan & Roger G. Brooks, *Innovation vs. Evasion: Clarifying Patent Rights in Second-Generation Genes and Proteins*, 17 BERKELEY TECH. L.J. 1265, 1273 (2002).

92. Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112 para. 1, “Written Description” Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001) (footnote omitted).

93. *Id.*

94. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002) (holding that the deposit of biological materials in a public depository satisfies the written description requirement).

95. *Id.* at 1324–25.

96. *In re Bell*, 991 F.2d 781, 785 (Fed. Cir. 1993).

acid sequence alone did not render obvious the claimed DNA sequence.⁹⁷ Under similar facts, the court in *In re Deuel* found claims directed to DNA coding for heparin binding growth factors (HBGFs) were not obvious, despite the presence of prior art disclosure of a partial amino acid sequence and a method for using that information to obtain the corresponding DNA molecule.⁹⁸ The court stated:

A general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search No particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA⁹⁹

The Federal Circuit's stringent application of the written description and enablement requirements, in combination with lenient application of the obviousness requirement, leads to the expected outcome that DNA patents will be "numerous but extremely narrow."¹⁰⁰ In the absence of prior art explicitly describing or suggesting the precise DNA sequence, "anyone who has isolated and characterized a novel DNA molecule is certain to receive a patent on it."¹⁰¹ But the patentee will be allowed only to claim that molecule, "as the Federal Circuit appears to regard other related molecules as inadequately described until their [precise] sequence is disclosed."¹⁰²

Since the doctrine of equivalents is derived from the obviousness standard, it logically follows that inventors will not be able to utilize this doctrine to expand the scope of patent protection beyond narrow claims to the disclosed molecules. The doctrine of equivalents applies where the differences between the patented technology and the accused infringing product are "insubstantial."¹⁰³ Courts have formulated various tests to determine whether the differences are substantial. The test adopted by the Supreme Court in *Graver Tank & Manufacturing Co. v. Linde Air Products Co.* is whether the accused element "performs substantially the same function in substantially the same way" to achieve substantially the same result.¹⁰⁴ An alternative test is the "known interchangeability" test, which asks whether one of ordinary skill in the art would consider the accused element to be reasonably interchangeable with the limitation

97. *Id.* at 784.

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

99. *Id.* at 1558.

100. Burk & Lemley, *supra* note 70, at 1181.

101. *Id.*

102. *Id.*

103. *Hilton Davis Chem. Co. v. Warner-Jenkinson Co.*, 62 F.3d 1512, 1519 (Fed. Cir. 1995) (en banc), *rev'd on other grounds*, 520 U.S. 17 (1997).

104. *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 609 (1950).

described in the patent.”¹⁰⁵ Because reasonable interchangeability relies on the PHOSITA, “the less certain the court perceives a field to be the less scope will be given to patents under the doctrine of equivalents.”¹⁰⁶ The Federal Circuit has stated that biotechnology is an inherently uncertain discipline, suggesting that the reasonable interchangeability test is likely to lead to a narrow interpretation of the doctrine of equivalents.¹⁰⁷

Recent case law suggests reluctance on the part of the Federal Circuit to apply the doctrine of equivalents in the biotechnology context. In *Amgen Inc. v. Hoechst Marion Roussel*, the district court held that the accused protein infringed Amgen’s patent under the doctrine of equivalents even though it differed by one amino acid from the claimed sequence.¹⁰⁸ Amgen had obtained a patent on the 166 amino acid sequence of human erythropoietin without realizing that the amino acid at position 166 is cleaved off before the protein is secreted from the cell.¹⁰⁹ The defendants produced a protein with the identical amino acid sequence for the first 165 positions, but without the amino acid at position 166. The court held that the accused protein infringed Amgen’s patent under the doctrine of equivalents because the two proteins had “the same conformational structure and biological activity.”¹¹⁰ On appeal, the Federal Circuit held that the presumption of prosecution history estoppel applied, vacating and remanding the decision for analysis under the doctrine of prosecution estoppel as set forth in *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki*.¹¹¹ On remand, the district court held that Amgen was not estopped from asserting the doctrine of equivalents and upheld its ruling that the patent had been infringed under this doctrine.¹¹² Since the Federal Circuit did not reach the merits on this case, the Federal Circuit’s position regarding the doctrine of equivalents in the biotechnology context is not clear. Nevertheless, the Federal Circuit’s depiction of the level of skill in the art of biotechnology suggests that it will eschew expansive application of this doctrine.

105. Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1654–55 (2003); see also *Hilton Davis*, 62 F.3d at 1519.

106. Burk & Lemley, *supra* note 105, at 1655.

107. *Id.*

108. *Id.*; see also *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69 (D. Mass. 2001).

109. *Id.* at 86.

110. *Id.* at 133.

111. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003) (citing *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki*, 535 U.S. 722 (2002)).

112. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 287 F. Supp. 2d 126, 160 (D. Mass. 2003).

*B. Discrepancies Between Federal Circuit Jurisprudence
and Scientific Reality*

The Federal Circuit's reliance on chemical cases to ascertain the validity and scope of biotechnology patents is based on its assessment that nucleic acid molecules are chemical substances they should treat the same as other compounds. But commentators have observed that DNA and RNA are not merely chemical substances, "but also biochemical information that can be derived from other biochemical information" via common research techniques.¹¹³ Additionally, "DNA sequences that were the subject of patent claims in . . . [the early days of biotechnology] typically consisted of cloned genes that enabled the production of proteins through recombinant DNA technology."¹¹⁴ Because "[p]atents on the genes encoding these proteins promised exclusivity in the market for the protein itself, . . . patents on DNA sequences seemed analogous to patents on new chemical compounds."¹¹⁵ However, "[a]s DNA sequence discovery has moved beyond targeted efforts to clone particular genes to large-scale, high-throughput sequencing of entire genomes, . . . DNA sequences . . . look less like new chemical entities than they do like new scientific information."¹¹⁶ Thus, technological advances have considerably strained the analogy, calling into question the rationality of the Federal Circuit's rigid application of established precedent in the chemical arts when deciding biotechnology patent cases.

