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Genes 101: Are Human Genes Patentable Subject Matter?

Andrew Bowman
University of Richmond

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by Andrew Bowman*

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I. INTRODUCTION

[1] Genes are the fundamental building blocks of all living things. They dictate hair color, eye color, even susceptibility to cancer.[1] As such, genes inherently possess untold power. The ability of a sole company to

* J.D. Candidate 2013, University of Richmond School of Law. I would like to thank Professor Kristen Osenga for her helpful comments and insight in publishing this comment.

[1] *See* Patrick Sulem et al., *Genetic determinants of hair, eye and skin pigmentation in Europeans*, 39 NATURE GENETICS 1443, 1444, 1446, 1448 (2007); Richard Wooster et al., *Localization of a Breast Cancer Susceptibility Gene, BRCA2, to Chromosome 13q12-13*, 265 SCI. 2088, 2089 (1994).

wield this omnipotence makes a human gene patent highly sought after.[2] Notwithstanding the other requirements for patentability, the eligibility of human genes as 'inventions' worthy of patent protection under 35 U.S.C. § 101 has recently been called into question. In *Association for Molecular Pathology v. U.S. Patent and Trademark Office* ("the *Myriad* decision"), the Federal Circuit answered in the affirmative.[3] In arriving at this conclusion, the majority rejected the biological significance of the information contained in the deoxyribonucleic acid ("DNA") molecule in favor of a purely structural approach.[4] The court incorrectly concluded that an isolated DNA molecule is "markedly different" from native DNA because of minor structural differences.[5] The court discounted the fact that both the isolated DNA and the relevant portion of the native DNA contain the same sequence of nucleotides and therefore the same biological information.[6] While the Federal Circuit incorrectly considered this issue by narrowly looking at DNA structure, there is an alternative comprehensive approach that considers both important properties of DNA. This comment proposes a totality-of-the-circumstances approach to analyzing biological molecules under § 101 such that both the structure

[2] Gene patents have broad implications in both the scientific and medical communities; they permit the monopolization of scientific research and genetic testing on that specific gene. *See generally* SECRETARY'S ADVISORY COMM. ON GENETICS, HEALTH, AND SOC'Y, DEP'T OF HEALTH & HUMAN SERVS., GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 28-31 (2010), *available at* http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_patents_report_2010.pdf; Mildred K. Cho et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3, 5-7 (2003).

[3] (*Myriad II*) 653 F.3d 1329, 1334 (Fed. Cir. 2011).

[4] *Id*. at 1352-53.

[5] *See id.* at 1353.

[6] *See id*.

and its information is examined. Part II of this note reviews relevant precedent in patent law. Part III analyzes the Federal Circuit's *Myriad* decision, and Part IV explains the potential effects of the recent Supreme Court decision *Mayo Collaborative Services v. Prometheus Laboratories*. Finally, in Part V, the patent eligibility of human genes is examined. Analyzing this issue under the proposed totality-of-the-circumstances approach, this article concludes that isolated human genes are not patentable.

II. GENE PATENT PRECEDENT

[2] In order to obtain a patent, an invention must comply with Title 35 requirements for patentability.[7] Subject matter eligible for patent protection is defined in § 101—the invention must be a "new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."[8] When enacting this statute, Congress intended it be interpreted broadly in order to cover "anything under the sun made by man."[9] While incredibly broad, the Court has recognized three main limitations: an inventor cannot patent the laws of nature, physical phenomena, or abstract ideas.[10] "The concepts covered by these exceptions are 'part of the storehouse of knowledge of all men . . . free to all men and reserved exclusively to none.'"[11]

[7] 35 U.S.C. § 101 (2006).

[8] *Id.*

[9] S. REP. NO. 82-1979, at 5 (1952).

[10] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980).

[11] Bilski v. Kappos, 130 S. Ct. 3218, 3225 (2010) (quoting Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948)).

[3] Interpreting these exceptions, the Court in *Diamond v. Chakrabarty* was faced with the issue of whether a human-made, genetically engineered bacterium was patentable subject matter.[12] The Court extended the prohibition on the patenting of the laws of nature to include the products of nature.[13] To be patentable, the invention must be a product of human ingenuity; it must be "markedly different" from what exists in nature, "having a distinctive name, character, [and] use."[14] Thus, the Court concluded that by adding two oil-degrading plasmids Chakrabarty had created a new bacterium sufficiently different from that occurring in nature.[15]

[4] In enunciating its "markedly different" standard, the *Chakrabarty* Court adopted the standard promulgated in *Hartranft v. Wiegmann*.[16] The issue in *Hartranft* was whether a polished seashell was an article of manufacture.[17] After harvesting, raw seashells were acid etched, ground to expose their interior layer, and then polished.[18] The Court held that even though the shells had undergone changes, they still had the same "name, character, [and] use" as a shell picked up off the ground.[19] Thus,

[12] 447 U.S. at 305.

[13] *Id*. at 313; *see also* H.R. REP. NO. 1129, at 7 (1930); S. REP. NO. 315, at 6 (1930).

[14] *Diamond*, 447 U.S. at 309-10 (quoting Hartranft v. Wiegmann, 121 U.S. 609, 615 (1887)).

