No. 2010-1406

IN THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, THE AMERICAN COLLEGE OF MEDICAL GENETICS, THE AMERICAN SOCIETY FOR CLINICAL PATHOLOGY, THE COLLEGE OF AMERICAN PATHOLOGISTS, HAIG KAZAZIAN, MD, ARUPA GANGULY, Ph.D, WENDY CHUNG, MD, Ph.D, HARRY OSTRER, MD, DAVID LEDBETTER, Ph.D, STEPHEN WARREN, Ph.D, ELLEN MATLOFF, M.S., ELSA REICH, M.S., BREAST CANCER ACTION, BOSTON WOMEN'S HEALTH BOOK COLLECTIVE, LISBETH CERIANI, RUNI LIMARY, GENAE GIRARD, PATRICE FORTUNE, VICKY THOMASON, and KATHLEEN RAKER,

Plaintiffs-Appellees,

v.

UNITED STATES PATENT AND TRADEMARK OFFICE,

Defendant,

MYRIAD GENETICS, INC.,

Defendant-Appellant, and

(caption continued on inside cover)

Appeal from the United States District Court for the Southern District of New York, in case no. 09-CV-4515, Senior Judge Robert W. Sweet

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BRIEF FOR THE UNITED STATES AS AMICUS CURIAE IN SUPPORT OF NEITHER PARTY

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Defendants-Appellants.

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INTEREST OF THE UNITED STATES

The United States submits this brief as *amicus curiae* pursuant to Fed. R. App. P. 29(a). The extent to which basic discoveries in genetics may be patented is a question of great importance to the national economy, to medical science, and to the public health. This appeal consequently implicates the expertise and responsibilities of a wide array of federal agencies and components, including the Patent and Trademark Office (PTO), the National Institutes of Health (NIH), the Antitrust Division of the Department of Justice, the Centers for Disease Control and Prevention, the Office of Science and Technology Policy, and the National Economic Council, among others. The PTO was a defendant below with respect to plaintiffs' constitutional claims, but was not named as a defendant with respect to the statutory issues now before this Court.

QUESTIONS PRESENTED

1. Whether human-engineered DNA molecules, such as cDNAs, are patent-eligible subject matter under 35 U.S.C. § 101.
2. Whether isolated but otherwise unmodified genomic DNA is patent-eligible subject matter under section 101.

STATEMENT

A. Patents for Genes and Genetic Inventions

1. In Diamond v. Chakrabarty, 447 U.S. 303 (1980), the Supreme Court established that the man-made products of genetic engineering are eligible for patent protection under 35 U.S.C. § 101. The Patent and Trademark Office responded to Chakrabarty by granting patents on a wide range of engineered DNA molecules and useful genetic methods.

The district court's opinion in this case includes a helpful description of the relevant principles of molecular biology and genetics. See A119-A139.[1] Briefly, deoxyribonucleic acid (DNA) is the chemical molecule that encodes the instructions required by living cells to produce the proteins essential for their structure and function. DNA thus directly or indirectly controls nearly every aspect of an organism's physiology. The basic structure of DNA comprises two complementary strands of repeating chemical units, known as "nucleotides" or "bases," bound together like a ladder and twisted into a distinctive double-helix.

[1] The prefix "A" denotes a citation to the addendum to appellants' opening brief.

An organism's complete set of DNA is its "genome." With qualifications not relevant here, a "gene" is any section of DNA that, through its nucleotide sequence, governs the expression of a particular protein. Only certain portions of a gene's sequence, known as "exons," actually code for the protein that the gene expresses. The remaining portions include upstream and downstream regulatory regions — information that governs, for example, how much of the protein the cell should make and when it should be made — and non-coding intervening sequences, known as "introns," that may also contain information relevant to the expression of the gene. Genes are the "basic units of heredity," A121, that enable organisms to transmit to future generations the blueprint for making all essential proteins.

DNA can be extracted from the natural cellular environment in which it occurs through established laboratory techniques. A127. A particular segment of DNA of interest, such as a gene, can then be excised from the extracted material. The result of this laboratory process — a DNA molecule excised from the genome and separated from its cellular environment — is commonly termed "isolated DNA." The specifications of the patents at issue in this litigation define the

term "isolated DNA" in a manner generally consistent with this usage. See, e.g., U.S. Patent No. 5,747,282, col. 19, lines 8-18.

2. The first United States patents relating to DNA molecules issued at approximately the same time as the Chakrabarty decision and were directed primarily to recombinant DNA vectors — i.e., man-made constructs of nucleic acids useful for cloning molecules of interest in host cells, such as bacteria or yeast. Patents that claimed man-made complementary DNA molecules (cDNA) in combination with vectors began to issue in 1982. See, e.g., U.S. Patent No. 4,322,499 (1982) (claiming a recombinant DNA plasmid containing a cDNA).