The Federal Circuit's adherence to a doctrine of structural foreseeability in biotechnology cases indicates that the court perceives biotechnology as an uncertain art, where the results of experimentation are largely outside the control of those who practice it.¹¹⁷ The court's interpretation of the disclosure requirements suggests that "biotechnology researchers need a very high degree of assurance before they are capable of replicating an invention."¹¹⁸ Similarly, "biotechnologists apparently need genetic sequences explicitly described in the prior art to render a molecule obvious."¹¹⁹ This characterization of the science of biotechnology arguably does not accurately reflect modern reality. Commentators have pointed out that the search for a particular cDNA sequence coding for a protein among a large number of possibilities is a routine practice

113. See, e.g., Arti Kauer Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77, 138 (1999); Eisenberg, *supra* note 50, at 784–85.

114. Eisenberg, *supra* note 50, at 784.

115. *Id.*

116. *Id.* at 785.

117. Burk & Lemley, *supra* note 70, at 1193.

118. *Id.* at 1191.

119. *Id.*

in molecular biology.¹²⁰ But the court's holding in *In re Deuel* demonstrates that the prior art disclosure of a method for obtaining a particular sequence is insufficient to satisfy the obviousness test if it is not possible to predict from the prior art the precise sequence that will be found. Thus, the ease with which one may be able to ascertain the specific DNA sequence coding for a particular protein has little bearing on the determination of whether the DNA molecule itself is obvious.¹²¹

The Federal Circuit's focus on structural disclosure when addressing the obviousness of gene discoveries has been the subject of substantial criticism.¹²² Professor Andrew Chin cleverly demonstrated the fallacy of the Federal Circuit's line of reasoning by publishing a digital document that discloses the sequences of 11 million oligonucleotides and general methods of making and using them taken from the research literature.¹²³ Chin noted that by simply appending a list of structural formulae to references describing techniques for making and using DNA, it may be possible to render all of the listed molecules unpatentable in light of this prior art.¹²⁴ He observed:

While the reference is of little interest to the scientific community, it has proven to be of significant interest to the biotechnology patent bar, having been cited in connection with at least one issued patent and 25 pending U.S. patent applications. That mere artful drafting should bear on the validity of so many oligonucleotide patent claims calls into question the patent system's view of the prior art relative to these claims.¹²⁵

120. See, e.g., John M. Lucas, *The Doctrine of Simultaneous Conception and Reduction to Practice in Biotechnology: A Double Standard for the Double Helix*, 26 AIPLA Q.J. 381, 418 (1998) (“[M]aking the inventions of *Amgen*, *Fiers* and *Lilly* today would be routine.”); Anita Varma & David Abraham, *DNA is Different: Legal Obviousness and the Balance Between Biotech Inventors and the Market*, 9 HARV. J.L. & TECH. 53, 73 (1996).

121. Burk & Lemley, *supra* note 70, at 1180.

122. See, e.g., Rebecca S. Eisenberg & Robert P. Merges, *Opinion Letter as to the Patentability of Certain Inventions Associated with the Identification of Partial cDNA Sequences*, 23 AIPLA Q.J. 1, 33 (1995) (arguing that DNA sequences might be deemed prima facie obvious, even without structurally similar sequences in the prior art, just as past decisions have held novel chemicals prima facie obvious when the prior art discloses structurally similar compounds, because the prior art provides motivation to use familiar methods to construct the claimed inventions in both types of cases, despite the Federal Circuit's apparent reluctance to follow this line of reasoning in *In re Bell* and *In re Deuel*); see also Varma & Abraham, *supra* note 120, at 78–79; Jeffrey S. Dillen, *DNA Patentability: Anything but Obvious*, 1997 WIS. L. REV. 1023, 1041; Arti K. Rai, *Engaging Facts and Policy: A Multi-Institutional Approach to Patent System Reform*, 103 COLUM. L. REV. 1035, 1071 (2003).

123. Andrew Chin, *Artful Prior Art and the Quality of DNA Patents*, 57 ALA. L. REV. 975 (2006).

124. *Id.* at 977.

125. *Id.* at 978 (footnote omitted).

The ease with which scientists can now access genomic databases to obtain sequence information underscores the problem with the Federal Circuit's treatment of gene patents. Even though discontinuous genes are interrupted by non-protein coding regions ("introns"), making them different from the raw DNA sequence, they may still be obvious in light of the genome's publication, since introns are readily identifiable to those skilled in the art.¹²⁶

III. POLICY CONSIDERATIONS REGARDING GENE PATENTS

A. *Theoretical Perspectives*

A standard argument for patents emphasizes their role in providing incentives to invest in the expensive and risky endeavor of making inventions.¹²⁷ Patent law "seeks to address the 'public goods' problem that arises in regard to creative activity."¹²⁸ Temporary monopoly rights allow inventors to enjoy the fruits of discoveries that are costly to produce but virtually costless to imitate and use once created.¹²⁹ In some cases, however, the benefits of a patent greatly exceed the costs of invention and scientists may compete with each other to be the first to discover and patent the invention, which can lead to wasteful duplicative research efforts early in the invention process.¹³⁰ Patents also impact the incentives of follow-on developers to build upon early discoveries to produce new innovations. Thus, proper application of the patent system requires careful weighing of costs and benefits in order to strike the optimal balance that maximizes the social welfare.

An alternative theory of patent law promoted by Edmund Kitch, known as the prospect theory of patent law, holds that the primary purpose of the patent system is not to generate ex ante incentives to create, but rather to encourage efficient development and commercialization of nascent inventions.¹³¹ Kitch argues that, absent patent protection for upstream inventions, no one will invest in development for fear that the fruits of such investment will produce unpatentable information appro-

126. Haas, *supra* note 58, at 158–59.

127. Kenneth J. Arrow, *Economic Welfare and the Allocation of Resources for Invention*, in *THE RATE AND DIRECTION OF INVENTIVE ACTIVITY: ECONOMIC AND SOCIAL FACTORS* 609, 616–19 (1962), available at <http://www.rand.org/pubs/papers/2006/P1856.pdf>.

128. Burk & Lemley, *supra* note 70, at 1158.

129. *Id.*

130. See Matthew Erramouspe, *Staking Patent Claims on the Human Blueprint: Rewards and Rent-Dissipating Races*, 43 *UCLA L. REV.* 961, 976 (1996).

131. Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 *J.L. & ECON.* 265, 266 (1977).

priable by competitors.¹³² Kitch's theory postulates that giving one party the power to control and orchestrate all subsequent use and research related to the patented technology will not lead to underdevelopment or underinvestment, but rather to efficient licensing and avoidance of duplicative R&D investments.¹³³ "A prospect theory therefore suggests that patents should be granted early in the invention process, and should have a broad scope and few exceptions."¹³⁴

The notion that "broad, monopoly-conferring rights on nascent [biomedical] invention can provide a necessary spur to further innovation may well have merit."¹³⁵ Given the high cost associated with biopharmaceutical R&D, and the difficulty of recovering all of that cost in an end product drug patent, relatively upstream patent rights may promote innovation.¹³⁶ "[T]he research path from initial discovery of a potentially relevant DNA sequence or receptor to identification of a drug that is ready for clinical testing can be quite risky, lengthy, and expensive. If the initial discovery is not protected by a broad patent, the R&D path may produce knowledge that is appropriable by competitors."¹³⁷ In addition, in response to the argument that multiple research paths are necessary to fully exploit the potential of an upstream discovery, Kitch's theory provides for the possibility of different research paths. Kitch posits that the upstream patent holder would coordinate future development with a number of different developers, each of whom might pursue a different research path.¹³⁸

The most problematic assumption underlying Kitch's development-oriented theory is that licensing agreements will be fairly easy to negotiate. The notion that "broad upstream patent rights will promote coordinated licensing depends on unrealistic assumptions" and may not adequately account for the high transaction costs associated with imperfect information, disparate value assessments, and strategic behavior on the part of the negotiating parties.¹³⁹ The holder of an upstream patent may have an overinflated sense of the value of the basic research discovery and may not adequately take into account the expense and risk required to develop and commercialize the discovery. There is also a danger that "pioneer patent holders will simply misappropriate the confidential research plans of follow-on researchers once they are disclosed

132. *Id.* at 276.

133. *Id.*

134. Burk & Lemley, *supra* note 105, at 1604.

135. Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 BERKELEY TECH. L.J. 813, 828 (2001).

136. *Id.* at 828–29.

137. *Id.* at 820.

138. Kitch, *supra* note 131, at 276.

139. Rai & Eisenberg, *supra* note 29, at 297.

in the course of license negotiations.”¹⁴⁰ Transaction costs are compounded by the fact that a downstream developer of a basic research discovery typically must negotiate with several different upstream patent holders.¹⁴¹

Kenneth Arrow has argued that competition, not monopoly, best spurs innovation and suggests a much more limited role for intellectual property rights than the one advocated by prospect theorists.¹⁴² Arrow theorizes that patent rights should be narrowly circumscribed to particular implementations of an invention, and should generally not give the patentee the right to control competition in an economic market.¹⁴³ A related theory, cumulative innovation, contemplates patents on small inventions, but prefers giving less complete rights over those inventions than would prospect theory.¹⁴⁴ Merges and Nelson assert that competition should be favored over prospect theory’s reliance on broad pioneer patents in most technological areas.¹⁴⁵ They argue that competition spurs innovation much more effectively than monopolies because it allows multiple inventors to work simultaneously and because use of an idea by multiple inventors, unlike use of a tangible resource, is not mutually exclusive.¹⁴⁶

Anticommons theory challenges competition theory by focusing on the undesirable consequences that result when patent rights become so narrow and fragmented that no single entity can access the technology necessary to conduct research in their field.¹⁴⁷ Relying on Michael Heller’s concept of the anticommons,¹⁴⁸ some patent scholars have argued that granting too many different patent rights could impede the development of new products where the developer must negotiate licenses with several different patent holders in order to make the product.¹⁴⁹ Anticommons problems can occur either horizontally (i.e., patents covering different elements that must be integrated into a final product) or vertically (i.e., patents covering different steps in a cumulative innovation process).¹⁵⁰ Closely related to the anticommons problem is the problem of “patent thickets,” in which overlapping claims in dif-

140. *Id.*

141. *Id.*

142. *See* Arrow, *supra* note 127, at 619–20.

143. Burk & Lemley, *supra* note 105, at 1605.

144. *Id.* at 1610.

145. Robert P. Merges & Richard L. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 843–44 (1990).

146. *Id.* at 884.

147. Heller & Eisenberg, *supra* note 16.

148. *See* Michael A. Heller, *The Tragedy of the Anticommons: Property in the Transition from Marx to Markets*, 111 HARV. L. REV. 621 (1998).

149. *See, e.g.*, Heller & Eisenberg, *supra* note 16; Rai, *supra* note 10, at 192–94.

150. Burk & Lemley, *supra* note 105, at 1624.

ferent patents have the potential to block development of a product that incorporates multiple inventions.¹⁵¹

B. *Biotechnology and the “Tragedy of the Anticommons”*

Professors Michael Heller and Rebecca Eisenberg have identified biotechnology as an area in which the proliferation of intellectual property rights among a number of patentees may create a “tragedy of the anticommons.”¹⁵² They contend that patent claims result in upstream strangleholds that have the potential to significantly impede downstream technological development.¹⁵³

Preclinical and clinical investigation may be hindered by the hundreds of thousands of patent applications that have been filed on early-stage genomics research.¹⁵⁴ Ownership rights to a single gene that is one of many causative factors in a disease could create an opportunity to extract rents from those wishing to develop a diagnostic test or therapy.¹⁵⁵ This leads to higher development costs and ultimately results in higher medical costs and decreased availability for those in need.¹⁵⁶

For instance, a pharmaceutical company that is interested in developing a therapeutic compound for a particular genetic disease might have to seek licenses from every entity that holds patents on the relevant genes or even single nucleotide polymorphisms (SNPs)¹⁵⁷ found within the relevant genes.¹⁵⁸ Similarly, the maker of a gene chip that tests for thousands of different SNPs might have to seek licenses from several different SNP patent owners.¹⁵⁹ Licensing patent rights might not solve the anticommons problem because high transaction costs may result from developers having to negotiate licenses with multiple upstream patent holders. As Heller and Eisenberg have emphasized, disagreement about the relative values of an upstream invention and an improvement on it is likely because the negotiating parties are scientists who may overestimate the value of their scientific contribution while underestimating

151. See Carl Shapiro, *Navigating the Patent Thicket: Cross Licensing, Patent Pools, and Standard Setting*, in 1 *INNOVATION POLICY AND ECONOMY* 119, 121 (Adam B. Jaffe et al. eds., 2001).

