COMMENTS

Uncommon Genes, Unpatentable Subject Matter

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> "More than twenty years of pure policy arguments [against patents on human gene sequences] have gotten nowhere in the courts, and Congress has shown no inclination to put the lucrative biotechnology genie back into the bottle."[1]

I. INTRODUCTION

In a landmark decision on March 29, 2010, Judge Sweet of the Southern District of New York ruled on the first case challenging patents granted by the United States Patent and Trademark Office (USPTO) for gene sequences.[2] The plaintiffs[3] challenged the validity of Myriad Genet-

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1. John M. Conley & Roberte Makowski, *Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents (Part I)*, 85 J. PAT. & TRADEMARK OFF. SOC'Y 301, 307–08 (2003).

2. Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010).

3. The plaintiffs include the Association for Molecular Pathology, the American College of Medical Genetics, the American Society for Clinical Pathology, the College of American Pathologists, Dr. Haig Kazazian (University of Pennsylvania School of Medicine), Dr. Arupa Ganguly (University of Pennsylvania), Dr. Wendy Chung (Columbia University), Dr. Henry Ostrer (New York University School of Medicine), Dr. David Ledbetter (Emory University), Dr. Stephen Warren (Emory University), Ms. Ellen Matloff (Yale Cancer Genetic Counseling Program), Ms. Elsa Reich (Department of Pediatrics at New York University), Breast Cancer Action, Boston Women's Health Book Collective, Ms. Lisbeth Ceriani (patient), Ms. Runi Limary (patient), Ms. Genae Girard (patient), Ms. Patrice Fortune (patient), Ms. Vicky Thomason (patient), and Ms. Kathleen Raker (patient). *Id.* at 186–89.

ics'[4] patents on the BRCA1 and BRCA2 genes.[5] Myriad holds exclusive licenses for the patents claiming both the BRCA gene sequences and the mutations associated with those sequences.[6] These licenses grant Myriad the sole authority to test patients for BRCA mutations.[7] Because mutations in the BRCA genes correlate with a genetic predisposition to certain types of cancers,[8] the plaintiffs alleged that the grant of exclusionary rights to Myriad for the BRCA gene sequences inhibited patient access to medically relevant diagnostic tests and unnecessarily increased the cost associated with such tests.[9] Six different breast-cancer patients claimed they either received limited testing or could not afford tests due to Myriad's enforcement of its patent rights.[10] In this case, Judge Sweet sided with the plaintiffs, holding that, as a matter of law, Myriad's patents claiming the BRCA1/2 gene sequences are invalid.[11]

The Myriad litigation is just one example of the ongoing debate over patents on DNA sequences. The Myriad decision is currently before the Federal Circuit and may make its way to the United States Supreme Court, giving the judiciary an opportunity to weigh and clarify a questionable USPTO policy. The debate has taken several forms involving legal, ethical, and public-policy concerns.[12] Members of the biopharmaceutical industry argue that patents are necessary to promote new genetic technologies.[13] In contrast, gene-patent opponents believe that human DNA patents are dubious patentable subject matter under both legal and ethical rationales.[14] The USPTO grants gene-sequence patents on the grounds that the isolated and purified gene, extracted from the cell, con-

4. Plaintiffs asserted claims against the USPTO, Myriad Genetics, and the directors of the University of Utah Research Foundation. *Id.* at 189–90.

5. BRCA is the shorthand name for Breast Cancer Susceptibility Gene. BRCA1 refers to the first gene sequence identified that is associated with breast cancer. BRCA2 refers to the second gene identified. *Id.* at 201–03.

6. *Id.*

7. *Id.*

8. *Id.* at 203 (noting that women with BRCA1/2 mutations have an increased risk of developing breast cancer (up to 85% chance) and ovarian cancer (up to 50% chance)).

9. *Id.* at 204. Women who were unable to afford the full out-of-pocket cost for Myriad's tests were denied testing because, although other laboratories were able to perform the tests at a much lower cost, Myriad's patent rights barred those laboratories from offering similar tests. *Id.*

10. *Id.* at 188–89.

11. *Id.* at 232.

12. *See generally* SEC'Y'S ADVISORY COMM. ON GENOMICS, HEALTH & SOC'Y (SACGHS), REVISED DRAFT REPORT ON GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS (2010) [hereinafter SACGHS REPORT].

13. *E.g.*, Gregory C. Ellis, *Emerging Biotechnologies Demand Defeat of Proposed Legislation that Attempts to Ban Gene Patents*, 15 RICH. J.L. & TECH. 1, 1–3 (2008).

14. *See generally* Lori B. Andrews & Jordan Paradise, *Gene Patents: The Need for Bioethics Scrutiny and Legal Change*, 5 YALE J. HEALTH POL'Y L. & ETHICS 403 (2005).

stitutes something different from DNA as it is found in nature.[15] Consequently, if "isolated" DNA is never found in nature, it should be amenable to patent protection. This construction is problematic, however, because there is no functional difference between a DNA sequence found in the cell and a DNA sequence isolated from the cell.[16] Judge Robert H. Sweet, persuaded that the patents claimed genetic information as it is found in nature, interpreted the BRCA gene sequences as products of nature.[17] Accordingly, he decided that gene sequences are a form of unpatentable subject matter and held that Myriad's gene patents were invalid.[18]

Human gene sequences are not only products of nature, but also products of cultural heritage. Although the USPTO fails to effectively balance the competing business and human interests associated with DNA sequence patents, the international community tries to weigh these interests appropriately.[19] To date, however, the ethics-based doctrine of Common Heritage has been largely ineffective in overriding competing business interests.[20] The basic tenet of Common Heritage supposes that certain resources are part of the common heritage of humanity, and that communal property rights, rather than individual rights, are appropriate for such resources.[21] Although the doctrine has been cited as an ethical bar to gene patents, as generally conceptualized, this application of the doctrine is suspect for at least two reasons. First, the idea of a common human genome is an abstraction; only identical twins share a common genome.[22] Second, a common genome is not the subject of patent claims over gene sequences.[23]

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15. *See* Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001) [hereinafter Utility Examination Guidelines], *available at* http://www.uspto.gov/web/offices/com/sol/og/2001/week05/patutil.htm.

16. Unlike a situation where a researcher has altered the genetic composition of an organism to something that is not found in nature, a merely isolated gene sequence has not been altered to have a different function. The DNA sequence is the same whether it is contained within the cell or whether it exists in a test tube.

17. Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 232 (S.D.N.Y. 2010).

18. *Id.*

19. *See* Andrews & Paradise, *supra* note 14, at 403–04.

20. Pilar N. Ossorio, *The Human Genome as Common Heritage: Common Sense or Legal Nonsense?*, 35 J.L. MED. & ETHICS 425, 425–26 (2007). For a more general discussion of the opposition to gene patents, see Ellis, *supra* note 13. "[S]o-called moral opposition against gene patents . . . rarely amounts to any meaningful proposals of reform." *Id.* at 8.

21. For example, the seabed is considered to be the property of all humanity.

22. *See infra* Part V.

23. *See* Ossorio, *supra* note 20, at 431 (noting that each individual's genome is different from another individual's and that gene-sequence patents only cover very short DNA regions contained within a particular genome).

This Comment argues that although human gene sequences do not reflect a common human heritage, such sequences do reflect human cultural heritage. A patent that unfairly restricts access to basic genetic information generates wealth for the patent holder without regard to an individual's right to basic knowledge—knowledge that can be characterized and afforded legal protection as intangible cultural heritage. Much discussion is directed at the biological properties of DNA, but very little attention is given to the relationship between a human gene and its cultural derivation. While it is true that patent claims encompass only individual genes and gene fragments, these genetic regions and mutations result from human cultural and genetic evolution.[24] Genetic mutations distinguish individuals by virtue of different family genealogies.[25] Similarly, genetic mutations differentiate groups of people that share a common cultural heritage.[26] Any gene sequence is part of an individual's family history and group affiliation.