Applicants eventually began to seek, and PTO began to grant, patents directed not only to synthetic DNA molecules such as cDNAs but also to isolated but otherwise unaltered genomic DNA itself — that is, genomic material excised from an organism's genome and isolated from the cellular environment in which it normally occurs, but without material change to its naturally occurring chemical structure and function. The first such patents claimed genes directly, without the rubric of isolation or purification. See, e.g., U.S. Patent No. 4,472,502 (1984) (claiming the Lactobacillus bacteria malolactic gene). The first

patent using the term "isolated DNA" appears to have issued in 1987, although it was directed to a recombinant vector rather than genomic DNA. See U.S. Patent No. 4,680,264, claim 27 (1987). It is believed that PTO issued the first patent claiming isolated but otherwise unmodified human genomic DNA in the same period.

In 2001, PTO published revised examination guidelines for the "utility" requirement of section 101. See Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001). The guidelines attracted a number of public comments regarding the patent eligibility of isolated genes, and the agency's response to those comments represents the only written articulation of the agency's views on the subject. PTO stated that, if the specification of a patent discloses a particular use for a gene — e.g., that the specified gene expresses a useful protein — then "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. at 1093. PTO stated that a DNA molecule that has been "isolated" in this way is not a product of nature "because that DNA molecule does not occur in that isolated form in

nature." Ibid.; see also Reply in Support of Gov't Mot. for Judgment on Pleadings, docket no. 245, at 11 ("The USPTO's position on this question remains as set forth in its Utility Guidelines[.]").

3. Until this case, no court had previously addressed whether such an isolated DNA molecule is patentable subject matter under 35 U.S.C. § 101. Cf. Intervet, Inc. v. Merial Ltd., 617 F.3d 1282, 1293 (Fed. Cir. 2010) (Dyk, J., concurring in part) (observing that "thus far the question has evaded judicial review"). Nor has the United States previously expressed its view on that question in litigation.

B. The Challenged Claims

At issue in this case are fifteen claims drawn from seven United States patents relating to the human genes known as Breast Cancer Susceptibility Genes 1 and 2, or "BRCA1" and "BRCA2."[2] See generally A172-A178 (discussing the disputed patents and claims). Located on human chromosomes 17 and 13, respectively, the BRCA1 and BRCA2

[2] The United States is a co-owner of four of the patents-in-suit. See A26 n.4. As part of the settlement of an inventorship dispute between Myriad and NIH in 1995, however, the government granted an exclusive license under those patents to Myriad. That result is anomalous: NIH ordinarily does not grant exclusive licenses under DNA patents for diagnostic applications.

genes express proteins that assist in the repair of damaged DNA and the suppression of tumors. Mutations in these genes are associated with significantly increased risks of breast and ovarian cancer. See A146-A147. The district court declared all of the challenged claims invalid under 35 U.S.C. § 101, holding that the challenged composition claims are directed to unpatentable products of nature, see A214-A228, and that the method claims are directed to unpatentable abstract ideas, see A228-A242.

Several of the composition claims in the patents-in-suit are limited to cDNAs that encode the BRCA proteins. See, e.g., U.S. Patent No. 5,747,282, claim 2.

Other claims at issue, however, would encompass isolated but otherwise unmodified human genomic DNA itself. The district court identified claim 1 of the '282 patent as representative of the challenged composition claims:

> An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

A173. A "polypeptide" is a protein or protein fragment; "SEQ ID NO:2" is the amino-acid sequence of the BRCA1 protein as it occurs in nature.

See '282 patent, col. 19, lines 41-50. The specification defines the term "isolated DNA" to include not only cDNAs and similar man-made constructs, but also genomic DNA that has merely been "separated from other cellular components which naturally accompany a native human sequence" and "removed from its naturally occurring environment." Id. at col. 19, lines 8-18. Likewise, the patent defines "encode" (synonymous with "coding for") to include the ability of a DNA molecule "in its native state" to express the desired protein. See id. at col. 19, lines 1-5.

Accordingly, claim 1 of the '282 patent encompasses *any* isolated DNA molecule whose nucleotide sequence codes for the natural BRCA1 protein. See also U.S. Patent No. 5,837,492, claim 1 (same, BRCA2). This would include an ordinary BRCA gene isolated from a tissue sample taken from a woman in a hospital.

SUMMARY OF ARGUMENT

Section 101 marks the "threshold" of the patent system. Bilski v. Kappos, 130 S.Ct. 3218, 3225 (2010). It not only "defines the subject matter that may be patented," ibid., but simultaneously defines what must remain in "'the storehouse of knowledge of all men * * * free to all men and reserved exclusively to none,'" ibid. (quoting Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948)); see Bonito Boats, Inc. v. Thundercraft Boats, Inc., 489 U.S. 141, 151 (1989) (the patent laws "determine not only what is protected, but also what is free for all to use"). The boundary between eligible and non-eligible subject matter is defined, in significant part, by the settled principle that the patent laws do not embrace laws of nature, physical phenomena, or abstract ideas. See Bilski, 130 S.Ct. at 3225.