152. See Heller & Eisenberg, *supra* note 16.

153. *Id.*

154. Demaine & Fellmeth, *supra* note 4, at 308–09.

155. *Id.*

156. *Id.*

157. SNPs are DNA sequence variations that occur when a single nucleotide in a genetic sequence is altered. See Human Genome Project Information, SNP Fact Sheet, http://www.ornl.gov/sci/techresources/Human_Genome/faq/snps.shtml (last viewed Nov. 3, 2007).

158. Rai, *supra* note 10, at 193.

159. *Id.*

that of the developer.¹⁶⁰ The gene or SNP patent holder may also be tempted to act strategically by holding out for a supracompetitive price that far exceeds the contribution of the patented discovery to the value of the commercial product.¹⁶¹

Indeed, contrary to Kitch's prospect theory, "there are indications in the biopharmaceutical industry that development through tailored licensing [of upstream patents] will be difficult to achieve."¹⁶² The director of research at one pharmaceutical company estimated that there were more than fifty proteins possibly involved in cancer on which the company is not working because agreements with upstream patent holders could not be concluded.¹⁶³ Upstream patents may thus serve as a tax on innovation and reduce value creation in the industry through waste of resources on bargaining and other transaction costs.¹⁶⁴ Some of the observed increase in R&D spending by pharmaceutical companies may represent payments for access to upstream science of the kind that used to be freely available to downstream developers but now must be obtained through license agreements and research collaborations between the pharmaceutical sector and universities and biotechnology companies.¹⁶⁵ The willingness of private firms in a patent-sensitive industry to engage in efforts to enhance the public domain by disclosing information about the genome¹⁶⁶ is persuasive evidence to support the view that patent rights in upstream genetic research could significantly impede subsequent research and product development.¹⁶⁷

Gene patents may also stymie basic and clinical research. Gene patent holders may require licenses from researchers seeking to study gene function or the prevalence of mutations in the patented gene in the population.¹⁶⁸ Patent rights may also hamper the ability of scientists to duplicate and verify published results because other scientists refuse to

160. Heller & Eisenberg, *supra* note 16, at 701.

161. See Rai, *supra* note 10, at 193.

162. Rai, *supra* note 135, at 831–32.

163. See Andrew Pollack, *Bristol-Myers and Athersys Make Deal on Gene Patents*, N.Y. TIMES, Jan. 8, 2000, at C2 (discussing comments by Peter Ringrose, chief scientific officer at Bristol-Myers).

164. Cockburn, *supra* note 65, at 18; see Rai & Eisenberg, *supra* note 29, at 302 n.68 (discussing *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004), *cert. denied*, 543 U.S. 1015 (2004), which demonstrates that the developers of Vioxx and Celebrex did not require an exclusive license from the upstream patentee to motivate their investments in developing cox-2 inhibitors).

165. Cockburn, *supra* note 65, at 18.

166. See discussion *supra* Introduction.

167. Demaine & Fellmeth, *supra* note 4, at 298–99.

168. See Lori Andrews, *Patenting Life*, J. OF LIFE SCI., May 2007, available at <http://www.tjols.com/article-200-4.html> (noting that in one survey, half of gene patent holders said they would require a license for researchers to study the prevalence of mutations in the patented gene in the population).

share information, data, or materials.¹⁶⁹ In addition, fragmented patent rights among basic researchers may impair the collaborative research necessary to understand the complex relationships among the various genetic elements involved in intracellular regulatory pathways.

Indeed, academic and industrial researchers have expressed frustration with the proliferation of patent claims.¹⁷⁰ Concerns over biotechnology patenting prompted the research arm of the National Academies of Science to commission a study on the effects of patenting in the biomedical sciences.¹⁷¹ The study found that ensuring access to research tools such as unique drug targets (i.e., “any cell receptor, enzyme, or other protein implicated in a disease, thus representing a promising locus for drug intervention”) was of particular concern.¹⁷² DNA chips were singled out as being particularly expensive, forcing most small companies to partner with other firms.¹⁷³ The potential impact of gene patents on the availability of genetic testing has led the American College of Medical Genetics to conclude that genes should not be patentable.¹⁷⁴ Similarly, the American Medical Association notes that “some physicians fear [that] if too many genes receive patents, genetic testing of patients could become prohibitively expensive . . . [and] may never be used effectively to help patients.”¹⁷⁵

The costs incurred by gene patents arguably exceed the potential benefits. Much DNA sequence information is freely disclosed in the public domain, both by nonprofit institutions and by private firms. Moreover, patents may not be necessary to prompt scientists to discover new genes, since a large portion of basic genomics research is supported by public funds and technological innovations have significantly reduced the time and expense associated with finding and sequencing new genes: “If a discovery is likely to be made and disclosed promptly even without

169. *Id.* (noting that twenty-eight percent of geneticists surveyed reported that they were unable to duplicate published research because other academic scientists refused to share information, data, or materials).

170. See NAT'L INSTS. OF HEALTH, REPORT OF THE NATIONAL INSTITUTES OF HEALTH (NIH) WORKING GROUP ON RESEARCH TOOLS (June 4, 1998), available at <http://www.nih.gov/news/researchtools/index.htm> (exploring the extension of patent rights to research tools and noting that many scientists believe that this is impeding technological advancement).

171. NAT'L RESEARCH COUNCIL, NAT'L ACADS. OF SCI., A PATENT SYSTEM FOR THE 21ST CENTURY 17, 59 (Stephen A. Merrill et al. eds., 2004).

172. John P. Walsh et al., *Effects of Research Tool Patents and Licensing on Biomedical Innovation*, in PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285, 310 (Wesley M. Cohen & Stephen A. Merrill eds., 2003).

173. *Id.* at 302.

174. American College of Medical Genetics, Position Statement on Gene Patents and Accessibility of Gene Testing (1999), <http://genetics.faseb.org/genetics/acmg/pol-34.htm>.