[15] *Id*. at 310.

[16] *Id.* at 309-10 (citing *Hartranft*, 121 U.S. at 609).

[17] *Hartranft*, 121 U.S. at 613.

[18] *Id*. at 611.

[19] *Id*. at 615.

the polished shells were not transformed into a different article of manufacture.[20]

[5] The seashells in *Hartranft* are similar to the inoculant created in *Funk Brothers Seed Co. v. Kalo Inoculant*.[21] In *Funk Brothers*, the Court sought to determine the validity of a patent for an inoculant containing several species of bacteria that were not mutually inhibiting.[22] As the bacteria in the inoculant were identical to the bacteria as they existed in nature, the patent claimed the naturally occurring properties of the bacteria; the fact that when combined they do not inhibit the desirable properties of each other.[23] Thus, the invention was held not patentable subject matter as it sought to claim the laws of nature.[24] In the shadow of this precedent, the Federal Circuit took it upon themselves to decide the issue of whether human genes are patentable subject matter.

III. THE *MYRIAD* DECISION

[6] The controversy began in 2009 when Association for Molecular Pathology[25] filed a declaratory judgment action against Myriad Genetics,

[20] *Id*.

[21] *See* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948).

[22] *Id*. at 128.

[23] *Id*. at 131.

[24] *Id*. at 132.

[25] Association for Molecular Pathology was the first named party in the case. Other plaintiffs include the American College of Medical Genetics, the American Society for Clinical Pathology, Breast Cancer Action, Boston Women's Health Book Collective, eight doctors, and six women seeking breast cancer genetic testing. Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad I*), 702 F. Supp. 2d 181, 186-89 (S.D.N.Y. 2010).

the University of Utah Research Foundation, and the U.S. Patent and Trademark Office (collectively "Myriad") alleging fifteen claims, spanning seven patents, were invalid as unpatentable subject matter.[26] The patents at issue covered segments of "isolated DNA" and cDNA[27] from the BRCA1 and BRCA2 genes as well as methods for "analyzing" or "comparing" segments of isolated DNA to determine the presence of mutations.[28] The BRCA1 and BRCA2 genes encode proteins integral in the repair of DNA breaks.[29] Certain mutations in these genes have been observed to correlate to one's susceptibility to breast and ovarian cancer.[30]

[7] Recognizing the case's significance, the district court concisely stated the issue: "[a]re isolated human genes . . . patentable?"[31] The district court held human genes not patentable under § 101 because "DNA represents the physical embodiment of biological information" and thus falls under the law of nature exception to § 101.[32] Myriad appealed to the Federal Circuit.[33]

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[26] *Id*. at 184 (challenging the validity of claims 1, 2, 5, 7, and 20 of U.S. Patent 5,747,282, claims 1, 6, and 7 of U.S. Patent 5,837,492, claim 1 of U.S. Patent 5,693,472, claim 1 of U.S. Patent 5,709,999, claim 1 of U.S. Patent 5,710,001, claim 1 of U.S. Patent 5,753,441, and claims 1 and 2 of U.S. Patent 6,033,857).

[27] Isolated DNA is a nucleotide segment removed from the chromosome and separated from the extraneous cellular components. *See infra* Part V.D. cDNA is a piece of artificially created DNA. *Id.*

[28] *Myriad II*, 653 F.3d 1329, 1334-35 (Fed. Cir. 2011).

[29] Kiyotsugu Yoshida & Yoshio Miki, *Role of BRCA1 and BRCA2 as regulators of DNA repair, transcription, and cell cycle in response to DNA damage*, 95 CANCER SCI., 866, 866-68 (2004).

[30] *Myriad II*, 653 F.3d at 1339; *see also* Wooster, *supra* note 1, at 2089.

[31] *Myriad I*, 702 F. Supp. 2d at 185.

[32] *Id*.

[33] *Myriad II*, 653 F.3d at 1333.

A. Federal Circuit: Judge Lourie's Majority Opinion

[8] In his opinion Judge Lourie characterizes three types of DNA: native DNA, isolated DNA, and cDNA.[34] Native DNA is the single DNA molecule that composes each chromosome.[35] Native DNA, as the name suggests, is the form of DNA exactly as found in nature.[36] It contains both coding exon and non-coding intron regions of many genes.[37] It is found covalently bonded to a complementary strand of DNA and wound around histones, proteins which "package" or condense the DNA into chromatin.[38] Isolated DNA, on the other hand, is native DNA in which the histones have been removed and a sequence, containing an entire gene, has been cut out of the chromosomal structure.[39] Finally, cDNA is a form of synthetic DNA, made by humans in a laboratory, containing only protein coding regions of DNA.[40]

[9] Examining the patent eligibility of each of these types of DNA, Judge Lourie quickly decided the fates of genomic DNA and cDNA. He correctly distinguished native DNA as existing in nature, thus preventing

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[34] *Id*. at 1351-53.

[35] *Id*. at 1351.

[36] *Id*.

[37] *Id*. at 1339.

[38] *Myriad II*, 653 F.3d at 1338 fig.4.