In attempting to apply that principle here, the district court erroneously cast doubt on the patent-eligibility of a broad range of man-made compositions of matter whose value derives from the information-encoding capacity of DNA. Such compositions — e.g., cDNAs, vectors, recombinant plasmids, and chimeric proteins, as well as countless industrial products, such as vaccines and genetically modified crops,

created with the aid of such molecules — are in every meaningful sense the fruits of human ingenuity and thus qualify as "'human-made inventions'" eligible for patent protection under section 101. J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124, 130 (2001) (quoting Diamond v. Chakrabarty, 447 U.S. 303, 313 (1980)). The district court therefore erred in invalidating the challenged composition claims, such as claim 2 of the '282 patent, that are directed solely to cDNAs.

The district court correctly held, however, that genomic DNA that has merely been isolated from the human body, without further alteration or manipulation, is not patent-eligible. Unlike the genetically engineered microorganism in Chakrabarty, the unique chain of chemical base pairs that induces a human cell to express a BRCA protein is not a "human-made invention." Nor is the fact that particular natural mutations in that unique chain increase a woman's chance of contracting breast or ovarian cancer. Indeed, the relationship between a naturally occurring nucleotide sequence and the molecule it expresses in a human cell — that is, the relationship between genotype and phenotype — is simply a law of nature. The chemical structure of

native human genes is a product of nature, and it is no less a product of nature when that structure is "isolated" from its natural environment than are cotton fibers that have been separated from cotton seeds or coal that has been extracted from the earth.

The scope of Section 101 is purposefully wide and its threshold is not difficult to cross. See Bilski, 130 S.Ct. at 3225. New and useful methods of identifying, isolating, extracting, or using genes and genetic information may be patented (subject to the prohibition against patenting abstract ideas), as may nearly any man-made transformation or manipulation of the raw materials of the genome, such as cDNAs. Thus, the patent laws embrace gene replacement therapies, engineered biologic drugs, methods of modifying the properties of plants or generating biofuels, and similar advanced applications of biotechnology. Crossing the threshold of section 101, however, requires something more than identifying and isolating what has always existed in nature, no matter how difficult or useful that discovery may be.

ARGUMENT

A. Section 101 Embraces Only "Human-Made Inventions."

Section 101 of the Patent Act "defines the subject matter that may be patented." Bilski v. Kappos, 130 S.Ct. 3218, 3225 (2010). The statute provides: "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 therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. "'In choosing such expansive terms * * * modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope.'" Bilski, 130 S.Ct. at 3225 (quoting Diamond v. Chakrabarty, 447 U.S. 303, 308 (1980)).

The patent laws do not, however, embrace the products and processes of nature itself. "He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes." Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948). Whether understood as an interpretation of section 101 or as a judicially recognized exception to it, this principle has "defined the

reach of the statute as a matter of statutory *stare decisis* going back 150 years." Bilski, 130 S.Ct. at 3225. Thus, "a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of * * * nature, free to all men and reserved exclusively to none.'" Chakrabarty, 447 U.S. at 309 (quoting Funk Brothers, 333 U.S. at 130); see also, e.g., Diamond v. Diehr, 450 U.S. 175, 185-86 (1981); Gottschalk v. Benson, 409 U.S. 63, 67 (1972); Le Roy v. Tatham, 14 How. 156, 175 (1853).

The Supreme Court has twice addressed the application of these principles to innovations in biotechnology. In Chakrabarty, the Court held that a genetically engineered microorganism useful for digesting oil spills was a patentable manufacture or composition of matter under section 101. The Court emphasized that "the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly it is

patentable subject matter under § 101." 447 U.S. at 310. In J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124 (2001), the Court held that human-developed plant breeds are eligible for patent protection under section 101. Id. at 131. In each case, the Supreme Court stressed that "'the relevant distinction'" for purposes of section 101 is not "'between living and inanimate things, but between products of nature * * * and human-made inventions.'" J.E.M. Ag Supply, 534 U.S. at 130 (quoting Chakrabarty, 447 U.S. at 313). This settled distinction between "products of nature" and "human-made inventions" provides the touchstone for resolving this appeal.