175. American Medical Association, Gene Patenting (2004), <http://www.ama-assn.org/ama/pub/category/print/2314.html>.

patent incentives, there is little point in enduring the social costs of exclusionary rights.”¹⁷⁶

Potential negative effects arising from the patenting of upstream genomics research are particularly concerning given the fact that “there are few safety valves built into the patent system that constrain the rights of patent holders in favor of competing interests of the public.”¹⁷⁷ Indeed, “[u]nlike copyright law, patent law has no fair use defense that permits socially valuable uses without a license,”¹⁷⁸ and “[u]nlike trade secret law, patent law has no defense for reverse engineering.”¹⁷⁹ And unlike both copyright and trade secret law, independent creation is not a defense to patent infringement.¹⁸⁰ Moreover, the Federal Circuit has eschewed expansive application of the safety valves that do exist in the patent system. In *Madey v. Duke University*, the court applied the experimental use defense quite narrowly, holding that any purpose to commercialize products resulting from use of the patented technology precludes reliance on the defense.¹⁸¹ The court stated that so long as the infringing use of the patented technology was “in furtherance of the alleged infringer’s legitimate business and is not solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry, the act does not qualify for the very narrow and strictly limited experimental use defense.”¹⁸²

Patent scholars have suggested various strategies designed to mitigate the anticommons problems associated with patents on upstream biomedical research. These proposals include broadening the interpretation of the experimental use exemption to infringement liability;¹⁸³ introducing a fair use doctrine into patent law;¹⁸⁴ applying a compulsory

176. Eisenberg, *supra* note 113, at 795.

177. *Id.* at 796.

178. *Id.*

179. *Id.*

180. *Id.*

181. *Madey v. Duke Univ.*, 307 F.3d 1352, 1361 (Fed. Cir. 2002).

182. *Id.* at 1362.

183. See, e.g., Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 CHI. L. REV. 1017, 1076–78 (1989) (suggesting that in the case of improvement research, firms ought to be allowed to use patented upstream research in exchange for reasonable royalties from commercially valuable improvements); Janice Mueller, *No “Dilettante Affair”: Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1 (2001).

184. See, e.g., Maureen O’Rourke, *Toward a Doctrine of Fair Use in Patent Law*, 100 COLUM. L. REV. 1177, 1230–34 (2000) (proposing a five-part test for a finding of patent fair use that considers: (i) the nature of the infringement (indirect versus direct infringement likely arising from reverse engineering); (ii) the purpose of the infringing use; (iii) the nature and strength of the market failure that prevents a license from being concluded; (iv) the impact of the use on the patentee’s incentives and overall social welfare; and (v) the nature of the in-

licensing scheme where the patented invention must be used to make improvements;¹⁸⁵ and enacting a scheme whereby intellectual property rights are enforced by liability rules (i.e., rules that address infringement by requiring payment of damages), rather than property rules (i.e., rules that simply enjoin infringement).¹⁸⁶ Other suggestions include revising the utility requirement for gene patents¹⁸⁷ and protecting follow-on improvers from infringement liability via a more expansive application of the reverse doctrine of equivalents.¹⁸⁸

All of these suggestions require the Federal Circuit to reformulate one or more of the existing rules or standards. In addition, many of the proposed schemes require judicious implementation by the Federal Circuit, which would be called on to make difficult subjective determinations regarding the optimal balance of rights between upstream patent holders and countervailing interests. Thus, the potential of the above proposed strategies to solve the anticommons problem is largely dependent on the willingness of the Federal Circuit to modify the existing patent doctrinal framework. The court has thus far shown little interest in taking such a bold step.

Some commentators have argued that measures aimed at solving the anticommons problem will do more harm than good and that society is better off maintaining the status quo with regard to biotechnology patents. Various counterarguments have been made in response to calls for changes to the current gene patenting regime. Biotechnology firms contend that they need patents to raise capital from investors so that they can conduct research, and to compel pharmaceutical companies to collaborate

fringing subject matter (whether it represents an actual advancement or is merely taking advantage of market lead time)).

185. See, e.g., John H. Barton, *Patents and Antitrust: A Rethinking in Light of Patent Breadth and Sequential Innovation*, 65 ANTITRUST L.J. 449, 458 (1997) (suggesting that improvers that make significant contributions be given a “dependency license” which requires only the payment of reasonable royalties).

186. See, e.g., Irving N. Feit, *Biotechnology Research and the Experimental Use Exception to Patent Infringement*, 71 J. PAT. & TRADEMARK OFF. SOC’Y 819, 840 (1989) (suggesting payment of damages based on commercial advantage).

187. See, e.g., Sean C. Pippen, *Dollars and Lives: Finding Balance in the Patent “Gene Utility” Doctrine*, 12 B.U. J. SCI. & TECH. L. 193, 223–24 (2006) (proposing a “substantial similarity” test for utility, which would preclude patenting the DNA sequence whose function is substantially similar to that of the naturally occurring DNA sequence in order to distinguish between isolated or purified naturally occurring genes and genes materially altered by human manipulation).

188. See Robert P. Merges, *A Brief Note on Blocking Patents and Reverse Equivalents: Biotechnology as an Example*, 73 J. PAT. & TRADEMARK OFF. SOC’Y 878, 887–88 (1991) (suggesting that the reverse doctrine of equivalents be applied to all situations where courts find that a follow-on improver has done “very substantial additional research” such that the “value added” of the improvement is large).

with them.¹⁸⁹ Meanwhile, universities claim that they need patents because the biotechnology firms who are their licensees need patents.¹⁹⁰

The PTO has been a strong advocate in favor of biotechnology patents. The PTO's position on gene patents is reflected in an essay by John J. Doll, the PTO's Commissioner for Patents and then Director of Biotechnology Examination:

It is only with the patenting of DNA technology that some companies, particularly small ones, can raise sufficient venture capital to bring beneficial products to the marketplace or fund further research. A strong U.S. patent system is critical for the continued development and dissemination to the public of information on DNA sequence elements.¹⁹¹

These sentiments were later echoed by Todd Dickinson, the Director of the PTO, in remarks made before the Subcommittee on Courts and Intellectual Property of the House Judiciary Committee: "Without the funding and incentives that are provided by the patent system, research into the basis of genetic diseases and the development of tools for the diagnosis and treatment of such diseases would be significantly curtailed."¹⁹²

The debate over the desirability of biotechnology patents arises in part because the biopharmaceutical industry maps onto both anticommons theory and prospect theory.¹⁹³ The sectors of the industry engaged in basic genomics research invoke anticommons theory while the sectors engaged in the development of drugs and other commercial end products invoke prospect theory.¹⁹⁴ The patenting of nucleotide molecules is troubling in light of the tools available for finding and identifying genetic sequences and the importance of preserving the biochemical information stored in such molecules for the public domain. Nevertheless, even if identifying a gene is relatively costless, turning upstream research discoveries into marketable products is often time-consuming, complex, risky, and expensive because of the process of characterizing the mechanism of action of its protein product and validating the discovery as a

189. Rebecca S. Eisenberg, *Patents, Product Exclusivity, and Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 *FORDHAM L. REV.* 477, 479 (2003).