[39] *Id*. at 1351-52. Judge Lourie also incorrectly lumps isolated cDNA with isolated genomic DNA. When considering isolated DNA, isolated cDNA should not be considered along with isolated genomic DNA. Isolated cDNA is simply a shortened form of cDNA, and therefore should be analyzed as cDNA for the purposes of § 101.

[40] *Id*. at 1338-39.

patenting.[41] As native DNA is devoid of any human innovation or modification, it is not patent-eligible subject matter under § 101.[42] Judge Lourie also correctly found cDNA to be patentable subject matter.[43] The creation of cDNA requires extensive human intervention and modification; it is quintessentially man-made.[44] Therefore, Judge Lourie held it should be afforded patent protection under § 101.[45]

[10] On the other hand, determining the patent eligibilty of isolated genomic DNA sequences required a more intricate analysis. Examining isolated DNA, Judge Lourie compares it to its native counterpart from a chemical, as opposed to a biological, perspective.[46] From a chemical perspective, the differences in DNA structure were compared, not the differences in information content characteristic of a biological perspective.[47] Looking at the structure of the chromosomal DNA, Judge Lourie noted the chromosomes containing the BRCA1 and BRCA2 genes are approximately eighty million and one hundred fourteen million nucleotides in length, respectively.[48] Yet, the actual genes are merely fragments of the astronomically large strands of DNA comprising each

[41] *See id*. at 1351.

[42] *See id*.

[43] *See Myriad II*, 653 F.3d at 1350.

[44] *See id*. at 1338-39.

[45] *Id*. at 1350.

[46] *Id*. at 1351-53.

[47] *Id*.

[48] *Myriad II*, 653 F.3d at 1351-52.

chromosome.[49] When the BRCA1 and BRCA2 genes are removed in the creation of isolated DNAs, each are approximately 7,000 and 11,000 base pairs in length, respectively.[50] Judge Lourie states this extensive modification of the chemical structure of the genomic DNA makes isolated DNA's *structure* markedly different from that of native DNA.[51] And for purposes of patentability, it is the change in physical structure of the molecule, not the information that is conveyed, that is the proper gauge for determining the differences from native form.[52] Therefore, Judge Lourie concluded that the chemical bonds broken in the creation of isolated DNA are sufficient structural changes to warrant patent eligibility.[53]

B. Federal Circuit: Judge Moore's Concurrence-In-Part

[11] Arriving at the same conclusion as the majority, Judge Moore applied a slightly different, more skeptical, analysis of the science. As an initial matter, Judge Moore agreed that cDNA is patent eligible subject matter; it is made by man and is not found in nature.[54] Next, she

[49] BRCA2 is one of 720 genes composing the 115M bp of chromosome 13, and BRCA1 is just one of the 1773 genes on the 81M bp chromosome 17. NCBI Map Viewer, Chromosome 13, NAT'L CENTER FOR BIOTECHNOLOGY INFO., http://www.ncbi.nlm.nih.gov/mapview/maps.cgi?ORG=hum&MAPS=ideogr,est,loc&LINKS=ON&VERBOSE=ON&CHR=13 (last visited Mar. 19, 2012); NCBI Map Viewer, Chromosome 17, NAT'L CENTER FOR BIOTECHNOLOGY INFO., http://www.ncbi.nlm.nih.gov/mapview/maps.cgi?ORG=hum&MAPS=ideogr,est,loc&LINKS=ON&VERBOSE=ON&CHR=17 (last visited Mar. 19, 2012).

[50] *Myriad II*, 653 F.3d at 1351-52.

[51] *Id*. at 1352.

[52] *Id*. at 1353.

[53] *Id*. at 1352-53.

[54] *Id*. at 1364 (Moore, J., concurring).

examined the structural differences between isolated DNA and genomic DNA. Agreeing with the majority, she found that the removal of a segment of DNA from the chromosome is a significant modification,[55] but that modification only satisfies § 101 because the change imparts a whole new utility upon the isolated DNA molecule that is not present in the genomic DNA.[56] Judge Moore qualifies this determination as being heavily influenced by the historical practice and examination guidelines of the U.S. Patent Office allowing isolated DNA claims.[57] She notes that without this background, she might have found that an isolated gene is not patentable subject matter as it "serves the same ends devised by nature."[58]

C. Federal Circuit: Judge Bryson's Concurrence-In-Part and Dissent-In-Part

[12] Unlike the majority and concurring opinions, Judge Bryson concluded isolated DNA is not patentable subject matter as it is "not materially different from native genes."[59] Looking at the significance of the changes undergone in the creation of isolated DNA, he found the majority and concurrence placed too much emphasis on the breaking of a chemical bond.[60] Chemical bonds are broken regularly in a vast myriad of processes: during the cutting and cleaning of diamonds or the isolation of

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[55] *Myriad II*, 653 F.3d at 1364-65 (Moore, J., concurring).

[56] *Id*. at 1365.

[57] *Id*. at 1367 (citing Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093-94 (Jan. 5, 2001)).

[58] *Id.* at 1366-67.

[59] *Id*. at 1373-75 (Bryson, J., dissenting).