Human gene sequences can be conceptualized in three ways: as a molecular fragment, as genetic information, and as a product of cultural heritage.[27] This Comment uses the BRCA litigation as an organizing principle to discuss the importance of understanding human genes as something more than just biological material.[28] Part II addresses the background of the BRCA gene-patent case and the legal arguments against patenting gene sequences. Part III discusses the ethical objections to gene patents by focusing on common-heritage rationales. Further, Part III addresses the inadequacy of the Common Heritage Doctrine as applied to human gene sequences. Part IV highlights the international and domestic protections afforded to cultural heritage. Part V argues that because human genetic variation results from complex cultural and evolutionary processes, gene sequences should be protected from appropriation as intangible cultural heritage. Finally, Part VI offers some concluding thoughts.

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24. For a general discussion concerning the interplay between genetic forces, environmental impact, and cultural adaptation, see MARK A. JOBLING, MATTHEW HURLES & CHRIS TYLER-SMITH, HUMAN EVOLUTIONARY GENETICS: ORIGINS, PEOPLES & DISEASE 401–38 (Garland Science 2004).

25. *See id.*; *see* discussion *infra* Part V.

26. *See* JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 401–38.

27. *See* Debra Greenfield, *Intangible or Embodied Information: The Non-Statutory Nature of Human Genetic Material*, 25 SANTA CLARA COMPUTER & HIGH TECH. L.J. 467, 468–69 (2009) (discussing DNA as both a tangible molecule and intangible information).

28. As the focus of this Comment is conceptualizing genes as both biological and cultural products, it deals only with patents that directly claim a human gene or gene fragment. This Comment does not address the efficacy of gene-related product or method patents, nor does it address gene patents claiming the genetic material of other species.

II. BACKGROUND

A. Ass'n for Molecular Pathology v. USPTO

On March 29, 2010, Judge Sweet granted the plaintiffs' motion for summary judgment to declare invalid fifteen patent claims contained in seven of Myriad's BRCA patents.[29] The plaintiffs, represented by the American Civil Liberties Union (ACLU), included individuals from medical and advocacy organizations, as well as researchers, genetic counselors, and women either threatened by the risk of breast cancer or struggling to fight breast cancer.[30] The plaintiffs claimed that patents granted for the BRCA1 and BRCA2 gene sequences were unlawful under each of the following: (1) the Patent Act of 1952,[31] (2) Article I, Section 8, Clause 8, of the United States Constitution (the Patent and Copyright Clause), and (3) the First and Fourteenth Amendments of the United States Constitution.[32] In granting the plaintiffs' motion for summary judgment, Judge Sweet acknowledged the special significance of the claims before the court: "The resolution of the issues presented to this Court deeply concerns breast cancer patients, medical professionals, researchers, caregivers, advocacy groups, existing gene patent holders and their investors, and those seeking to advance public health."[33]

At trial, defense attorney Brian Poissant characterized the ACLU's position as an attack "on biotechnology patenting that warn[s] of the 'gruesome parade of horribles' that will happen if companies are given patents over biological phenomena."[34] Furthermore, he noted that "if a ruling were as broadly applied here as the ACLU [contends] then it could 'undermine the entire biotechnology sector.'"[35] Concerned, but not persuaded, Judge Sweet ruled for the plaintiffs, convinced that Myriad's patents claimed DNA as it is found in nature.[36] Judge Sweet concluded that natural products are "unsustainable as a matter of law and are deemed unpatentable subject matter under 35 U.S.C. § 101."[37]

Judge Sweet's trepidations mirror the public's concerns about the gene-patent debate.[38] The plaintiffs' legal challenges to the BRCA pa-

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29. Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 184–85 (S.D.N.Y. 2010).

30. *Id.* at 186–89.

31. 35 U.S.C. § 101 (2006).

32. *Molecular Pathology*, 702 F. Supp. 2d at 184.

33. *Id.* at 185.

34. Matt Jones, *Myriad, ACLU Clash over Gene IP in NY Court*, GENOMEWEB DAILY NEWS (Feb. 2, 2010), http://www.genomeweb.com/dxpgx/myriad-aclu-clash-over-gene-ip-ny-court.

35. *Id.*

36. *Molecular Pathology*, 702 F. Supp. 2d at 185.

37. *Id.*

38. *See* Andrews & Paradise, *supra* note 14, at 403–04 ("Intense opposition to gene patents is . . . coming from researchers, politicians, organized religions, indigenous groups, patient groups,

tents raise a difficult legal and ethical dilemma: should information about an individual's personal genetic identity be protectable as intellectual property for the purpose of promoting scientific innovation? On the one hand, resolving this thorny question in favor of the plaintiffs could affect the future of biomedical research.[39] Conversely, a resolution favoring the defendants affects both personal healthcare and autonomy.[40]

B. Why Do Gene-Sequence Patents Pass Muster Under the Patent Act?

The United States Constitution defines Congress's power "to promote the Progress of Science and useful arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[41] The exclusionary rights granted by the Constitution are thought to create incentives for invention and stimulate the public dissemination of scientific innovation.[42] Congress interprets exclusionary rights under the 1952 Patent Act (Patent Act) as encompassing "making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States"[43] for a current term of twenty years after the date of the patent application.[44] The Patent Act codified statutory conditions under which the USPTO grants inventors patent protection for their inventions and discoveries.[45] According to the Patent Act, four threshold requirements are necessary for the approval of patent protection: (1) patentable subject matter, (2) utility, (3) novelty, and (4) non-obviousness.[46]

An invention is patentable subject matter under § 101 of the Patent Act when a person "invents or discovers any new and useful process, machine, manufacture, or composition, or any new and useful improvement thereof . . . ."[47] Congress interpreted the patentable subject matter requirement broadly, including "anything under the sun that is made by man."[48] Although almost any "thing" qualifies as § 101 subject matter,

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and medical professional organizations. Patents covering human genetic material raise a variety of issues . . . regarding privacy, autonomy, religious freedom, and reproductive liberty.").

39. *See Molecular Pathology*, 702 F. Supp. 2d at 185.

40. *Id.*

41. U.S. CONST. art. I, § 8, cl. 8.

42. Diamond v. Chakrabarty, 447 U.S. 303, 308–09 (1980) (stating that the Patent Act was drafted in accordance with Thomas Jefferson's philosophy that "ingenuity should receive a liberal encouragement") (quoting 5 WRITINGS OF THOMAS JEFFERSON 75–76 (Washington ed. 1871)).

43. 35 U.S.C. § 154 (2006).

44. *Id.*

45. *Id.* §§ 101–103.

46. *Id.* This Comment is not concerned with the statutory requirements for novelty, utility, and non-obviousness.

47. *Id.* § 101.

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

the "human-made" requirement is a sticking point; laws of nature, abstract ideas, and natural phenomena fall outside the scope of patentable material.[49] Because genetic material exists in cells, some commentators have identified gene sequences as unpatentable products or laws of nature.[50] In 1911, however, Judge Learned Hand distinguished molecules as they exist in nature from molecules that have been manipulated through processes like purification and isolation.[51] Judge Hand articulated the purification–isolation rationale in *Parke-Davis & Co. v. H.K. Mulford Co.*[52] At issue in *Parke-Davis* was a patent for glandular adrenaline that required the isolation of adrenaline from the body and subsequent laboratory purification.[53] The court reasoned that although adrenaline exists within the body in a natural form, the isolation and purification of adrenaline from the gland was "for every practical purpose a new thing commercially and therapeutically."[54] Therefore, derivatives of natural products are appropriate patentable subject matter if they exhibit some new commercial property.[55]

In 1980, the Supreme Court decided *Diamond v. Chakrabarty* and extended the purification rationale of *Parke-Davis* to biotechnological manipulation of naturally occurring organisms.[56] In *Diamond*, the issue was whether a genetically modified bacterium qualified as a patentable

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49. *Id.*

50. *See, e.g.*, Eileen M. Kane, *Splitting the Gene: DNA Patents and the Genetic Code*, 71 TENN. L. REV. 707, 707 (2004).

51. Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 103 (C.C.S.D.N.Y. 1911). Although isolation and purification technically refer to two different processes (i.e., the physical separation of a molecule from its natural environment and then the removal of any associated substances to render a pure molecule), in the context of DNA, isolation and purification go hand in hand. DNA cannot be analyzed unless it is both separated from the body and the cell, as well as purified from biochemical compounds that inhibit further analysis. In this sense, DNA must necessarily be both separated and clean before a researcher can make any use of it.

52. *Id.*

53. *Id.* at 97.

54. *Id.* at 103. The court stated:

> Nor is the patent only for a degree of purity, and therefore not for a new "composition of matter." As I have already shown, it does not include a salt, and no one had ever isolated a substance which was not in salt form, and which was anything like Takamine's. Indeed, Sadtler supposes it to exist as a natural salt, and that the base was an original production of Takamine's. That was a distinction not in degree, but in kind. But, even if it were merely an extracted product without change, there is no rule that such products are not patentable. Takamine was the first to make it available for any use by removing it from the other gland-tissue in which it was found, and, while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically. That was a good ground for a patent.

Id.

55. *See id.*

56. Diamond v. Chakrabarty, 447 U.S. 303, 313 (1980).

manufactured product.[57] The Court held that "the patentee has produced a new bacterium with markedly different characteristics from any found in nature. . . . His discovery is not nature's handiwork . . . under § 101."[58] Although no court has extended the isolation and purification reasoning to DNA-sequence patents, the USPTO cites the above cases in support of issuing such patents on isolation and purification grounds.[59] But the "isolation and purification" of a DNA molecule does not change the informational content of the molecule.[60] The processes used to isolate and purify DNA are laborious, but the end product in isolated form is not functionally different from the molecule found within the cell.[61] The DNA product contains the same nucleotide sequence as the *in vivo* molecule: the informational content that a researcher hopes to determine. While it is true that the isolated molecule is different because it has been stripped of the material that inhibits its analysis, it is the informational content of DNA that makes the sequence useful. Identifying the sequence of the

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57. *Id.* at 309.

58. *Id.* at 310.

59. *See* Utility Examination Guidelines, *supra* note 15.

> Several comments state that while inventions are patentable, discoveries are not patentable. According to the comments, genes are discoveries rather than inventions. These comments urge the USPTO not to issue patents for genes on the ground that genes are not inventions. Response: The suggestion is not adopted. An inventor can patent a discovery when the patent application satisfies the statutory requirements. The U.S. Constitution uses the word "discoveries" where it authorizes Congress to promote progress made by inventors. The pertinent part of the Constitution is Article 1, section 8, clause 8, which reads: "The Congress shall have power * * * To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."
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> When Congress enacted the patent statutes, it specifically authorized issuing a patent to a person who "invents or discovers" a new and useful composition of matter, among other things. The pertinent statute is 35 U.S.C. 101, which reads: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title." Thus, an inventor's discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it.

Id.

60. Greenfield, *supra* note 27, at 467, 478 (2009) ("Although scientists, social scientists, and historians since the early 1950s have described deoxyribonucleic acid (DNA) sequences as information, this characterization has yet to be recognized by the law of intellectual property.").

61. *Id.* at 478–79.

> A thorough examination of the types of sequences that are actually being claimed and the manner in which they are claimed fails to establish any meaningful distinctions under the law. Instead, it reveals only an abstraction, a construct: "Thus stripped of its identity as 'natural,' the unencumbered gene becomes readily susceptible to the creation and layering upon it of a new legal identity as 'man-made' through scientific interventions."

Id. (quoting Jonathan Kahn, *What's the Use? Law and Authority in Patenting Human Genetic Material*, 14 STAN. L. & POL'Y REV. 417, 426 (2003)).

DNA fragment is the baseline step necessary before further useful discoveries can be achieved. Once this information is available, researchers can, for example, correlate the presence of mutations within the sequence with some particular outcome like increased risk of disease. A gene-sequence patent claiming the baseline nucleotide sequence of isolated DNA, therefore, prevents others from using the sequence information to create different tests or diagnostic technologies.

To illustrate, the challenged claims of BRCA patents cover four categories. First, the patents claim isolated, ancestral[62] forms of the BRCA genes and fragments of the BRCA genes consisting of at least fifteen nucleotides.[63] Second, they cover isolated forms of the BRCA genes that have mutations; the mutations may or may not be associated with an increased risk of cancer.[64] Third, the patents claim a method of analyzing a person's BRCA sequences to determine whether the sequences contain mutations.[65] Last, the patents claim a method of comparing a patient's BRCA gene sequences to the normal BRCA sequences in order to determine whether a genetic predisposition to breast cancer exists.[66] In other words, the patents exclude others from sequencing a patient's BRCA1 or BRCA2 gene, comparing that sequence to the BRCA reference sequences, and determining whether a patient has a heightened cancer risk.

III. WHY SHOULD GENE SEQUENCES BE INAPPROPRIATE PATENT SUBJECT MATTER?

A. Gene-Sequence Patents Negatively Affect Genetic Research and Healthcare

The plaintiffs in *Molecular Pathology* alleged that the BRCA patents effectually bar all other entities from providing genetic testing for the BRCA genes.[67] Additionally, these patents bar researchers from conducting further research of the BRCA genes.[68] This potential chill on fur-

62. Ancestral, or wild-type, forms of a particular gene refer to the initial sequence state of the gene that existed at some point in the past.

63. *See* Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 212–13 (S.D.N.Y. 2010). For ease of discussion, I have summarized the general content for some of Myriad's challenged patent claims in its '282, '441, and '857 patents as described by Judge Sweet in *Molecular Pathology*.

64. *See id.*

65. *See id.*

66. *See id.* at 213–14. Note also that one patent claims a method for determining the efficacy of a potential cancer therapeutic.

67. *See id.* at 206.

68. *Id.* I am not suggesting that Myriad enforces its patents against basic researchers; in fact, Myriad made public statements to the contrary. *Id.* Although Myriad does not currently enforce its

ther research is important because while Myriad's mutation detection tests covered many mutations associated with a heightened cancer risk, the tests did not cover all known mutations associated with that risk.[69] Myriad's patents effectively block other researchers from designing a test that would include mutations or sequence arrangements for which Myriad does not test. A failure to test for known mutations that correlate with cancer predisposition undermines the efficacy of diagnostic tests. Myriad's patents discourage, and if enforced, prohibit researchers from designing new tests based on new knowledge.

Gene-patent advocates counter the above claims in several ways, arguing that gene patents should be retained because: (1) gene patents are necessary to create incentives for biotechnological innovation,[70] and (2) empirical research has not demonstrated that gene patents chill further research or that patents increase the cost of, or access to, diagnostic tests.[71] Gene-patent advocates argue that patent protection is crucial to drive investment in areas such as biopharmaceutical innovation.[72] For example, biologics are drugs that have been derived from a living organism or cell or by recombinant DNA technology.[73] The research and development costs associated with bringing biologic drug therapies to the market are enormously high.[74] Given the significant investments necessary to carry out research and development, manufacturers often require a guarantee that those investments are recoverable.[75] The economic-investment argument, however, fails to separate the economic incentive provided by the patent on the gene sequence from the total economic incentive offered for the diagnostic or technological innovation.