B. Engineered DNA Molecules, Including cDNAs, Are Human-Made Inventions Eligible For Patent Protection.

Against this background, the district court was clearly mistaken in invalidating the challenged composition claims, such as claim 2 of the '282 patent, that are limited to cDNAs. The court further erred in implying that any isolated DNA molecule whose value derives from the information-encoding capacity of DNA must be deemed an unpatentable product of nature. See, e.g., A218, A221-A222. Molecules that are engineered by humans, including cDNAs, vectors, recombinant

plasmids, chimeric proteins, and similar fruits of the manipulation of genetic material, will almost invariably be patent-eligible subject matter. These molecules generally do not occur in nature, but are instead the synthetic results of scientists' manipulation of the natural laws of genetics.

cDNAs, for example, are synthetic molecules engineered by scientists to incorporate, in a single contiguous DNA segment, only the exons (i.e, protein-coding sequences) of a naturally occurring gene, and to exclude the intervening introns and other regulatory regions that normally separate the exons in genomic DNA. With rare exceptions (such as retroviruses that use cDNA-like structures to replicate themselves), such molecules do not occur in nature, either in isolation or as contiguous sequences contained within longer natural molecules, but instead must be synthesized by scientists in the laboratory from other genetic materials. See A134 (acknowledging that "cDNA is typically generated by scientists in a laboratory"); see generally Alberts et al., Molecular Biology of the Cell 503 & fig. 8-34 (4th ed. 2002) (describing the process of synthesizing double-stranded cDNA molecules). The utility of such molecules, moreover, is clear: because

cDNAs are stable DNA compounds that reflect only the coding sequences of a gene, they "can be used as a tool for biotechnological and diagnostic applications for which native DNA cannot be used." A135.

Likewise, recombinant vectors and similar biotechnological innovations are man-made constructs that permit the direct yoking of natural processes for mankind's purposes, such as coaxing a bacterial cell to express a human protein. See Alberts, Molecular Biology of the Cell, at 500-01. Like the genetically engineered microorganism in Chakrabarty, biological innovations of this kind are "not nature's handiwork," 447 U.S. at 310, and thus are patent-eligible subject matter under section 101.

Notably, plaintiffs have not challenged any of the claims in the patents-in-suit directed solely to recombinant vectors or similar molecules. Claim 8 of the '282 patent, for example, claims a "replicative cloning vector which comprises the isolated DNA of claim 1 or parts thereof and a replicon operative in a host cell." Just as the engineered microorganism in Chakrabarty included many (indeed, most) of the features of the natural bacterium from which it was created, the mere fact that a non-naturally occurring polynucleotide,

such as the recombinant vector in claim 8 of the '282 patent, incorporates nucleotide sequences whose significance is derived from nature does not mean the claim as a whole is directed to a product of nature. Cf. Diehr, 450 U.S. at 188 (for section 101 purposes, "claims must be considered as a whole").

It is possible that, in light of the prevailing level of knowledge in the biotechnological arts, future patent applications directed to cDNAs and simple recombinant vectors may be rejected as obvious. See generally In re Kubin, 561 F.3d 1351, 1358-61 (Fed. Cir. 2009). Such molecules, however, constitute man-made compositions of matter that are eligible for patent protection where the other requirements of Title 35 are satisfied.

C. Isolated But Otherwise Unmodified Genomic DNA Is Not A Human-Made Invention.

The same cannot be said, however, of genomic DNA merely isolated from a cell in the human body. Methods of identifying, isolating, and using such DNA molecules may be patented, as may any new and useful alteration of those molecules through human intervention. Genomic DNA itself, however, is a product of nature that

is ineligible for patent protection, whether or not claimed in "isolated" form.

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. The district court's judgment in this case, however, prompted the United States to reevaluate the relationship between such patents and the settled principle under Supreme Court precedent that the patent laws do not extend to products of nature. For the reasons below, the United States has concluded that isolated but otherwise unaltered genomic DNA is not patent-eligible subject matter under 35 U.S.C. § 101.

1. Unmodified Genomic DNA Is A Product Of Nature.

No one doubts that the native BRCA genes *in situ* are products of nature. The unique nucleotide sequence that induces human cells to express the BRCA1 protein was not invented by appellants or, for that matter, by scientists at NIH. Nor was the fact that certain mutations

in those sequences and not others (see, e.g., claim 7 of the '282 patent) are associated with an increased risk of breast and ovarian cancer. The BRCA genes, their deleterious alleles, and their relationship to breast cancer are the products of evolution, not human invention. Like the mutually non-inhibitive qualities of the bacterial strains in Funk Brothers, the cancer-inhibitive qualities of the BRCA gene products are "manifestations of laws of nature, free to all men and reserved exclusively to none." 333 U.S. at 130.

Indeed, the relationship between a naturally occurring nucleotide sequence and the molecule it induces a human cell to express — that is, the relationship between genotype and phenotype — is simply a law of nature. The fact that a particular segment of the human genome codes for the BRCA1 protein in a human cell, for example, rather than for adrenaline or insulin or nothing at all, is not within the power of science to alter. Such basic natural relationships may not be the subject of a patent.

2. "Isolation" Does Not Transform A Product Of Nature Into A Man-Made Invention.