[60] *Myriad II*, 653 F.3d at 1376.

the element lithium.[61] Even in genetics, the chemical bonds holding the DNA backbone together are broken and reformed on a regular basis.[62] The routine nature of breaking chemical bonds therefore makes them an arbitrary method for determining patentability of DNA, especially when the method has been expressly rejected in the past.[63]

[13] Rejecting the chemical approach of looking solely at structure, Judge Bryson likens the creation of isolated DNA to the snapping of a leaf from a tree.[64] When a person snaps a leaf from a tree, she breaks chemical bonds that had previously attached it to the branch. In doing so, she has imparted new characteristics and uses upon the leaf. It no longer can be used to convert the sun's energy into food, as nature would use it. Rather, it can be used for decoration, consumption, or a myriad of other uses. Yet, as Judge Bryson notes, even though the leaf was broken from the structure of the tree by man, and this breaking imparted a new utility not previously present, the leaf was created by nature, just as the tree was, and is therefore not patentable.[65] Isolated DNA should be considered in the same manner. Genomic DNA is created by nature. While breaking off a small segment may impart some new utility, it does not change the fact that nature created that segment. Therefore, Judge Bryson found DNA sequences isolated from genomic DNA unpatentable.[66]

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[61] *Id.* at 1375-77 (explaining that diamonds and lithium are not patentable, man-made inventions merely because they involve the breaking of chemical bonds).

[62] Topoisomerases, a type of enzyme, introduce nicks or double strand breaks into DNA to relieve supercoiling caused by DNA replication. ROBERT F. WEAVER, MOLECULAR BIOLOGY 658 (4th ed. 2008).

[63] *See Myriad II*, 653 F.3d at 1376 (Bryson, J., dissenting).

[64] *Id*. at 1377.

[65] *See id.*

[66] *Id*. at 1375.

IV. THE EFFECT OF *MAYO V. PROMETHEUS LABORATORIES*

[14] In light of the recent decision *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, the Federal Circuit was directed to reconsider its earlier decision that isolated human DNA is patentable.[67] While the *Mayo* decision related specifically to the patentability of processes claiming laws of nature, the Court's reasoning provides significant insight on analyzing patentability decisions directly implicating the laws of nature and § 101.[68] The Court's rejection of insignificant or inconsequential steps following the direct application of a law of nature further bolsters the notion that a substantial human innovative contribution is required for patentability.[69]

[15] Writing for the unanimous Court, Justice Breyer found Prometheus' patents claimed unpatentable subject matter.[70] The patents at issue claim methods for "optimizing [the] therapeutic efficacy" of treating certain autoimmune diseases.[71] The claimed methods sought to recapture the correlation between the amount of a drug administered and the resulting physiological effect.[72] The Court held this relationship alone

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[67] Ass'n for Molecular Pathology v. Myriad Genetics, No. 11-725, 2012 WL 986819, at *1 (Mar. 26, 2012) (vacating the judgment and remanding to the Federal Circuit for reconsideration).

[68] *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1294 (2012).

[69] *See id.* at 1297.

[70] *Id*. at 1305.

[71] *Id.* at 1295 (quoting U.S. Patent No. 6,355,623 (filed Apr. 8, 1999)).

[72] *Id.* at 1296.

was a law of nature and therefore not patentable.[73] In an attempt to circumvent a § 101 rejection, the claimed processes were drafted to include a transformative step to go beyond the law of nature.[74] While these superfluous steps would likely avoid § 101 rejection under *Bilski*'s "machine or transformation test," the Court found they "add[] nothing to the laws of nature that is not already present."[75] Thus, the Court held the addition of these "well-understood, routine, conventional" steps did not bestow patentability upon the law of nature.[76]

[16] In announcing this opinion, the Court reiterated a basic patent principle: patents should promote scientific innovation.[77] Thus, when examining patents involving the laws of nature, the scope of the claims should not be so broad as to "improperly t[ie] up the future use of the laws of nature."[78] To restrain further research into that law of nature would monopolize one of the "the basic tools of scientific and technological work"—directly contradicting a fundamental goal of patent law.[79]

[17] When the Federal Circuit reconsiders the patent eligibility of Myriad's isolated DNA claims, it should be cognizant of the similarities

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[73] *Mayo Collaborative Servs.*, 132 S. Ct. at 1297.

[74] *Id.*

[75] *Id.* at 1298.

[76] *Id.*

[77] *See id.* at 1301; *see also* U.S. CONST. art. 1, § 8, cl. 8 ("To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.").

[78] *Mayo Collaborative Servs.*, 132 S. Ct. at 1301.

[79] *Id.*

between Prometheus' and Myriad's patents; each involves a law of nature followed by a superfluous step. Just as the correlation between the quantity and effect of a drug is a law of nature, so too is a human gene.[80] Therefore, the added step of 'isolating' the whole gene from the chromosomal DNA should be analyzed like the "administering," "wherein," and "determining" steps of the Prometheus patents.