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patents against basic researchers, the patent claims are broad enough to allow Myriad to block basic research should it choose to do so. In *Metastasizing Patent Claims on BRCA1*, Kepler et al. performed a bioinformatics analysis for claim 5 of Myriad's U.S. Patent No. 5,747,282. Their results show that claim 5 extends the breadth of the '282 patent to portions of the genome beyond the BRCA1 gene itself. They estimate that the small nucleotide fragment identified in claim 5 is likely present at least once in every human gene. By the letter of the patent then, any genetic research using this particular nucleotide fragment would be infringing, irrespective of whether that research concerned BRCA1. Thomas B. Kepler, Colin Crossman & Robert Cook-Deegan, *Metastasizing Patent Claims on BRCA1,* 95 GENOMICS 312, 312–14 (2010).

69. *See Molecular Pathology*, 702 F. Supp. 2d at 206. The opinion suggests that Myriad currently tests for all known sequence mutations. The plaintiffs contend there was a period of time when Myriad failed to test for large rearrangements in the BRCA genes, despite knowledge that such mutational events are related to cancer predisposition. *Id.*

70. Ellis, *supra* note 13, at 3.

71. *Cf.* SACGHS REPORT, *supra* note 12, at 32–41.

72. Ellis, *supra* note 13, at 46.

73. *Id.* at 51.

74. *See id.* at 52–53 ("The incentive required to research and develop a biologic drug is no less than it would be for a traditional pharmaceutical drug. In actuality it is more.").

75. *Id.* at 54.

There is little clarity as to which is more valuable: the patent on the underlying gene sequence or a patent on the innovative use of that gene sequence. The biotechnological innovation likely entails a novel use, modification, or application of the underlying sequence.[76] On the one hand, if the value of the patented innovation is derived mainly from an innovative use, modification, or application, then claiming the underlying sequence does not add much value. Thus, if the patent on the underlying sequence offers little actual value to the patent holder, then the economic-incentive argument fails because the sequence patent is superfluous. Alternatively, if the value of the patent derives mainly from blocking other researchers from developing other innovative uses, modifications, or applications of the underlying gene sequence, then the patent is contrary to the policy for granting patents.[77] Under this scenario, the patent is valuable not because it provides an incentive to innovate, but because it prevents others from innovating.

In response to the concerns about the chilling effect of gene patents and a lack of empirical evidence demonstrating such an effect, the U.S. Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) conducted its own report to assess the validity of the assertion that gene-sequence patents actually block other researchers from innovating.[78] SACGHS commissioned the Revised Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests (Report) to evaluate the potential blocking function of sequence patents and problems associated with patient access to genetic testing.[79] The Report includes multiple empirical studies suggesting that a chilling effect on research currently exists.[80] The fear of patent holders enforcing exclusionary rights for patents granted on foundational research discoveries is a real concern for researchers.[81]

Molecular Pathology demonstrates how this fear impacts healthcare. Myriad asserted its exclusionary rights over other clinicians and

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76. The discovery of a particular gene sequence is not innovative. *See* Matthew Erramouspe, Comment, *Staking Patent Claims on the Human Blueprint: Rewards and Rent-Dissipating Races*, 43 UCLA L. REV. 961, 997 (1996).

77. Diamond v. Chakrabarty, 447 U.S. 303, 308–09 (1980).

78. SACGHS REPORT, *supra* note 12.

79. *Id.* SACGHS was chartered in 2002 by the Secretary of the U.S. Department of Health and Human Services as a forum for discussing the policy issues associated with issues surrounding genetic testing. The Committee consists of seventeen individuals with specific expertise in the following disciplines: biomedical sciences, human genetics, healthcare delivery, evidence-based practice, public health, behavioral sciences, social sciences, health services research, health policy, health disparities, ethics, economics, law, healthcare financing, and consumer issues. *Id.* at 1.

80. *Id.* at 83.

81. *See id.*

laboratories, limiting patient access to testing and testing validation.[82] The plaintiffs include six women, between the ages of thirty-two and fifty-two, who were adversely affected by Myriad's exclusive right to provide BRCA1/2 diagnostic testing.[83] These women were denied access to information about their own predisposition to aggressive cancers because the BRCA gene patent claims excluded other clinicians from performing additional tests or the same tests at lower cost, or confirming Myriad's test results.[84] Women were denied access to the full range of preemptive options that could have prevented the cancer from developing or spreading.[85] Myriad's enforcement of its BRCA patents negatively affected these patients.

Aside from the concerns about the clinical and research-blocking function of gene-sequence patents, some are disturbed by the appropriation and commoditization of DNA.[86] Although issuance of a patent does not confer property rights, the downstream effect is that patents generate wealth for patent holders.[87] When considering human genes, the concern is that patents allow individuals and organizations to make money from genetic information that is both personal and communal.[88] The debate rages on as to whether patent rights sufficiently balance the need to encourage genetic innovation against a perceived misappropriation of access to genetic knowledge.[89]

Unfortunately, there has been no satisfactory theory levied in which to ground the fears about gene patents. Although strong ethics-based arguments against DNA-sequence patents could bolster the cause for an

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82. Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 206 (S.D.N.Y. 2010).

83. *Id.*

84. Women may choose to have preemptive surgeries such as mastectomies after finding out the likelihood of developing breast cancer. If a woman does not have access to her personal risk assessment, she cannot make preemptive decisions.

85. *Molecular Pathology*, 702 F. Supp. 2d at 206.

86. *See* Ossorio, *supra* note 20, at 425 ("Many people can accept the plausibility of claims that all human beings have a profound interest in the human genome—that all people have a significant stake in how and whether the human genome is manipulated, and in what principles would guide its commercial exploitation.").

87. Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, 76 UMKC L. REV. 295, 302 (2007) (noting that there is often confusion as to the actual scope of rights associated with a patent grant: patent holders do not own genes; they merely own exclusionary rights against others wishing to use, make, or sell the inventions claimed in the patent application). There is an undoubtedly complicated relationship between the perceived strength of a company's IP portfolio and its market value. While this Comment does not attempt to discuss this phenomenon, it is interesting to note that Myriad's stocks dropped roughly 7% the day following the *Molecular Pathology* decision. Anand Basu, *Myriad Genetics Shares Fall After Court Denies Patents*, REUTERS (Mar. 30, 2010, 11:05 AM), http://www.reuters.com/article/idUSTRE62T35X20100330.

88. Ossorio, *supra* note 20, at 431.

89. *Molecular Pathology*, 702 F. Supp. at 185.

immediate change in subject-matter classification, no such ethical violation has been clearly identified.[90] While not prominent in U.S. policy discussions, the international community endorses the Common Heritage Doctrine to designate the human genome as the public property of all humanity.[91] This Doctrine was publicly adopted by the United Nations, the international Human Genome Organization (HUGO), and the Council of Europe.[92] While enticing at least in the abstract, the Doctrine fits uncomfortably as an ethical rationale for exempting gene sequences from patentable subject matter. Classifying the human genome as common heritage oversimplifies the reality of human genetic variation. Furthermore, when drawn to its legal end, the Common Heritage Doctrine has unsatisfactory property-based consequences.[93]