The basic composition claims at issue in this case are directed not to the wild-type or mutated BRCA genes *in situ* but to "isolated" DNA molecules that have the same chemical structure and function but have been extracted from the natural cellular environment.[3] The "isolated" limitation must therefore carry the entire weight of these claims: absent that limitation, claim 1 of the '282 patent, for example, would encompass the native BRCA1 gene in the human body, which likewise "cod[es] for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2" (*i.e.*, the naturally occurring BRCA1 protein).

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[3] Several of the disputed claims are framed in functional terms that would additionally encompass non-naturally occurring alleles of the BRCA genes and related cDNAs. Claim 1 of the '282 patent, for example, would encompass not only the isolated wild-type gene, but also a laboratory-synthesized DNA molecule that has a different nucleotide sequence from the wild-type gene but, because different codons may code for the same amino acids, nonetheless encodes the claimed BRCA1 polypeptide. Like other man-made molecules, synthetic alleles of this kind are clearly patent-eligible subject matter, and a claim limited to such alleles would survive scrutiny under section 101 (although it might be held obvious over the natural gene).

Yet the fact of "isolation" is inadequate for the task. The mere fact that genes do not occur in "isolated" form in nature does not provide a principled basis for patent-eligibility. See Intervet, 617 F.3d at 1294-95 (Dyk, J., concurring in part). Many natural products — coal beneath the earth, cotton fibers mixed with cotton seeds, the stigmas of the saffron flower — must be physically separated, i.e., "isolated," from their natural environments before becoming useful to mankind, but few would doubt that coal, cotton, and saffron are products of nature and not patent-eligible. Likewise, the unique nucleotide sequence that induces human cells to express the BRCA1 protein is no more an invention of appellants or NIH when captured in a test tube than in its natural context in the human body. The *process* of applying restriction enzymes to select and extract a naturally occurring segment of DNA in the human genome from its chromosomal environment (now well understood in the art) was undoubtedly patent-eligible when it was first conceived, and an improved process for doing so may be the subject of a patent in the future. But the isolated DNA segment *itself* remains, in structure and function, what it was in the human body.

Common sense would suggest that a product of nature is not transformed into a human-made invention merely by isolating it. The very term "isolated" suggests only that extraneous matter has been separated from the natural product of interest, not that the product itself has been transformed or altered into something man-made. The Supreme Court explicitly noted in Funk Brothers, for example, that the patentee had "isolated" the mutually non-inhibitive strains of bacteria "by certain methods of selection and testing." 333 U.S. at 130. Under appellants' theory, the isolated bacteria in Funk Brothers that exhibited valuable and previously unknown qualities in their isolated state would have been patentable in their own right. Yet the Court held that the quality "of inhibition or of non-inhibition in the bacteria" — a quality that was doubtless the consequence of genetic variation, though the fact was unappreciated at the time — was "the work of nature" and, accordingly, beyond the reach of the patent laws.[4] Ibid.

[4] Although appellants characterize Funk Brothers as an obviousness case, they correctly acknowledge (Br. 44) that the Court's reasoning relied on principles of patent eligibility. The Supreme Court has thus repeatedly cited Funk Brothers for the proposition that products of nature are not patent-eligible under section 101. See, e.g., Bilski, 130 S.Ct. at 3225; Chakrabarty, 447 U.S. 309-10.

The discovery of any number of basic natural phenomena could be recharacterized as the "invention" of an isolated "manufacture" or "composition of matter" under section 101. For example, many highly reactive elements on the periodic table, such as lithium, occur in nature only in chemical compounds (*i.e.*, salts). Not until 1818 was lithium, which has innumerable industrial applications, first isolated in metallic form by Sir Humphry Davy and W.T. Brande. See Krebs, The History and Use of Our Earth's Chemical Elements: A Reference Guide 48 (2d ed. 2006). That accomplishment marked a significant achievement in chemistry, but it did not entitle Davy and Brande to claim a patent on the third element in the periodic table. Cf. Funk Brothers, 333 U.S. at 130 (the "qualities of metals" are "part of the storehouse of knowledge of all men"). Courts in the early part of the 20th century repeatedly rejected claims for isolated natural elements as new "manufactures." See Gen. Electric Co. v. De Forest Radio Co., 28 F.2d 641 (3d Cir. 1928) (pure ductile tungsten, though previously thought impossible to produce, held unpatentable as a product of nature); In re Marden, 47 F.2d 957 (CCPA 1931) (same, pure ductile uranium); In re Marden, 47

F.2d 958 (CCPA 1931) (same, pure ductile vanadium); cf. In re Seaborg, 328 F.2d 996 (CCPA 1964) (upholding patent for element 95, americium, which does not occur in nature). The unacceptable implication of appellants' argument is that these cases were wrongly decided.[5]