[18] The step of 'isolating' DNA does not add sufficient novel subject matter to the inherent law of nature to enable patenting. In order to transform a law of nature into patentable subject matter, the subsequent steps must be more than conventional, obvious, routine, or insignificant.[81] Like the "determining" and "wherein" steps of the Prometheus patent, the isolation of genomic DNA does nothing to change the law of nature embodied by the isolated gene.[82] Rather, it is a universally known tool in molecular biology: exactly the type of "well understood, routine, conventional activity" already engaged in by the scientific community that was insufficient to transform patent eligibility in *Prometheus*.[83] The claims directed towards isolated BRCA1 and BRCA2 genes do nothing more than attempt to monopolize the market in a law of nature embodied as the genes. Therefore, the claims towards isolated DNA should be held not patentable subject matter.

V. ARE GENES PATENTABLE SUBJECT MATTER?

[80] *See id.* at 1296.

[81] *Id.* at 1298.

[82] *See infra* Part V.A.

[83] Dennis Crouch, Mayo v. Prometheus*: Natural Process + Known Elements = Normally No Patent*, PATENTLYO (Mar. 20, 2012), http://www.patentlyo.com/patent/2012/03/mayo-v-prometheus-natural-process-known-elements-normally-no-patent.html.

[18] Human genes, embodied as isolated DNA, are not patent-eligible subject matter. As the Supreme Court recently vacated the Federal Circuit's original *Myriad* ruling, they are again tasked with deciding whether isolated human DNA is patentable subject matter.[84] The majority in the first *Myriad* decision incorrectly relied solely upon a chemical perspective—considering changes to DNA's structure—when analyzing the differences between native and isolated DNA.[85] When examining the patent eligibility of DNA, the Federal Circuit should examine both its information and structure. The chemical perspective ignores the significance of the information content of DNA and, specifically, a gene. From a biological perspective, a piece of isolated DNA is *identical* to native DNA and, thus, fails the markedly different standard advanced by the court.[86] When rehearing the issue on remand, the Federal Circuit should consider all aspects of DNA, both structure and information, when examining the eligibility of biological molecules.

A. The Informational Significance of DNA

[19] DNA is the blueprint of life.[87] The information contained in DNA enables the creation of an entire human being.[88] The DNA molecule itself

[84] Ass'n for Molecular Pathology v. Myriad Genetics, No. 11-725, 2012 WL 986819, at *1 (Mar. 26, 2012).

[85] *See* Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 653 F.3d 1329, 1351-53 (Fed. Cir. 2011).

[86] *See, e.g.*, *Myriad I*, 702 F. Supp. 2d 181, 185 (S.D.N.Y. 2010).

[87] Robert Aronson & Jacqueline McMurtie, *The Use and Misuse of High-Tech Evidence by Prosecutors: Ethical and Evidentiary Issues*, 76 FORDHAM L. REV. 1453, 1469 (2007).

[88] *See* WEAVER, *supra* note 62, at 32.

is not incredibly complex; it is composed of a series of nucleosides[89] joined in a chain by a phosphate group.[90] Each nucleoside contains a deoxyribose sugar and one of four nitrogenous bases: adenine ("A"), thymine ("T"), cytosine ("C"), or guanine ("G").[91] Thus, the structure of DNA is composed of no more than repeating nucleotide segments of a nitrogenous base, the deoxyribose sugar, and the phosphate group arranged in a right-handed double helix.[92] DNA molecules exist in the nucleus double stranded, or hydrogen bonded to a complementary piece of DNA, and wound around histone proteins in the chromatin.[93] The histone's function is to package the large volume of DNA so that it can fit within the nucleus.[94] It simply binds the exterior of the DNA molecule and does not modify the DNA or its structure in any material way.[95]

[20] While this structure is important to DNA's function, it is the information contained in the nucleotide sequence—the order of the A, T,

[89] Nucleosides and nucleotides are different entities. A nucleotide contains a nucleoside as well as the phosphate group. *Id*. at 16-17. For the purposes of this comment, both are the functional equivalent.

[90] J.D. Watson & F.H.C. Crick, *Molecular Structure of Nucleic Acids*, 171 NATURE 737, 737-38 (1953).

[91] *Id*.

[92] *Id*.

[93] WEAVER, *supra* note 62, at 23; Tony Kouzarides, *Chromatin Modifications and Their Function*, 128 CELL 693, 693 (2007).

[94] Kouzarides, *supra* note 93, at 693.

[95] WEAVER, *supra* note 62, at 40-41 (explaining how DNA fits into the grooves on the surface of the histone octamer and is only held in place through interactions with the histone tails).

C, and Gs—that makes DNA invaluable to an organism.[96] When an organism activates a gene, it reads and copies the nucleotide sequence in the process of transcription and then uses the copied sequence to produce a protein during translation.[97] During transcription, the cell's machinery synthesizes a copy of the activated gene out of RNA.[98] Then, the structure of the RNA is modified, including the removal of introns, to create mRNA.[99] During translation, three base segments, known as codons, of the mRNA are 'read' such that a specific amino acid is incorporated into the nascent protein based on the sequence of the nucleotides within that codon.[100] The protein is then incorporated into one of millions of processes of the organism. Thus, by providing the blueprint for the creation of cellular proteins, the information contained in DNA is an important property that cannot be ignored.