B. The Common Heritage Doctrine

In *The Human Genome as Common Heritage: Common Sense or Legal Nonsense*, Pilar Ossorio reflects on the theoretical foundations of the Common Heritage Doctrine and discusses its applicability to the human genome.[94] She notes that the Doctrine embodies two rationales for protecting certain objects or resources as the public property of all humanity: (1) the Common Heritage Property Doctrine (CHPD) and (2) the Common Heritage Duties Doctrine (CHDD).[95] The following discussion about common heritage reflects Ossorio's research and insights about the two doctrinal forms. CHPD is the traditionally invoked doctrine to support ethical objections to DNA sequence patents.[96] Because "CHPD vests all people or all nations with equal *property* interests in a territory or resource," CHPD suggests that all people have a property interest in the human genome. [97] In contrast, CHDD recognizes individual property interests in a common resource.[98] CHDD imposes a duty to protect common resources from exploitation.[99] Thus, under CHDD, individuals have personal property interests in the human genome and those collective interests warrant a duty to protect the genome from exploitation.[100] While the application of CHPD to genetic information is problematic, CHDD

90. *See* Ossorio, *supra* note 20, at 429.
91. *Id.* at 425.
92. *Id.*
93. *Id.*
94. *Id.* at 425–26.
95. *Id.* at 427.
96. *Id.* at 428–29.
97. *Id.* at 427, 429.
98. *Id.* at 430.
99. *Id.*
100. *See id.*

offers a compatible theoretical basis for protecting gene sequences as intangible cultural heritage.[101]

CHPD was developed during the 1960s in response to concerns about disparate global power structure.[102] Representatives of less industrialized nations noted that benefits derived from resource exploitation become inequitably allocated.[103] Because wealthy nations benefit unfairly from resource exploitation, legal agreements between nations should be structured to account for benefit misallocation.[104] By incorporating redistributive measures such as taxes and transfer agreements into resource-exploitation agreements, the benefits would be more evenly distributed.[105] "Because of its particular history, the CHPD emphasized the distribution of benefits rather than the distribution of burdens or duties that might be associated with maintaining a [common heritage] resource."[106] In other words, CHPD recognizes that because of the global power structure, less powerful nations do not receive the benefits they are entitled to when common resources are exploited.[107]

Given the benefit-driven nature of CHPD-designated resources, conceptualization of the human genome as a CHPD resource suggests that DNA could be commercially exploited so long as the benefits of commercial exploitation are equitably distributed.[108] If a concern exists about whether gene sequences should be commoditized, then a theory that allows for exploitation of a common resource would be inconsistent with such an anti-gene-patent position. Notably, "[n]o codification of the CHPD prevents economic exploitation of the CH resources."[109] All the CHPD designation offers is the equitable distribution of benefits derived from commercial exploitation; it does not address whether commercial exploitation is an appropriate use of the resource.[110]

Alternatively, CHDD developed out of international concern for the protection of cultural and national heritage. The nationalist-preservationist development in Europe and England spurred this concern.[111] The CHDD language reflected this preservationist spirit and was codified in the Convention for the Protection of Cultural Property in the Event of Armed Conflict and the Convention for the Protection of the

101. *See id.* at 431.
102. *Id.* at 427–28.
103. *Id.*
104. *Id.*
105. *Id.* at 428.
106. *Id.*
107. *Id.*
108. *Id.* at 429.
109. *Id.*
110. *Id.*
111. *Id.* at 430.

World Cultural and Natural Heritage.[112] CHDD "reflects the rare situation in which a public resource is composed of incremental, individual holdings."[113] Resources such as cultural artifacts and natural wonders, though created or situated within a particular nation, should be protected from exploitation or degradation because they contribute to global culture.[114] "[T]he doctrine reflects the normative stance that interdependence—among human beings and between humans and the non-human natural world—ought to be recognized and nurtured in national and international policy."[115] Unlike the ideals of CHPD, the ideals of CHDD square satisfactorily with the protection of human gene sequences.[116] CHDD functions to protect and preserve important cultural resources.[117] It functions to allow private entities to hold cultural resources for the purpose of preserving them for future generations.[118]

Although CHDD is an underdeveloped doctrine, it incorporates the ideals underlying protective regimes for items of cultural heritage.[119] As argued below, gene sequences can be conceptualized as products of intangible cultural heritage, and CHDD offers a duty-based, as opposed to property-based, rationale for protecting genetic information. The use of this doctrine is still problematic, however, because it labels the human genome as a common resource in need of preservation.[120] As argued below, the designation of the human genome as a common-heritage resource is inappropriate because individual genes embody an uncommon heritage.

C. The Uncommon Heritage of Human Genes

Although attention is often directed at the molecular-biological structure and content of DNA sequences, little attention is given to the human cultural and evolutionary history of genetic-sequence information.[121] If CHPD is applied to gene-sequence patents, the rationale can be

112. *Id.*
113. *Id.*
114. *Id.* at 430–31.
115. *Id.* at 431.
116. *See id.*
117. *Id.* at 430.
118. *Id.* at 431.
119. *See id.*
120. *See id.* at 432.
121. Greenfield, *supra* note 27, at 471–72.

> Joining the social scientists and philosophers, scientists, engineers, biomedical researchers, and policy-makers have come to recognize that claims to DNA sequences can be perceived and characterized as intangible information, separate and thus distinguishable from the tangible molecule in which it is contained. DNA sequences can also be described or characterized as information which has materialized or is embodied as a mole-

attacked on the following grounds: (1) there is no one human genome common to all humanity; (2) gene patents protect limited regions, genes, or mutations that are only a small piece of genetic material common to any one human genome; and (3) human populations exhibit large amounts of genetic variation both within and among groups.[122] These attacks are difficult to overcome if the stated reason for sequence protection derives from an oversimplification of the meaning of genetic information. The conceptualization of gene sequences as part of a united whole, whether literally or symbolically, provides little incentive to change an accepted intellectual property regime.

1. There Is No One Human Genome

In 2001, the Human Genome Project provided researchers access to a complete sequence of the entire human genome.[123] Project contributors compiled a draft sequence patching together sequence data for every human gene.[124] The complete sequence of the human genome—a spectacular accomplishment—gives researchers access to a resource for understanding human genetic evolution.[125] The term "genome" refers to the entire amount of genetic information contained within our cells, including nuclear DNA and cytoplasmic mitochondrial DNA.[126] Nuclear DNA is diploid, meaning that we inherit one copy from each of our parents; thus, we each have two nuclear genomes that can be distinguished on the basis of genetic variation.[127] Additionally, each of those genomes contains unique mutations and variations that are different from all other individuals. The human genome discloses the identity of human genes as differentiated from those of other species; it is only common to all humans in that sense. In other words, the human genome is different than either the mouse genome or the dog genome, but the gene sequences found in my genome do not match those found in any other person's ge-

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> cular structure. Simply, when considering the nature and character of human DNA, "the medium is . . . the message." Despite this recognition and the growing literature devoted to the implications of human genetic material as information, intellectual property law to date has not treated it as such, but continues to allow the privatization of human genetic material in the form of patents based upon a limited and archaic definitional understanding of DNA sequences as simply biological "wet" material.

Id.

122. *See* David B. Resnik, *The Human Genome: Common Resource but Not Common Heritage, in* ETHICS FOR LIFE SCIENTISTS 195, 200–01 (Michiel Korthals & Robert J. Bogers eds., 2005).

123. *See* J. Craig Venter et al., *The Sequence of the Human Genome*, 291 SCIENCE 1304, 1304–51 (2001), *available at* http://www.sciencemag.org/content/291/5507/1304.full.

124. *Id.*

125. JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 25.

126. The mitochondrial genome is a haploid molecule inherited only through the maternal line.

127. JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 25.

nome sequence. Although it may seem obvious, the human genome is "common" only as an abstraction, not a literal entity.