Similarly, Hans Dehmelt won the Nobel Prize in physics in 1989 for being the first to isolate a single electron free of the atom, an accomplishment with useful applications in atomic clocks and other devices. Dehmelt undoubtedly could have patented his process and apparatus for isolating an electron in free space, as well as any method for exploiting the characteristics of electrons thus isolated, assuming

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[5] Appellants erroneously suggest (Br. 44 n.3) that De Forest Radio and the Marden cases involved considerations of obviousness rather than patentable subject matter. In fact, those decisions were expressly predicated on the ineligibility of natural products for patent protection. See, e.g., De Forest Radio, 28 F.2d at 643 ("What he discovered were natural qualities of pure tungsten. Manifestly he did not create pure tungsten, nor did he create its characteristics. These were created by nature and on that fact finding the reasoning as to the validity of the product claims will be based."); Marden, 47 F.2d at 957 ("Uranium is a product of nature, and the appellant is not entitled to a patent on the same, or upon any of the inherent natural qualities of that metal."); Marden, 47 F.2d at 959 ("The quality of purity of vanadium or its ductility is a quality of a natural product and as such is not patentable.").

the other requirements of Title 35 were satisfied. But Dehmelt plainly did not invent the elemental unit of negative charge in the universe. Nonetheless, on appellants' theory, Dehmelt could have patented the isolated electron itself (as a "manufacture") and thereby arrogated to himself the exclusive right to conduct experiments in electron quantum physics for twenty years.[6]

Accordingly, PTO historically rejected isolation alone as the test for determining patent eligibility. In Ex parte Latimer, 46 O.G. 1638, 1889 Dec. Comm'r Patent 123 (1889), for example, the Commissioner rejected a claim for a fiber from the needles of the *Pinus australis* tree. The claim recited that the fiber was extracted "in full lengths from the silicious, resinous, and pulpy parts of the pine needles." Id. at 123. Stressing that the claimed fiber was identical to what occurred in nature, the Commissioner concluded that "it is a natural product and can no more be the subject of a patent in its natural state when freed

[6] The Supreme Court in Chakrabarty observed that Newton could not have patented the law of gravity, 447 U.S. at 309; surely that prize does not still await the first scientist to isolate the graviton.

from its surroundings than wheat which has been cut by a reaper."[7] Id. at 127.

Likewise, in Ex parte Berkman, 90 U.S.P.Q. 398 (1951), the Board held ineligible for patent protection a "physiologically active material * * * derived from fresh raw plant material * * * being further characterized by being substantially free of cellulosic material, electrolytes and enzymes." Id. at 399. Although the claimed material was "actually isolated," id. at 400, the Board concluded that "claims to a

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[7] As the Supreme Court noted in Chakrabarty, the Commissioner's decision in Latimer led to a widespread conviction in the early part of the 20th century that all plant products, including artificially bred plants, were unpatentable products of nature. See 447 U.S. at 311-12. Congress responded in part by enacting the Plant Patent Act of 1930, which granted a limited form of patent protection to the inventors of human-created, asexually reproducing plants. Id. at 312-13; see 35 U.S.C. § 161. The accompanying Senate Report explained in detail why, in Congress's judgment, it was permissible to extend patent protection to such *artificially* bred plants: "It is obvious that nature originally creates plants but it cannot be denied that man often controls and directs the natural processes and produces a desired result." S. Rep. No. 71-315, at 6-7 (1930). Just as a chemist "avail[s] himself of the physical and chemical qualities inherent in the materials used and of the natural principles applicable to matter" to develop "new compositions of matter which are patentable under existing law," the Senate report reasoned, a plant breeder "avails himself of *the natural principles of genetics* and of seed and bud variations" and "cultivates the plants in his own laboratory under his own eye." Id. at 7 (emphasis added).

product formed by nature's processes are as a rule held to be invalid, even when invention can be recognized in the method of isolating them or otherwise obtaining them from the environment in which they are found in nature." Id. at 401. These decisions state the correct rule.

3. Isolated Genomic DNA Is Not Patent-Eligible Merely Because It Is A Literal Composition Of Matter.

Appellants urge (Br. 31) that an isolated gene is patentable subject matter because it is a complex chemical polymer, a literal composition of matter. But that does not make an isolated gene a "new and useful * * * composition of matter" within the meaning of 35 U.S.C. § 101 any more than the fact that the mathematical method in Benson was a literal "process" could have made that method eligible for patenting. See also Ex Parte Latimer, supra. The Supreme Court recently reiterated that, although the terms of section 101 are normally construed in accordance with their "ordinary, contemporary, common meaning," Bilski, 130 S.Ct. at 3226, the Court has "deviate[d]" from that ordinary meaning where necessary to accommodate the settled exceptions for "laws of nature, physical phenomena, and abstract ideas," ibid. Indeed, the Supreme Court did so in Bilski itself, holding

that the claimed method of hedging financial risk, though a literal process, was not a "process" within the meaning of section 101. See also American Fruit Growers, Inc. v. Brogdex, 283 U.S. 1, 11-12 (1931) (orange treated with borax to prevent mold, though the product of an industrial process, was not a patent-eligible "manufacture").