[21] It is important to note that transcription does not occur while the gene exists in its double stranded form as it would around histones. In order for the gene to be activated for transcription, the histone proteins are stripped away by the cell's machinery and the DNA strands are separated in what is known as the "transcription bubble."[101] Thus, when the actual informational content of the DNA is being accessed, the gene exists in a markedly similar state to that of isolated DNA—single stranded and unbound to proteins.

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[96] *Id*. at 32 (explaining how the DNA sequence informs the creation of a protein).

[97] *See id*. at 40-46.

[98] WEAVER, *supra* note 62, at 40-41.

[99] *Id*. at 401.

[100] *Id*. at 44-46.

[101] *Id*. at 41, 369-71.

B. The Chemical Versus Biological Perspective

[22] When examining the patent eligibility of human genes, there are two possible ways the subject matter can be examined—from a chemical or biological perspective. The chemical perspective can be characterized by looking strictly at the structure of the molecules composing DNA.[102] It looks solely at the molecular structure of DNA, the layout of the nucleotides and backbone, as well as any subsequent modification by humans. Adopting this perspective, Judge Lourie, writing for the majority, concluded that simply breaking the DNA backbone and the unzipping of the double stranded structure amounted to a "markedly different" change from the genomic DNA.[103] Examining the structure without regard to the information content it holds ignores a fundamental property of DNA.

[23] On the other hand, the biological perspective examines the information content of the gene. It looks not at the structure but at the information that structure reveals. DNA is known as the 'blueprint of life' because it contains information that dictates the creation of an entire organism.[104] While the structure does play a minor role in determining this information content, it is the genetic sequence, or order of the nucleotides within each gene, that contains the information.[105] By simply

[102] *See, e.g.*, *Myriad II*, 653 F.3d 1329, 1353 (Fed. Cir. 2011).

[103] *See id.* at 1354. Judge Lourie's reliance on a chemical perspective could be explained by his background in chemistry; he holds a master's degree in organic chemistry and a Ph.D. in chemistry. Biography of Alan D. Lourie, Circuit Judge, UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT, http://www.cafc.uscourts.gov/judges/alan-d-lourie-circuit-judge.html (last visited Jan. 16, 2012).

[104] *See generally* WEAVER, *supra* note 62, at 32 (characterizing the process by which DNA results in the creation of proteins).

[105] *See id.*

modifying the structure of the chromosome, i.e., excising a whole gene, no change is made to the information content of each gene.[106] The unchanged genetic sequence and information content in the isolated DNA would fail the "markedly different" standard when compared to the sequence and information contained in the genomic DNA.

[24] To exemplify this dichotomy between structure and information, consider an analogy from copyright law. Consider a book. A book is copyrightable with regard to the author's exact portrayal of the information it contains.[107] This is due in part to the fact that the societal value of the book is not in its structure—its number of pages, type of cover, or method of binding. Rather, the author's original portrayal of the information in the book is what makes the book useful and deserving of a copyright.[108] Thus, if a person copies a chapter of that book, she is an infringer.[109] This infringer did not modify that chapter in any way. She simply removed a piece of what already existed in the book and attempted to pass it off as her own. While the chapter has a "markedly different" structure than the whole book, the portrayal of the information contained in the chapter is identical to what previously existed in the book. The presence of that exact portrayal prevents the infringer from getting a new copyright even though the structure of the book is different because the significance of the book is not in its structure but in its content.[110]

[25] The same result should be obtained in patent law, where genomic DNA is the book and isolated DNA is the chapter. Native DNA, like a

[106] *See id.*

[107] Feist Publ'ns, Inc. v. Rural Tel. Serv. Co., 499 U.S. 340, 348 (1991).

[108] *Id*.

[109] 17 U.S.C. § 501(a) (2006).

[110] *See id.*

book composed of many chapters, is a unitary collection of many genes in a single strand of DNA.[111] Likewise, isolated DNA is a chapter; the largest pieces of isolated DNA contain at most a single gene.[112] As previously noted, the significance of DNA, both to the human body and for commercial exploitation, is mainly in its informational content, not its physical structure.[113] Examining DNA's patent eligibility solely based on its structural differences is the functional equivalent of granting copyrights on books based on the physical structure of the text. When examined in this informational context, the information contained in the isolated DNA is not "markedly different" from the relevant portion of the genomic DNA, just as the information's portrayal in the chapter is not "markedly different" from the information's portrayal in the entire book. Indeed, they are exactly the same. Thus, just as one could not obtain a copyright for simply removing the chapter of a book, one cannot obtain a patent for simply isolating a specific sequence of DNA containing a gene.

C. Isolated DNA is not Patentable Subject Matter

[26] When determining whether a piece of DNA is patent eligible subject matter, the court should take a totality-of-the-circumstances approach, examining both the structure and information of the DNA.

[111] *See generally* WEAVER, *supra* note 62, at 3.

[112] *Myriad II*, 653 F.3d 1329, 1338 (Fed. Cir. 2011). A potential counterargument is that certain isolated DNAs are composed of substantially smaller portions of a gene, i.e., segments ranging from 10-100 nucleotides in length. In this case, it can be argued that these smaller segments of DNA impart a markedly different utility upon the isolated DNA such that they should be afforded patent protection. This is the functional equivalent of borrowing a string of three words from the text of a book. It is virtually impossible to demonstrate that such a string is copyrightable; those three words likely are not a unique portrayal by an author. In this way, they have a unique utility for each use just as smaller segments of isolated DNA have a different function than the entire gene.

