
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, PhD, WENDY CHUNG, MD, PhD, HARRY OSTRER, MD, DAVID LEDBETTER, PhD, STEPHEN WARREN, PhD, 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,

and

MYRIAD GENETICS, INC.,

Defendant-Appellant,

and

LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation,

Defendants-Appellants,

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

**BRIEF FOR THE BIOTECHNOLOGY INDUSTRY ORGANIZATION AND
THE ASSOCIATION OF UNIVERSITY TECHNOLOGY MANAGERS
AS AMICI CURIAE SUPPORTING REVERSAL**

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CERTIFICATE OF INTEREST

Counsel for the Biotechnology Industry Organization and the Association of University Technology Managers certifies the following:

1. The full names of every party or amicus represented by us are:
Biotechnology Industry Organization

Association of University Technology Managers
2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by us is:
Not applicable
3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by us are:
None
4. The names of all law firms and the partners or associates who appeared for the party or amicus now represented by us in the trial court or agency or are expected to appear in this Court are:

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Dated: October 29, 2010


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STATEMENT OF INTEREST

The Biotechnology Industry Organization (“BIO”) is the country’s largest biotechnology trade association, representing over 1100 companies, academic institutions, and biotechnology centers in all 50 States and countries around the world. BIO members undertake research and development of biotechnological healthcare, agricultural, environmental, and industrial products. BIO members range from start-up businesses and university spin-offs to Fortune 500 corporations. The vast majority of BIO’s members are small companies that have yet to bring products to market or attain profitability, and thus rely heavily on venture capital and other private investment. Patents on isolated DNA molecules are frequently critical to a biotech company’s ability to attract the investment necessary for development of innovative therapeutic, diagnostic, environmental, renewable energy, and agricultural products.

The Association of University Technology Managers (“AUTM”) is the largest association of university technology transfer professionals, with members from over 350 universities, research institutions, teaching hospitals, and government agencies worldwide, as well as hundreds of companies involved with managing and licensing innovations derived from academic and nonprofit research.

The issues raised in this case are of great importance to BIO’s and AUTM’s members. BIO and AUTM have no commercial interest in the parties to this

action. None of the parties nor the University of Utah Research Foundation is a member of BIO or AUTM.

All parties have consented to the filing of this brief.

INTRODUCTION

“[C]ourts should not read into the patent laws limitations and conditions which the legislature has not expressed.” *Diamond v. Chakrabarty*, 447 U.S. 303, 308-309 (1980) (internal quotation marks omitted). The district court regrettably did just that, ignoring Congress’s intent that statutory subject matter under Section 101 expansively include all products of human ingenuity. *Id.* at 309-310.

Isolated DNA molecules are unquestionably “composition[s] of matter,” 35 U.S.C. §101; the district court’s ruling that they are nonetheless categorically unpatentable rested on three fundamental errors.¹ *First*, the court incorrectly treated isolated DNA molecules as merely “purified” forms of naturally-occurring substances; in fact, they are new, man-made chemical compositions that do not occur in nature. *Second*, even if isolated DNA molecules could be treated as purified versions of naturally-occurring DNA, the process of isolation requires such a level of human intervention and so alters their character and use as to make them patentable under settled law. *Third*, the district court was led astray by the comparison of DNA sequences to “information”—a common metaphor that is useful in conveying complex science to laypersons, but that does not change the fact that DNA remains a chemical compound, not an alphabet or a language. The utility of isolated DNA molecules derives from their chemical structure, which is,

¹ *Amici* address the product claims in this case, not the method claims.

and can only be, developed by human ingenuity using complex scientific expertise and equipment. As a result, isolated DNA molecules are patentable subject matter.

Unless reversed, the district court's ruling will seriously harm the U.S. biotechnology industry, which consists largely of small firms that are engaged in foundational research and dependent on private investment, not product revenues, to fund their work. Patent protection is essential to the ability of biotechnology firms to secure such private investment. If this Court affirms the district court's categorical rejection of the patentability of isolated DNA molecules, it would cast a cloud of uncertainty over thousands of similar patents and compromise the ability of biotechnology firms to pursue groundbreaking discoveries in human healthcare, renewable energy, and sustainable agriculture; it would also harm university research and innovation by impeding the transfer of technology from the academy to industry. Conversely, there is no basis for Plaintiffs' contention that patenting isolated DNA molecules stifles scientific innovation. Numerous recent studies confirm that such patents have not interfered with scientific progress; on the contrary, they safeguard and encourage innovation by ensuring that U.S. research entities can obtain the necessary capital to perform critical biotechnology research.