190. *Id.*

191. John J. Doll, *The Patenting of DNA*, 280 *SCIENCE* 689, 690 (1998).

192. *Gene Patents and Other Genomic Inventions: Hearing Before the Subcomm. on Cts. & Intell. Prop. of the H. Comm. on the Judiciary*, 106th Cong. 11–12 (2000) (statement of Q. Todd Dickinson, Under Secretary of Commerce for Intellectual Property & Director of the U.S. Patent & Trademark Office).

193. Burk & Lemley, *supra* note 105, at 1676.

194. *See id.*

drug target. This validation process is the necessary first step in developing new therapeutics targeting the gene. Developing biotechnology end products, particularly in the pharmaceutical sector, also involves long development times and high development costs.¹⁹⁵ Therefore, strong patent rights are necessary in order to provide the necessary incentives to turn basic research discoveries into clinical end products.

Drug patents make development profitable by providing market exclusivity.¹⁹⁶ But patents on upstream technologies that feed into drug development, such as genomic information and databases and newly identified drug targets, impose costs on drug development.¹⁹⁷ Therefore, the optimal approach to biotechnology patents is one in which the genetic commons is preserved for basic research while at the same time incentives to develop new diagnostics and therapeutics are maintained. In Part IV below, I argue that this balance will be achieved by revisiting the Federal Circuit's application of the obviousness standard. It is not necessary to create a more stringent obviousness test specific to biotechnology. Instead, the existing doctrinal framework should be applied in a way that complies with the principles set forth in the recent Supreme Court decision in *KSR v. Teleflex* and is consistent with the current knowledge and capabilities of the biotechnology PHOSITA.

IV. A CALL FOR A NEW APPROACH

A. *KSR v. Teleflex* and the Biotechnology PHOSITA

In *KSR v. Teleflex*,¹⁹⁸ a unanimous Supreme Court issued a mandate to the Federal Circuit to abandon its rigid application of the "teaching, suggestion or motivation" (TSM) test¹⁹⁹ for obviousness in favor of a more expansive and flexible approach that takes into account the inferences and creative steps that the PHOSITA in the relevant field would employ.²⁰⁰ The patent at issue in *KSR v. Teleflex* covered brake, gas, and clutch pedals in cars that are adjustable within the foot well so that

195. See *id.* (explaining that both stringent regulatory oversight exercised by the FDA and inherent uncertainty about the functionality of biotechnology products makes product development risky and uncertain).

196. Eisenberg, *supra* note 189, at 480.

197. *Id.* at 480–81 ("These discoveries are like so many siphons at the feeding trough of new drugs, draining away profits in many different directions.").

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

199. Under the TSM test, a patent claim is only proved obvious if "some motivation or suggestion to combine the prior art teachings" can be found in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art. See, e.g., *Al-Site Corp. v. VSI Int'l, Inc.*, 174 F.3d 1308, 1323–24 (Fed. Cir. 1999).

200. *KSR v. Teleflex*, 127 S. Ct. at 1739–41.

drivers of different heights can comfortably reach them. Key to the patent was a combination of an adjustable pedal assembly with an electronic sensor that detects the position of the pedal.²⁰¹ A prior art patent taught everything but the application of the electronic sensor, and other patents described the sensor.²⁰²

In holding that the patent at issue was obvious, the Court cautioned against “overemphasis on the importance of published articles and the explicit content of issued patents” when applying the TSM test.²⁰³ The Court observed that, “[a] person of ordinary skill is also a person of ordinary creativity, not an automaton.”²⁰⁴ It rejected the Federal Circuit’s longstanding rule that a patent claim cannot be proved obvious by showing that it was “obvious to try,” stating:

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.²⁰⁵

The Court concluded its opinion by observing that if exclusive rights are granted to the results of ordinary innovation, patents might stifle rather than promote technological progress.²⁰⁶

KSR v. Teleflex is the most recent example of the Supreme Court’s increasing willingness to challenge the Federal Circuit’s patent jurisprudence. In 2005, a unanimous Supreme Court vacated the Federal Circuit’s interpretation of the preclinical research exemption of 35 U.S.C. § 271(e)(1) in *Merck KGaA v. Integra Lifesciences I, Ltd.*, concluding that the safe harbor provision was somewhat broader than the Federal Circuit had read it to be.²⁰⁷ The safe harbor provision permits the use of patented inventions primarily manufactured via recombinant DNA, recombinant RNA, hybridoma technology, or other genetic techniques when employed solely to develop and submit information required by federal law.²⁰⁸ Merck had conducted research using materials covered by Integra’s patents in order to identify potential therapeutic candidates for human testing.²⁰⁹ Merck claimed safe harbor protection

201. *Id.* at 1734.

202. *Id.* at 1735–36.

203. *Id.* at 1741.

204. *Id.* at 1742.

205. *Id.*

206. *Id.* at 1746.

207. *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005).

208. 35 U.S.C. § 271(e)(1) (2000).

209. *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 863 (Fed. Cir. 2003).

because its ultimate goal was to submit its product to the Food and Drug Administration (FDA) for approval, for which it would need to generate data required by federal law.²¹⁰ The Federal Circuit rejected Merck's safe harbor defense on the ground that Merck's research was in the pre-clinical phase, and thus did not directly generate data required by the FDA.²¹¹ The Supreme Court reversed, holding that, in certain situations, the exemption is sufficiently broad to protect the use of patented products for experiments that are not ultimately submitted to the FDA.²¹²

Shortly thereafter, only months before *KSR v. Teleflex*, the Supreme Court decided *Medimmune v. Genentech*.²¹³ In that case, the Court again reversed the Federal Circuit, overturning its rule that a patent licensee must terminate or breach its license agreement before seeking declaratory judgment jurisdiction to challenge the validity of the patent.²¹⁴ These recent decisions indicate that an era of active Supreme Court review of Federal Circuit decisions has begun.²¹⁵

Thus, the time is ripe for the Federal Circuit to implement a new approach to biotechnology cases by incorporating the principles espoused by the Supreme Court into its obviousness analysis and other patent doctrines conceptually linked to the PHOSITA. Specifically, the Federal Circuit should adopt a more expansive interpretation of the scope and content of the prior art. The prior art should include not merely that which is explicitly delineated in the genomics research literature, but also the inferences that the PHOSITA would draw from these data. This would require the court to diligently adhere to the principle that identification of the PHOSITA is a fact-specific inquiry that must be made on a case-by-case basis.