[113] *See supra*, Part IV.A.

While both the District Court for the Southern District of New York and the Federal Circuit deemed these approaches mutually exclusive, the Supreme Court historically rejected the rigid application of a single test when deciding issues of patentability.[114] In *KSR International v. Teleflex Inc.*, the Court rejected the exclusive application of the "teaching, suggestion, or motivation test" when determining issues of obviousness under § 103.[115] Similarly, in *Bilski v. Kappos*, the Supreme Court held when determining patentability of processes under § 101, the "machine-or-transformation test" was not the sole test for patentability.[116] While just a microcosm of the Court's decisions, these cases demonstrate the Court's proclivity for denying the application of narrow rules in patent law. This sort of narrow application is precisely the analysis the lower courts performed when the district court looked solely at information and the Federal Circuit looked solely at structure.[117] By considering both the structure and the information content, neither the immense biological significance of the nucleotide sequence nor the significance of structural modifications is discounted.

[27] Applying the "markedly different" standard in this fashion reveals isolated genomic DNA is not sufficiently different from genomic DNA to be the subject of patent protection. Examining both from biological and chemical perspectives reveal that the information contained in the isolated DNA, and the vast majority of its structure, is identical to that of genomic DNA. While there are four covalent bonds cleaved in the creation of

[114] *See e.g.*, KSR Intern. Co. v. Teleflex Inc., 550 U.S. 398 (2007); Bilski v. Kappos, 130 S. Ct. 3128 (2010).

[115] 550 U.S. at 407, 415.

[116] *Bilski*, 130 S. Ct. at 3231.

[117] *See Myriad I*, 702 F. Supp. 2d 181, 185 (S.D.N.Y. 2010); *Myriad II*, 653 F.3d 1329, 1351-52 (Fed. Cir. 2011).

isolated DNA, this minor structural change is insufficient to outweigh the near identity of the two molecules to be considered "markedly different."

i. Information Content is Identical

[28] Examining the information contained in the isolated DNA, it is not "markedly different" from the information contained in the genomic DNA. DNA contains information in its nucleotide sequence; the sequence dictates the creation of a specific protein.[118] Thus, for the information content to be markedly different, the isolated DNA sequence must code for a protein sufficiently different from that found in nature.

[29] Because of the nature of isolated genomic DNA, the protein resulting from transcription of the gene is identical to that resulting from transcription of native DNA. Isolated DNA is produced by removing a specific genomic DNA sequence, usually an entire gene, from the rest of the cellular components.[119] The piece of DNA 'isolated' was actually created by nature, with the exact same sequence, introns, and promoters.[120] Therefore, with sequence identity to the native DNA, the isolated DNA contains the same information as found in the native gene.

[30] This is exemplified by the '282 Patent where Claim 1 covers all isolated DNAs that encode for the BRCA1 protein.[121] While the claim does not specify a sequence, the specification discloses the nucleotide

[118] *See supra* Part V.A.

[119] U.S. Patent No. 5,747,282 col. 19 (filed Mar. 24, 1995). Claim 1 claims a sequence of isolated DNA found in Seq. Id. No. 2. Example 6 of the specification clarifies that the sequence contained in Seq. Id. No. 2 is the entire region containing the BRCA1 gene. *Id.* at cols. 19, 153.

[120] *Id*. at col. 19.

[121] *Id*. at col. 153.

sequence of BRCA1 exactly as it is found in native DNA.[122] The information contained the isolated DNA was not created by the ingenuity of man, rather it is the product of millions of years of evolution, devoid of any human input. Therefore, the information contained in the isolated BRCA1 DNA is not "markedly different" from its genomic counterpart, and thus under *Chakrabarty*, the isolated DNA is not patent eligible subject matter.

ii. Structure is Insignificantly Different

[31] Aside from looking at the DNA's information content, significant structural changes to the DNA could render it patentable subject matter. For instance, the synthesis of synthetic DNA, such as cDNA, has such a different structure from what is found in nature that it is rendered patentable. Yet, the process of isolating genomic DNA in no way creates a "new . . . composition of matter" required by § 101. In fact, the isolated DNA contains the exact same nucleotides, in the exact same sequence, as existed in the genomic DNA *in vivo*.[123] The process of isolation is described as the "remov[al] from its naturally occurring environment."[124] Thus, modification of the sequence is not performed. Isolation simply removes what had already existed in the cell.

[32] This is exemplified by the claims of the '282 patent. Claim 1 covers an isolated DNA coding for the BRCA1 protein.[125] As the claims of the patent are read in light of the specification, the claimed isolated DNA would be composed of a portion of the genomic DNA, removed

[122] *Id*. at cols. 5-6.

[123] *Id*. at col. 19 (defining "isolated" as simply the removal of naturally occurring DNA with no modification).

[124] U.S. Patent No. 5,747,282 col. 19 (filed Mar. 24, 1995).