The Supreme Court has long ago applied the same principle to compositions of matter. In Cochrane v. Badische Anilin & Soda Fabrik, 111 U.S. 293 (1884), for example, the plaintiff obtained a patent for a process of artificially manufacturing alizarine, a red dye that naturally occurs in the root of the madder plant, and for the artificial alizarine (identical to natural alizarine) that was the result of the claimed process. Although alizarine is a literal "composition of matter," the alleged infringer defended, *inter alia*, on the ground that the dye "is a natural product, having a well-known definite constitution; that it is not a composition of matter, within the meaning of the statute, but has been well known in the arts, from time immemorial, for the purpose of dyeing." Id. at 297. The Supreme Court upheld the process claim but rejected the patentee's claim for the alizarine compound itself,

explaining: "While a new process for producing it was patentable, the product itself could not be patented, even though it was a product made artificially for the first time, in contradistinction to being eliminated from the madder root. Calling it artificial alizarine did not make it a new composition of matter, and patentable as such, by reason of its having been prepared artificially, for the first time * * * *." Id. at 311.

Likewise here: a new process for producing an isolated gene may be patented, as may a new process for using such an isolated gene. But the natural product itself cannot be patented, even though it is separated from the genome artificially for the first time.

4. Isolated Genomic DNA Is Not Rendered Patentable On The Theory That It Is "Pure."

Appellants also defend the challenged claims on the basis of an old line of cases holding that compounds extracted from nature may, in narrow circumstances, be patented in purified form. See, e.g., Kuehmsted v. Farbenfabriken of Elberfeld Co., 179 F. 701 (7th Cir. 1910); Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95 (S.D.N.Y. 1911), aff'd, 196 F. 496 (2d Cir. 1912). Whether this line of authority

survives the Supreme Court's decisions in Chakrabarty and Funk Brothers is open to doubt.

Regardless, these cases do not hold that natural products may be patented whenever they are extracted from impure environments. Rather, they provide that patent eligibility may arise when a natural compound has been so refined and purified through human intervention as to become a substance *different in kind* from the natural product. In Parke-Davis, for example, Judge Learned Hand stressed that the claimed form of adrenaline was so different in therapeutic operation from impure forms that it "was a distinction not in degree, but in kind." 189 F. at 103. See also In re Merz, 97 F.2d 599 (CCPA 1938) (rejecting a claim for pure ultramarine as lacking any new and different features over impure ultramarine, but noting that if an applicant "produces an article of such purity that it differs not only in degree but in kind it may be patentable"); In re King, 107 F.2d 618, 620 (CCPA 1939) (rejecting a claim for vitamin C purified from lemon juice, explaining: "Lemon juice has been known for ages as a satisfactory

specific for scurvy. * * * Difference in degree of purity itself does not predicate invention.").

It may be that "purification" — depending on what is meant by that term — can in some cases transform a natural substance into a new compound sufficiently different in kind from its natural ancestor to cross the threshold of section 101.[8] But this case involves no such transformation. The "pure" human BRCA1 polynucleotide claimed in the '282 patent is structurally identical to the DNA segment that occurs in the human body, apart from the fact of its isolation itself. Indeed, the structural identity of the isolated gene and the wild-type gene is the very point of the patent. As the district court noted, "the entire premise behind Myriad's genetic testing is that the claimed isolated DNA retains, in all relevant respects, the identical nucleotide sequence found in native DNA," thereby rendering it valuable for medical diagnostic and therapeutic applications. A224.

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[8] A chemical alteration of a bioactive molecule to improve absorption by the body, for example, could be described as "purification" and would likely satisfy section 101. Merely sorting the proverbial wheat from the chaff, however, would not.

Likewise, the function of the claimed isolated BRCA genes is exactly the same as the function of the identical DNA segments in the body. Two of the composition claims at issue are literally defined by their natural biological function: the capacity to express BRCA1 and BRCA2 proteins. See '282 patent, claim 1 (BRCA1); '492 patent, claim 1 (BRCA2). It is that intrinsic natural function, common to both the isolated and native forms of the gene, which makes the gene attractive to appellants and important to the medical community.