210. *Id.*

211. *Id.* at 866.

212. *Merck KGaA*, 545 U.S. at 206–07.

213. *Medimmune, Inc. v. Genentech, Inc.*, 127 S. Ct. 764 (2007).

214. *Id.* at 773–74.

215. Gregory A. Castanias, et al., *A Review of Recent Decisions of the United States Court of Appeals for the Federal Circuit: Area Summary: Survey of the Federal Circuit's Patent Law Decisions in 2006: A New Chapter in the Ongoing Dialogue With the Supreme Court*, 56 AM. U. L. REV. 793, 814–16 (2007). Castanias stated:

[T]he single most important lesson from the Supreme Court's recent dialogue with the Federal Circuit may be this: The Supreme Court is still 'supreme', even when it comes to issues of patent law that fall within the aegis of 'the specialized court'. That lesson may have been forgotten in the early years of the Federal Circuit, when patent cases were not reviewed frequently, and later, when the Federal Circuit was affirmed by the Supreme Court on the major issues of the day. But the world has changed

Id. at 814–16.

B. *Potential Impact of a "Common Sense" Approach
on the Patent Landscape*

Gene patents may not be able to withstand an obviousness inquiry that incorporates the concepts articulated by the Supreme Court in *KSR v. Teleflex*. A common sense approach would ask not just whether the specific claimed sequence is disclosed in the prior art but also whether identifying the gene would be routine given currently available resources and techniques. Arguably, such activity is well within the realm of "ordinary creativity" of the biotechnology PHOSITA.

At the same time, such an approach should have an impact on patent doctrines conceptually linked to the obviousness standard. There should be relaxation of the disclosure requirements to allow patentees to claim not merely that which is explicitly described in the patent but also molecules that the PHOSITA could easily derive from the disclosed structures. This line of reasoning also suggests more expansive application of the doctrine of equivalents to allow patentees protection from infringement by products that the PHOSITA would clearly recognize as functional equivalents to the claimed molecules. In sum, such modifications to the obviousness test, disclosure requirements, and doctrine of equivalents would result in fewer, but broader and more powerful, biotechnology patents. In addition, biotechnology patenting would be pushed downstream, away from basic genomics discoveries and toward products that have more direct clinical applications.

How might the above described approach play out in practice? While a newly discovered gene may not be patentable, certain diagnostic and therapeutic products derived from genetic materials may be novel and non-obvious. For instance, diagnostic kits which detect the presence of the gene or its protein product would still be patentable so long as the kit was developed through ingenious labor.²¹⁶ In addition, new therapeutic compositions incorporating the gene, such as nanoparticle delivery vehicles containing DNA constructs, would be eligible for patents. And of course, novel chemical compounds which function to activate or inhibit the gene *in vivo* would be patentable.

Expressed protein products downstream from newly discovered genes also would arguably withstand the obviousness analysis and thus be available for patenting. A protein folds into a complex three-dimensional structure whose characteristics cannot always be predicted based on its amino acid sequence.²¹⁷ In addition, proteins frequently undergo post-translation modification by enzymes which add or remove amino acids from the proteins, generating products which are arguably

216. See Haas, *supra* note 58, at 159.

217. *Id.*

non-obvious even if the gene sequences from which they are derived are known.²¹⁸ Moreover, intracellular regulatory mechanisms sometimes intervene during the process of translating mRNA into the amino acid sequences comprising proteins, leading to unforeseeable expression products such as mRNA molecules forming hairpin secondary structures as the bases in the RNA strand associate with themselves.²¹⁹ Such hairpin sequences enable a single RNA to code for two different proteins, both a full-length protein when the strand remains linear and a truncated protein when the hairpin forms and interrupts translation of the RNA into protein.²²⁰ These types of regulatory mechanisms might make the structure of the protein unpredictable, and hence patentable, even if the gene itself is not eligible for patenting.

Relaxation of the disclosure requirements and/or expansion of the doctrine of equivalents may also allow for broader patent protection for non-obvious inventions. Patentees should be able to get patent protection not just for structures claimed in the patent, but also for molecules that the PHOSITA would recognize as obvious functional equivalents. At the same time, follow-on improvers would have opportunities to patent non-obvious modifications to the original patented products.

One area in which such an opportunity may arise is the field of protein engineering, which involves modifying the nucleotide sequence of a gene so that it expresses a protein with a slightly different amino acid sequence.²²¹ Such “second generation” designer proteins may have clinical advantages over their natural analogs.²²² At present, scientists can modify amino acid sequences with precision, utilizing a technique called site-directed mutagenesis.²²³ The capabilities of protein engineering are limited, however, because researchers cannot know the results that such modifications will have on the protein’s function in advance, and the development of second-generation proteins typically involves trial and error.²²⁴ For persons skilled in the art, the effect that even so-called “conservative amino acid substitutions” would have on a protein’s biological activity remains unpredictable.²²⁵ A protein with an amino acid

218. *Id.*

219. *See* DAVID FRIEFELDER & GEORGE M. MALACINSKI, *ESSENTIALS OF MOLECULAR BIOLOGY* 376–79 (2d ed. 1993).

220. *Id.*

221. Antony L. Ryan & Roger G. Brooks, *Innovation vs. Evasion: Clarifying Patent Rights in Second-Generation Genes and Proteins*, 17 *BERKELEY TECH. L.J.* 1265, 1266 (2002).

222. *See id.* at 1270 (noting that second-generation designer proteins now on the market include Eli Lilly’s Humalog (an analog of human insulin), Genentech’s TNKase (an analog of tissue plasminogen activator) and Amgen’s Infergen (an analog of human alpha interferon)).