[125] *Id*. at col. 153.

from the cellular proteins, coding for BRCA1. The isolated piece of genomic DNA is disclosed to be 24,026 base pairs long, including the promoter and introns.[126] The disclosed sequence even includes several regions where the sequence is unknown, designated by repeating 'v's in the patent.[127] Accordingly, the structure of the claimed isolated DNA and the genomic DNA are identical.

[33] While the main structure of the DNA is identical, there is one minor difference. Four covalent bonds have been cleaved that held the segment-to-be-isolated into the DNA backbone.[128] The cleaving of these four bonds, according to Judge Lourie, creates a "markedly different" molecule.[129] But, examining the roots of the markedly different standard, this is the wrong conclusion. The markedly different standard adopted by the Federal Circuit comes from the Supreme Court's holdings in *Chakrabarty* and *Hartranft*.[130] This standard originated in *Hartranft* to determine whether a seashell had undergone sufficient physical change to be converted from a natural object to a manufacture.[131] The Court held that even the etching away of layers of shell via acid was not sufficient to fulfill the markedly different standard, because at its root, the shell was still a shell.[132] In the case of isolated DNA, the breaking of four bonds, in

[126] *See, e.g., id*. at fig. 10A-10H.

[127] *Id*. at col. 54.

[128] *Myriad II*, 653 F.3d 1329, 1351 (Fed. Cir. 2011).

[129] *Id*. at 1352.

[130] *See generally* Diamond v. Chakrabarty, 447 U.S. 303 (1980); Hartranft v. Wiegmann, 121 U.S. 609 (1887).

[131] *Hartranft*, 121 U.S. at 614-15.

[132] *Id*. at 615.

light of the hundreds of thousands of bonds present in the entire molecule, is insignificant. It is certainly a less extensive change than the acid removal of entire layers of shell in *Hartranft*. Therefore, the breaking of these bonds cannot be considered to create a "markedly different" DNA molecule.

D. cDNA is Patentable Subject Matter

[34] The significant structural changes to the cDNA molecule outweigh the informational identity thus permitting its patenting under § 101. cDNA is a form of artificial DNA that is synthesized according to the mature mRNA transcript of a gene.[133] The mature mRNA has undergone significant changes following transcription, most notably the excision of the introns, which can remove thousands of nucleotides.[134] For example, the BRCA1 gene is shortened from 80,000 nucleotides in genomic form to just 7,000 nucleotides in the mRNA as a result of splicing.[135] Scientists then take this mRNA, using reverse transcriptase, create a synthetic DNA molecule composed only of the coding exons that is found nowhere in nature.[136]

[35] Under the totality of the circumstances approach, cDNA is patentable subject matter. While cDNA codes for the exact same protein

[133] WEAVER, *supra* note 62, at 64.

[134] Excision of the introns shortens the BRCA1 gene from 81,188 nucleotides in length to 7,224 nucleotides. *See e.g.*, *Homo sapiens breach cancer 1, early onset (BRCA1), transcript variant 1, mRNA*, NIH NCBI GENBANK, http://www.ncbi.nlm.nih.gov/nuccore/NM_007294.3 (last visited Jan. 16, 2012).

[135] *Id.*

[136] *See* SAMBROOK & RUSSELL, MOLECULAR CLONING: A LABORATORY MANUAL §§ 11.1-11.19 (3d ed. 2001) (describing theory and current protocols for synthesizing cDNA).

as it is found in humans, the magnitude of the structural changes to the gene itself as well as its synthetic nature make it markedly different from anything found in a human. As noted before, the significance in DNA's information content requires significant structural modification to a native sequence to permit patenting.[137] Unlike isolated DNA, which is derived from natural, genomic DNA, cDNA is synthesized by man in a test tube.[138] It requires the specific isolation of the target mRNA intending to be replicated as well as the hybridization of a polythiamine primer to the polyadenine tail to foster the binding of the synthesis enzyme.[139] The result is a molecule of DNA that exists with no introns, unlike the corresponding DNA sequence in the body.[140] The combination of its synthetic nature and modified sequence amounts to sufficient changes to the cDNA's structure to overcome the information identity and make it patent-eligible subject matter.

VI. CONCLUSION

[36] Mired in the complexities of eukaryotic genetics, the straightforward question of whether human genes are patentable is easily lost. The significance of each element of DNA has led each legal mind to consider this issue to conclude differently. The district court and Federal Circuit's dissent champion the supremacy of DNA's information content. The majority and concurrence in the Federal Circuit supports the structural changes. But, ignoring either the structure or the information undermines the importance of these fundamental properties. Through a totality-of-the-circumstances approach, both information and structure are weighed in order to determine whether the molecule as a whole is "markedly

[137] *See supra* Part IV.A.

[138] *See generally* WEAVER, *supra* note 62, at 65.

[139] SAMBROOK & RUSSELL, *supra* note 136, § 11.12.

[140] *Myriad II*, 653 F.3d 1329, 1339 (Fed. Cir. 2011).

different" from genomic DNA, not just whether one property differs. Under this analysis, isolated genomic DNA is not patentable subject matter because of the structural changes undergone are relatively insignificant in light of the molecules identical information content, and cDNA is patentable subject matter because of the drastic, man-made manipulations of the molecule's structure.