Under these circumstances, the contention that a "purified" gene is patent-eligible merely because it does not occur in "pure" form in nature is essentially indistinguishable from the "isolation" rationale, and fails for the same reasons. A product of nature is unpatentable because it is not the inventive work of humankind. That essential rule cannot be circumvented by drafting claims for the same natural product removed from its natural environment and proclaiming the result "pure."[9] If section 101's "product of nature" limitation on patent-

[9] The CCPA in In re Bergstrom, 427 F.2d 1394 (CCPA 1970), overturned PTO's rejection of a patent for purified prostaglandins, emphasizing that the pure forms did not exist in nature. See id. at 1401. The court's analysis, however, was framed largely in terms of

eligibility means anything, it must mean that the mere act of culling a natural product from its environment to uncover or exploit its preexisting natural qualities or functions — however useful those qualities or functions may be — is insufficient to create patentable subject matter. The fundamental question under section 101 is whether the inventor has created something through the application of human ingenuity or merely exposed something previously unappreciated in nature. See J.E.M. Ag Supply, 534 U.S. at 134; Chakrabarty, 447 U.S. at 313. In this case, the answer is the latter.

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whether the claimed invention was "new" within the meaning of sections 101 and 102, not whether it constituted a patent-eligible "composition of matter" under Supreme Court case law. See generally id. at 1400-01. This Court has consequently understood Bergstrom as an inherent anticipation case. See Schering Corp. v. Geneva Pharmaceuticals, 339 F.3d 1373, 1381 (Fed. Cir. 2003); see also In re Bergy, 596 F.2d 952, 961 (CCPA 1979) (noting that Bergstrom "in effect treated the [§ 101] rejection as if it had been made under § 102"). Moreover, Bergstrom, which predated the Supreme Court's decision in Chakrabarty, did not discuss or purport to overrule previous CCPA cases, such as In re King and In re Merz, supra, establishing that the mere act of purifying a natural molecule does not render the result patent-eligible.

5. Isolated Genomic DNA Is Not Patent-Eligible Merely Because It Is Useful Or Requires Investment To Identify.

Finally, appellants urge that isolated genomic DNA has practical uses that native DNA does not, and that section 101 should be construed in a manner that provides an incentive for companies to identify, describe, and develop those uses into commercial applications that promote the public welfare. This contention, however, rests on several erroneous premises.

First, while isolated genomic DNA may have more potential applications than human genes in their natural context, the same is equally true of mined coal, separated cotton fibers, pure metallic lithium, ductile uranium, and other products of nature whose industrial value to mankind likewise arises when they are extracted from their naturally occurring environments. A person who invents a new and useful industrial application for isolated genomic DNA — or any other product of nature — is entitled to seek a process patent for that application. But the underlying natural compound itself is not patent-eligible.

Similarly, appellants' assertion that patent protection for raw isolated genomic DNA provides an incentive to make discoveries of value to society, see Br. 3-4, does not distinguish isolated genes from other, clearly unpatentable products of nature. Granting patent protection for previously unknown mineral ores or plants growing in the wild, for example, would surely encourage private investment in mining and botanical expeditions, but it does not follow that minerals and wild plants are patent-eligible subject matter under section 101. See Chakrabarty, 447 U.S. at 309 ("[A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter."); see also Ex parte Foster, 1951 Dec. Comm'r Patent 15 (1951) (previously unknown plant discovered in the wild in South America was not patentable subject matter).

Crossing the threshold of section 101 requires something more than identifying and isolating what has always existed in nature, no matter how difficult or useful that discovery may be. Nearly every biotechnological or pharmaceutical application of genomic DNA will involve a welter of potentially patentable products and methods: engineered DNA molecules, including cDNAs; processes of extraction

and purification; optimized pharmaceutical compounds (pills, vaccines); methods of preparing and administering the same; and so on. These may include very broad and fundamental claims (e.g., "method of treating cancer by administering an effective amount of compound X"). Claims directed to such "human-made inventions," Chakrabarty, 447 U.S. at 313, properly capture what the inventor has in fact contributed to society, without precluding the public's access to "the basic tools of scientific and technological work," Benson, 409 U.S. at 67.

CONCLUSION

For the foregoing reasons, the Court should reverse the district court's invalidation of the composition claims that are limited to cDNAs and similar man-made constructs, but affirm the district court's conclusion that the claims encompassing isolated human genomic DNA are invalid.

Respectfully submitted,

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October 29, 2010

CERTIFICATE OF COMPLIANCE
WITH FED. R. APP. P. 29(d) AND 32(a)(7)(B)

I hereby certify that the foregoing amicus brief complies with the type-face and volume limitations set forth in Federal Rules of Appellate Procedure 29(d) and 32(a)(7)(B) because the type face is Century Schoolbook, proportionally spaced, fourteen-point font, and the number of words in this brief is 6,979, according to the count of Corel WordPerfect 14.

s/ Mark R. Freeman
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CERTIFICATE OF SERVICE

I hereby certify that on October 29, 2010, I caused copies of the foregoing amicus brief to be filed with the Court by hand delivery. In addition, I caused copies to be served upon the following counsel by first-class U.S. mail and electronic mail:

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