2. What Do Gene Patents Protect?

Often, gene-patent claims encompass only a small portion of human genetic information.[128] As noted above, the BRCA patents claim the gene sequences that code for BRCA proteins and small nucleotide fragments of those sequences.[129] Importantly, gene-patent claims often extend not only to one identified sequence, but also to various mutations that may affect gene or protein function.[130] Sometimes claims also extend to undiscovered mutations.[131] To return to the BRCA example, mutations found within the BRCA sequence are associated with predispositions to breast and ovarian cancers.[132] Diagnostic tests like those used in BRCA-variant identification rely on the presence or absence of certain mutations to predict disease predisposition.[133] For these patents, the identification of the sequence mutations makes the BRCA patents valuable. Because mutations, by definition, reflect points of differentiation between individuals,[134] it is inappropriate to assume that human commonality is a viable rationale for eliminating patent protection for gene sequences.

IV. INTERNATIONAL AND DOMESTIC PROTECTIONS FOR CULTURAL HERITAGE

As noted in Part III.B, CHPD does not address concerns about genetic appropriation. Because it fails to account for the economic exploitation of public resources, CHPD will not allay fears about human genetic commercialization.[135] But a cultural-heritage theory, consistent with the

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128. *See, e.g.*, U.S. Patent No. 5,747,282 col.154 ll.56-58 (filed June 7, 1995).

129. Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 212–13 (S.D.N.Y. 2010). Additionally, the term "gene patent" has been used to refer to numerous types of claims, including divergent products and processes. *See* Holman, *supra* note 87, at 312.

> Some of the broadest product claims assert per se coverage to any isolated polynucleotide corresponding to a naturally-occurring human genetic sequence, which might be a full-length protein encoding gene, a gene fragment, a regulatory region, or a genomic region of unknown function. . . . Many product claims broadly encompass any polynucleotide encoding a naturally occurring protein, or even any polynucleotide claiming any variant of a naturally occurring protein.

Id.

130. *Molecular Pathology*, 702 F. Supp. 2d at 212–13 ("Claim 6 of the '492 patent, however, is considerably broader than claim 1 and is directed to any DNA nucleotide encoding any mutant *BRCA2* protein that is associated with a predisposition to breast cancer.").

131. *See id.*

132. *Id.* at 185.

133. *Id.*

134. JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 46–86.

135. Ossorio, *supra* note 20, at 430.

ideals of CHDD, can allow for the protection of genetic resources. The international community created several legal regimes to protect cultural heritage from appropriation and commercial exploitation.[136] Additionally, although U.S. law centers mostly on property-based protections for tangible cultural artifacts, some legal precedent exists in U.S. federal Indian law to afford protection for intangible cultural heritage.

Inevitably, a discussion about cultural heritage requires an attempt to define the term "culture." Culture is enormously complex and anthropologists have vigorously debated a satisfactory definition for over a century.[137] Despite its elusive definition, most people have a general sense of what culture encompasses. Culture might be defined as including all aspects of a group of people's past, present, and future. It is the tangible art, writings, and architecture made by a particular group, but it is also the intangible knowledge, traditions, and beliefs held by that group.[138] Cultural heritage, then, is both the tangible and intangible culture passed down from generation to generation.[139]

A. The International Community Recognizes and Protects Intangible Cultural Heritage

The international community recognizes the importance of offering legal protections for both tangible and intangible cultural heritage.[140] The 2003 United Nations Educational, Scientific, and Cultural Organization (UNESCO) Convention on the Safeguarding of Intangible Cultural Heritage[141] (2003 UNESCO Convention) seeks to protect intangible cultural heritage, ensure respect and appreciation of culturally derived materials, increase global awareness of its importance, and facilitate international cooperation and assistance.[142] The 2003 UNESCO Convention was enacted in 2006 and features more than 100 state parties.[143] It covers "practices, representations, expressions, knowledge, skills—as well as

136. *See* discussion *infra* Part IV.A.

137. *See* Peter K. Yu, *Cultural Relics, Intellectual Property, and Intangible Heritage*, 81 TEMP. L. REV. 433, 441 (2008).

138. *See id.* at 443.

139. *See id.* ("Although the protection for cultural heritage initially focused primarily on [tangible culture], such protection has now been extended to [intangible culture]."). It is important to note that a cultural artifact might be both tangible and intangible cultural heritage. For example, a rare manuscript might be protectable both as a physical artifact of manufacture and as a representation of the history, tradition, or ideology of the people at the time and place where it was written. *See id.*

140. *See id.*

141. UNESCO Convention for the Safeguarding of the Intangible Cultural Heritage art. 1, Oct. 17, 2003, 2368 U.N.T.S. 35 [hereinafter 2003 UNESCO Convention], *available at* http://unesdoc.unesco.org/images/0013/001325/132540e.pdf.

142. Yu, *supra* note 137, at 434.

143. *Id.*

the instruments, objects, [artifacts,] and cultural spaces associated therewith . . . ."[144]

In 2005, many signatories of the 2003 UNESCO Convention adopted the Convention on the Protection and Promotion of the Diversity of Cultural Expressions (2005 UNESCO Convention).[145] The 2005 UNESCO Convention aims to create beneficial conditions wherein cultures can flourish independently and interact freely with other cultures.[146] Moreover, it encourages cultures and countries to engage in an ongoing dialogue.[147] Additionally, in 2007, the United Nations adopted the Declaration on the Rights of Indigenous Peoples (DRIPS).[148] DRIPS articulates specific protectable rights of indigenous groups.[149] Under DRIPS, those groups have "the right to maintain, control, protect and develop their cultural heritage, traditional knowledge and traditional cultural expressions, as well as manifestations of their sciences . . . including human and genetic resources."[150] In codifying the above conventions and declaration, the international community demonstrated its concern for protecting cultural heritage from misappropriation.

B. Limited Domestic Protection Exists for Cultural Heritage

Protection of cultural heritage in the United States developed out of concern for protecting Native resources from commercial exploitation.[151] Currently, most legislation focuses on protecting tangible cultural resources,[152] but the Native American Graves Repatriation Act of 1990 (NAGPRA)[153] affords legal protection to both "sacred objects" and "cultural patrimony."[154] Unlike earlier legislation that dealt with policing illicit trade of art and cultural products,[155] NAGPRA was passed with the

144. 2003 UNESCO Convention, *supra* note 141, at art. 2, para. 1.

145. UNESCO Convention on the Protection and Promotion of the Diversity of Cultural Expressions, Oct. 20, 2005, 45 I.L.M. 269, *available at* http://unesdoc.unesco.org/images/0014/001429/142919e.pdf; Yu, *supra* note 137, at 434.

146. Yu, *supra* note 137, at 434.

147. *Id.*

148. Declaration on the Rights of Indigenous Peoples, G.A. Res. 61/295, U.N. Doc. A/RES/61/295 (Sept. 13, 2007), *available at* http://www.un.org/esa/socdev/unpfii/documents/DRIPS_en.pdf.

149. Yu, *supra* note 137, at 435.

150. *Id.*

151. Stephen D. Osborne, *Protecting Tribal Stories: The Perils of Propertization*, 28 AM. INDIAN L. REV. 203, 218 (2003).

152. *See id.*

153. Native American Graves Protection and Repatriation Act, 25 U.S.C. §§ 3001–3013 (2006).

154. Osborne, *supra* note 151, at 220.

155. *Id.* at 217. The Antiquities Act of 1906 established criminal penalties for individuals that destroyed or stole antiquities from federal land. Because the Antiquities Act was rarely enforced,

express purpose of recognizing tribal rights to Native American remains and associated artifacts.[156] NAGPRA requires federally funded institutions to inventory collections of human remains and funerary objects to determine cultural affiliation.[157] If such remains are affiliated with a federally recognized tribal entity, the institution must repatriate the remains and objects.[158] NAGPRA recognizes that Native American property rights exist in objects of cultural heritage and that these rights are inalienable.[159] In identifying a category of items as "cultural patrimony," NAGPRA acknowledges a communal interest in cultural resources.[160]

Although U.S. law is generally concerned with affording individual-based property protections, NAGPRA highlights at least the possibility that U.S. law can accommodate community-based rights for cultural heritage.[161]

V. HUMAN GENE SEQUENCES ARE INTANGIBLE CULTURAL HERITAGE

Humans do not comprise a single randomly mating population; there are patterns of genetic variation—or structure—that reflect a history of geographical, linguistic, ethnic, cultural, and religious nonrandom assortment.[162] Because these differences in experience helped to shape differences within our genes, gene sequences should be recognized as a form of intangible cultural heritage.