223. *Id.* at 1269–70.

224. *Id.* at 1270.

225. *Id.* at 1283.

substitution that has no perceptible effect on biological activity would likely infringe a patent on the original protein. But a designer protein with substantially improved biological activity or with an entirely new and useful property would likely not be considered by the PHOSITA to be an obvious improvement over the naturally occurring protein, and thus would not infringe.

C. *Ramifications for the Biopharmaceutical Industry*

The common sense approach to biotechnology patents outlined above would alleviate certain anticommons problems currently existing within the field. Newly found genes would be freely available for future research, aiding the ability of scientists to engage in collaborative projects designed to elucidate the complex regulatory pathways involved in disease processes. The revised paradigm would also reduce the cost of developing DNA microarrays by eliminating the need for chip makers to negotiate licenses with the numerous gene and SNP patent holders whose sequences reside on the chip. This may make gene chips cheaper and more accessible, which would further facilitate the progress of biomedical research because scientists believe that microarrays are crucial to unlocking the secrets of human genetic variation.²²⁶ The proposed approach would also eliminate costs incurred when upstream gene patent holders extract rents from biopharmaceutical companies for the right to develop drug candidates targeting patented genes.

Revoking the availability of gene patents may have the negative effect of stifling disclosure about newly discovered genomic information. In the absence of patent protection, researchers may resort to trade secrecy in order to maintain a proprietary interest in their discoveries. This may not be a serious problem within academia, where other incentives are in place to encourage disclosure. Academic scientists may be motivated by prestige, prizes, and academic awards, including tenure.²²⁷ They may also be motivated by the love of science and the possibility of making a positive contribution to their field.²²⁸ But the revised regime may lead to reduced disclosure of basic research findings by researchers working for biotechnology companies, who will maintain such findings as trade secrets if they cannot obtain patent protection for their discoveries.

226. See Eric S. Lander, *Scientific Commentary: The Scientific Foundations and Medical and Social Prospects of the Human Genome Project*, 26 J.L. MED. & ETHICS 184, 187 (1998) (predicting future uses of microarrays to “tease apart the genetic factors contributing to heart disease, cancer risk, schizophrenia, manic depression, and attention deficit disorder”).

227. See Burk & Lemley, *supra* note 105, at 1586 (discussing inventor motivation generally but including academic incentives).

228. *Id.*

Concerns about disclosure are mitigated by the fact that trade secret protection does not prevent other researchers from independently discovering the gene and disclosing their findings. It is also important to note that filing a patent application does not lead to immediate disclosure of a newly discovered gene: a thirty-month delay may remain between patent filing and public disclosure of an invention.²²⁹ Moreover, disclosure of a new gene via a patent application does not ensure that it will be readily available for study by basic researchers because patent holders have the right to demand a license fee or to refuse requests to perform research on a patented gene that fail to fall under the narrow parameters of the experimental use exception set forth in *Madey v. Duke*.²³⁰ Furthermore, discoverers of new genes under the proposed regime will have incentives to disclose information about the gene in connection with patent filings on new inventions derived from the gene discovery, such as new protein products or diagnostic kits. Thus, while the unavailability of gene patents may lead to disclosure delays, arguably these costs are outweighed by the benefits of preserving new gene discoveries for the genetic commons.

Elimination of gene patents may also have a negative impact on small biotechnology companies, who rely on strong patent portfolios in order to attract capital investment and negotiate strategic partnerships with established biopharmaceutical companies. However, arguments that biotechnology companies require gene patents in order to remain viable may be overblown. Certain companies may be able to survive without intellectual property rights. For instance, some companies may be able to profit by providing access to publicly available sequence information that is easier or more efficient to use.²³¹

More importantly, patents on discoveries that are made further downstream are generally far more influential in motivating private firms to develop end products than upstream patents on basic research discoveries.²³² Much of the impetus for R&D in the biopharmaceutical industry is centered on drug discovery.²³³ The long biopharmaceutical product

229. An inventor may file a provisional patent application for an invention, which serves as a placeholder for up to one year and is not available to the public. Upon expiration of the provisional application, the inventor may convert the application to a non-provisional application, which is not published until another eighteen months have passed. *See* Manual of Patenting Examination Procedure, available at <http://www.uspto.gov/web/offices/pac/mpep/index.htm> (last viewed Nov. 3, 2007).

230. *See* discussion *supra* Part III.

231. Haas, *supra* note 58, at 161–62.

232. Rai & Eisenberg, *supra* note 29, at 296.

233. Eisenberg, *supra* note 189, at 477 (“If a biotechnology company looks for a while like they are up to something other than staking out claims that will permit them to tap into drug profits, they often eventually seem to change their business model, or else they get folded into a company that is more squarely focused on profiting from drug development.”).

development process typically generates additional downstream patents that are more meaningful to the profit expectations of private investors than patents on the initial basic discoveries.²³⁴ Thus, the fear that new products would never be developed if the early discoveries from which they sprang remained unpatented arguably is not in line with contemporary R&D and patenting practices in the biopharmaceutical industry.²³⁵

CONCLUSION

The ENCODE consortium's recently released findings suggest that we have only scratched the surface of our understanding of the human genome. In order to tap into the enormous potential of genomics research to lead to medical breakthroughs, we must implement a new approach to biotechnology patents. The Supreme Court's mandate in *KSR v. Teleflex* to insert "common sense" into the obviousness analysis should serve as the guidepost for a more rational regime. Aligning the patent doctrinal framework with a realistic depiction of today's biotechnology PHOSITA will help to restore the genetic commons by eliminating strangleholds on upstream research.

Academic institutions and genomics companies may no longer be able to rely on gene patents to generate revenue under the approach proposed in this Article. However, I argue that there will be an overall net benefit to society in reducing the availability of patents on upstream genomics discoveries. A patent regime that recognizes the knowledge and capabilities of the biotechnology PHOSITA will eliminate barriers to collaborative research efforts aimed at elucidating the complexities of the human genome. This will facilitate advances in our understanding of the molecular basis of disease. In addition, reductions in the number of upstream patents will reduce the costs of developing new diagnostics and therapeutics, leading to reduced prices and increased access to medical end products.

234. Rai & Eisenberg, *supra* note 29, at 301.

235. *Id.* at 301–02.