Population genetics and anthropological genetics are disciplines that seek to understand how our genes reflect differences across populations and how evolutionary, environmental, and cultural processes have created that diversity within the human genome.[163] By analyzing genetic

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Congress enacted the Archaeological Resources Protection Act (ARPA) of 1979. Similar to the Antiquities Act, ARPA punished looting and desecration of culturally valuable sites and artifacts. Neither Act, however, explicitly recognized the communal cultural rights of Native American groups. *Id.* at 216–17.

156. *Id.* at 218.

157. *Id.*

158. *Id.* at 219.

159. *Id.* Under NAGPRA, "cultural patrimony" is:

> an object having ongoing historical, traditional, or cultural importance central to the Native American group or culture itself, rather than property owned by an individual Native American, and which, therefore, cannot be alienated, appropriated, or conveyed by any individual regardless of whether or not the individual is a member of the Indian tribe or Native Hawaiian organization and such object shall have been considered inalienable by such Native American group at the time the object was separated from such group.

25 U.S.C. § 3001(3)(D) (2006).

160. Osborne, *supra* note 151, at 219.

161. *See id.* at 228.

162. *See generally* JOBLING, HURLES & TYLER-SMITH, *supra* note 24.

163. *See id.*

diversity between human populations, researchers tell a story about human history and cultural heritage.[164]

A. Genes as Storytellers

Although the causal relationships and interactions between cultural and genetic evolution are quite complicated, consider one illustration of a cultural–genetic coevolutionary relationship involving human adaptation to dietary change. Lactase persistence is the ability of an adult to digest lactose, the primary sugar found in milk.[165] Although some adults are able to digest lactose beyond weaning, most adults lose that ability due to a rapid postweaning decrease in production of intestinal lactase, the enzyme that breaks down lactose.[166] The effects of accumulated lactose in the intestine are associated with what we commonly refer to as lactose intolerance.[167] The permanent reduction in lactase production after weaning is common to all mammals and was the ancestral state of all humans until about ten thousand years ago.[168] Currently, however, large numbers of people across the world retain the ability to produce lactase as adults.[169]

The worldwide distribution of lactase persistence is highly nonuniform; the highest prevalence rates occur in European and African pastoralist groups, while lower rates are found in the Middle East, the Mediterranean, and in south and central Asia.[170] The lowest persistence rates are found among Native Americans, Pacific Islanders, and in people of sub-Saharan Africa and southeast Asia.[171] The phenotype of lactase persistence correlates with cultures that have historically used fresh milk, and it has long been thought to be associated with human adaptation to dietary change spurred by the advent of agriculture in the Middle East.[172]

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164. *See id.*

165. Dallas M. Swallow, *Genetics of Lactase Persistence and Lactose Intolerance*, 37 ANN. REV. GENETICS 197, 198 (2003).

166. JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 414.

167. *Id.*

168. *See* Edward Hollox, *Genetics of Lactase Persistence—Fresh Lessons in the History of Milk Drinking*, 13 EUR. J. HUM. EVOLUTIONARY GENETICS 267, 267 (2005); *see also* J. Burger et al., *Absence of the Lactase-Persistence-Associated Allele in Early Neolithic Europeans*, 104 PROC. NAT'L ACAD. SCI. 3736, 3737–38 (2007) (genotyping Neolithic human skeletal remains for eight individuals and finding only the ancestral allelic state present for lactase persistence).

169. *See generally* JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 415–18 (providing an overview of lactase persistence research); Hollox, *supra* note 168, at 267–69 (reviewing research directed at whether the genetic locus underwent recent positive selection); Swallow, *supra* note 165, at 197–219 (offering a more detailed review of the genetic basis for lactase persistence).

170. JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 416.

171. *Id.*

172. *See id.* at 415–18; Swallow, *supra* note 165, at 197–219; *see also* Hollox, *supra* note 168, at 267–69.

Several hypotheses attempt to explain the geographic distribution of lactase persistence.[173] One theory posits that if groups displayed strong cultural transmission of milk consumption from generation to generation, selective pressures following the adoption of dairying would account for the rapid spread of the persistence trait.[174] The linear cultural transmission (strong reliance on milk consumption as opposed to other types of dietary consumption) would account for the population-specific distribution of the lactase-persistence trait.[175] This example illustrates the lineage and culturally specific structuring of genetic diversity across human populations.

The lactase-persistence mutation is an example of a genetic mutation directly correlated with a change in human behavior, but all genes are influenced by choices people make and reactions to cultural or environmental stress.[176] Genetic heritage is deeply intertwined with cultural heritage, and BRCA mutations, like all other genetic mutations, reflect unique historical events common to a particular group of people.[177]

BRCA1 was the first gene discovered to be associated with hereditary breast cancer.[178] Although first named by Mary-Claire King's research team in 1991, Mark Skolnick and colleagues at Myriad Genetics successfully cloned BRCA1 in 1994 and BRCA2 in 1995.[179] The Skolnick team identified truncation mutations[180] within the coding regions[181] of the BRCA genes; many of these mutations introduce a stop codon[182] within the reading frame such that the mutated BRCA sequence produces a nonfunctional BRCA protein.[183] Cells containing defective BRCA proteins experience damage to double-stranded DNA.[184] Because BRCA proteins are involved in DNA repair, damaged DNA is repaired via an error-prone process that results in chromosomal rearrangements.[185] The

173. *See* JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 416–19.

174. *See id.*

175. *See* Hollox, *supra* note 168, at 267–69.

176. *See id.*

177. *See id.*

178. Steven A. Narod & William D. Foulkes, *BRCA1 and BRCA2: 1994 and Beyond*, 4 NATURE REVS. CANCER 665 (2004).

179. *Id.*

180. Truncation mutations are sequence changes within the DNA that create altered proteins.

181. The coding region (reading frame) refers to the segment of the DNA sequence that becomes translated into a protein.

182. Stop codons are strings of three consecutive nucleotides that signify the end of the gene. Stop codons essentially tell the enzymes that read and copy the DNA sequence during mRNA transcription to stop at that point. If a nucleotide mutation changes the wild-type codon into a stop codon, the resulting protein will be shorter and nonfunctional.

183. Narod & Foulkes, *supra* note 178, at 666.

184. *Id.*

185. *Id.*

resulting chromosomal instability is thought to be a crucial feature of carcinogenesis.[186] Although BRCA mutations were primarily studied for their association with aggressive forms of cancer, researchers continued to explore the historical and evolutionary significance of BRCA variants.[187]

Soon after the identification of the BRCA genes, researchers identified different BRCA mutations across several human populations, including those in Finland, France, Hungary, Israel, Russia, and the United States.[188] Similar to the lactase-persistence mutation, population-specific BRCA variants originated at different times and in different parts of the world; these variants were passed down within families and migrated to new places with their human carriers.[189] Research shows that many BRCA mutations are "identical by descent,"[190] meaning that mutations found in different individuals derive from a common ancestor, not by mere coincidence.[191] If a mutation is identical by descent, one can extrapolate the date when the mutation arose; thus, in locating the mutation in one geographic area at one particular point in time, it is possible to learn which individuals are more likely to be affected and to design background-specific screening methods to detect predispositions to breast and ovarian cancers.[192]

For example, in 2008, F. Marroni and colleagues estimated the age of a BRCA1 mutation thought to be a founder allele—or first mutation of the ancestral state—originating in Tuscany.[193] They reconstructed the genetic history of the mutation from carrier families and determined that the most recent common ancestor likely lived in Tuscany roughly 750

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186. *Id.*

187. *See, e.g.*, N. Ah Mew et al., *Haplotype Analysis of a BRCA1: 185delAG Mutation in a Chilean Family Supports its Ashkenazi Origins*, 62 CLINICAL GENETICS 151, 151 (2002) (studying the significance of Ashkenazi founder mutations in a Chilean individual with no known Ashkenazi ancestry and noting that the founder mutation was likely carried by crypto-Jews of Sephardic origin to South America during Spain's sixteenth-century colonization effort).

188. *Id.*; Csilla I. Szabo & Mary-Claire King, *Population Genetics of BRCA1 and BRCA2*, 60 AM. J. HUM. GENETICS 1013, 1013 (1997).

189. Szabo & King, *supra* note 188, at 1013.

190. JOBLING, HURLES & TYLER-SMITH, *supra* note 24, at 503.

191. F. Marroni et al., *Reconstructing the Genealogy of a BRCA1 Founder Mutation by Phylogenetic Analysis*, 72 ANNALS OF HUM. GENETICS 310, 310 (2008). Additionally, there are instances where BRCA mutations arose independently in different populations at different points in time. *Id.*

192. *Id.* at 311.

193. *Id.* Marroni et al. looked at the BRCA1* 1499insA mutation and genotyped a DNA segment surrounding the mutation in fifty unrelated individuals. The segment contained numerous other mutations (in this case, short tandem repeats (STRs)). The STRs were used to construct haplotypes (individuals share a "haplotype" if they have the same pattern of mutations, or allelic states for a particular region of DNA). By comparing the length of the shared haplotypes between each pair of sampled individuals, Marroni and colleagues estimated the age of the most recent common ancestor carrying the founder allele. *Id.*

years ago.[194] Individuals carrying the founder mutation dispersed throughout Italy sometime after that date.[195] Given the estimated date, the dispersion of carrier individuals in Italy could have coincided with Lorenzo de' Medici's death in 1492.[196] Following his death, the preacher Girolamo Savonarola prophesized the Apocalypse and persecuted material pleasures.[197] Many Tuscan citizens left the city in search of better fortunes in response to intertown fighting and social unrest.[198]

This hypothesis, while fanciful, highlights why a person's genes are not merely a function of biology. Rather, genetic diversity represents choices made by individuals in response to particular cultural and historical circumstances. Who we choose to marry, how many children we choose to have, and where we choose to live are all decisions that influence the genetic makeup of our future descendents. Gene sequences, then, convey information about our cultural heritage. Because exclusionary rights granted by patents on gene sequences generate wealth for patent holders, cultural heritage is commoditized when patents are granted for human gene sequences. Such commoditization benefits the patent holder at the expense of the individual when access to an individual's genetic makeup is unfairly restricted.

The plaintiffs in *Molecular Pathology* were denied access to information about their susceptibility to cancer because the cost of the diagnostic test was prohibitively expensive.[199] As a result, they were denied access to knowledge about the specific mutations they carry. They were denied access to mutations shared by family members that resulted from a particular cultural trajectory. The plaintiffs were denied access to a part of their intangible cultural heritage. In this instance, patents directly conflict with personal rights to access information about an individual's past, present, and future.

B. Protecting Human Gene Sequences

Human DNA sequences identify two important pieces of information. First, sequences give researchers information about an individual's genetic makeup. Patents on gene sequences prevent clinicians from testing for genetic diseases unless they pay the patent holder for use rights. Second, DNA sequences represent an individual's cultural heritage, and

194. *Id.* at 315–16.

195. *Id.* at 316.

196. *Id.* Medici was an Italian statesman and de facto ruler of the Florentine Republic. His death marked the end of Florence's Golden Age. *Medici Family*, NEW WORLD ENCYCLOPEDIA, http://www.newworldencyclopedia.org/entry/Medici_family (last visited Mar. 19, 2011).

197. *Id.*

198. *Id.*

199. *See* Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 189 (S.D.N.Y. 2010).

patented genes misappropriate rights to that information. Because no logical distinction can be made between the gene sequence as it exists in the cell and the sequence after it has been isolated, the DNA sequence can be construed as both a product of nature and a piece of intangible cultural heritage. Gene-sequence patents should be invalidated because they grant exclusionary rights over naturally and culturally derived information.

In its recent amicus brief agreeing in part with the district court's ruling in *Molecular Pathology*, the U.S. Department of Justice (DOJ) reversed its former stance that isolated gene sequences are patentable subject matter.[200] The amicus brief stated that "the unique chain of chemical base pairs that induces a human cell to express a BRCA protein is not a 'human-made invention . . . .'"[201] While it is true that the gene sequence was not invented by the researcher that discovered it, the sequence can be conceptualized both as a product of nature and as a product of human ingenuity. Dynamic interplay between natural processes and human choice created the variation found in the human genome, and genes tell the story of our cultural heritage.

Intangible cultural heritage is protected under multiple international declarations and conventions.[202] These agreements protect intangible cultural heritage from misappropriation by encouraging member nations to respect the value of culturally derived information to its producers, their cultural descendents, and humanity.[203] Initially, cultural heritage was considered a form of personal property.[204] Attaching personal property rights to cultural heritage, however, is particularly problematic. Affording group rights to an article of culture creates a static right of ownership for a particular group.[205] Gene sequences contain mutations that may be shared by different groups either because the mutations were inherited or because they arose independently. Therefore, it would be impossible to tease apart the exact lineage of each individual and assign a property interest for each gene.

The protective interest over gene sequences is better construed as a common duty to protect human sequence data from commercial exploitation and appropriation. Unlike CHPD theory, the conflict of rights does

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200. Brief for the United States as Amicus Curiae in Support of Neither Party at 10, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (2010) (No. 2010-1460).

201. *Id.* "We acknowledge that this conclusion is contrary to the longstanding practice of the Patent and Trademark Office, as well as the practice of the National Institutes of Health and other government agencies that have in the past sought and obtained patents for isolated genomic DNA." *Id.* at 18.

202. *See supra* Part IV.

203. *Id.*

204. *Id.*

205. *See* Naomi Mezey, *The Paradoxes of Cultural Property*, 107 COLUM. L. REV. 2004, 2005 (2007).

not derive from inherent property rights to the whole genome. Rather, the conflict arises because exclusionary rights are granted over small pieces of information that either independently or collectively tell a story about an individual's cultural identity. Patent law inappropriately gives the patent holder the power to restrict or prohibit access to information that is both personal and communal.[206]

VI. CONCLUSION

The BRCA litigation has forced the courts to address the gene-patent debate head on. The case illustrates the harm posed by gene patents: individuals are denied access to genetic tests because a patent holder exercises exclusionary rights over a gene sequence. Patent law is designed to promote and create incentives for scientific innovation and to disclose important discoveries to the public. In this instance, however, patents on human gene sequences are both legally and ethically questionable, and the USPTO's current patent policy fails to weigh competing interests adequately. By deferring to business interests without critically evaluating the subject matter of gene-sequence patents, the USPTO grants exclusionary patent rights that directly conflict with access rights to intangible cultural heritage. DNA is more than a biological molecule; it contains information that uniquely identifies an individual's cultural and evolutionary history. As such, this information should be recognized and protected as a form of intangible cultural heritage.

206. For a related point, see Greenfield, *supra* note 27, at 468–69 ("Once removed from the control of the human body and populations, a DNA sequence regarded as pure information establishes a new hierarchy: whoever controls this intellectual product, the bio-power of the genome, assumes a new control over life.").