ARGUMENT

I. ISOLATED DNA MOLECULES ARE PATENTABLE SUBJECT MATTER

Congress has framed patent eligibility broadly, to include "any new and useful ... composition of matter." 35 U.S.C. §101. Although isolated DNA

molecules clearly are “composition[s] of matter,” the district court ruled them unpatentable because it believed them to be the “purification of a product of nature” and patentable only if they possessed “markedly different characteristics” from naturally-occurring DNA. A214 (quoting *Chakrabarty*, 447 U.S. at 310).

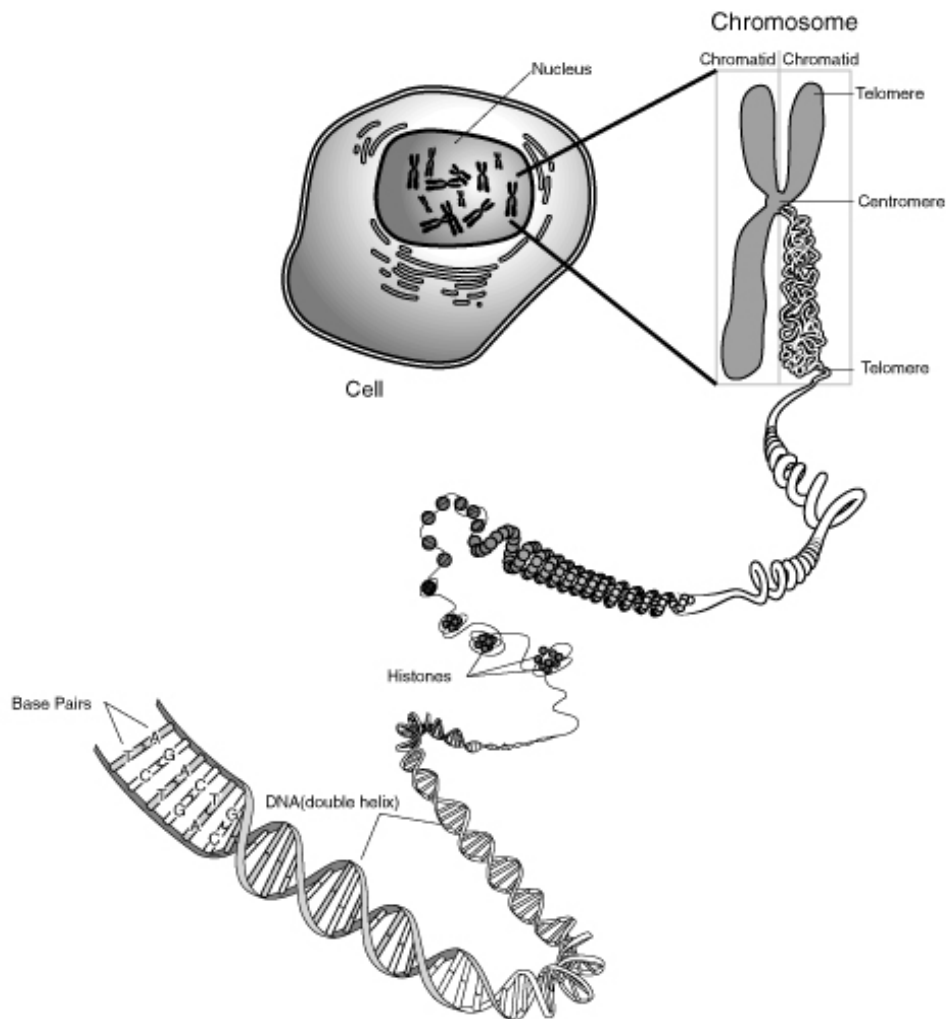
The district court’s analysis was doubly flawed. First, isolated DNA molecules are not the “purification” of naturally-occurring DNA. Rather, they are entirely different man-made molecules that do not appear in nature. Second, even if isolated DNA molecules could be considered “purified” forms of native DNA, the isolation process transforms the DNA into a new and different article with distinctive form, properties, and uses, rendering the isolated molecules patentable under longstanding precedent.

A. Isolated DNA Molecules Are New Man-Made Compositions Of Matter

The district court appeared to assume, without explanation, that isolated DNA molecules are merely the “purification” of naturally-occurring substances, rather than new substances all their own. A214. That was error. Isolated DNA molecules are freestanding chemical compounds that do not occur in nature, but rather are created by human ingenuity and, accordingly, are patentable.

Human DNA in its natural or “native” form exists as part of structures called chromosomes within the nucleus of human cells. Chromosomes are complex, stable structures consisting of extremely long strands of DNA bound together with

numerous proteins (such as histones), which give the chromosome compact form, regulate the functions of DNA, and account for half the molecular mass of the chromosome. Watson et al., *Molecular Biology of the Gene* 135 (6th ed. 2008) (“Watson”). DNA is composed of double-stranded chains of smaller components known as “nucleotides,” which form complementary “base pairs” in DNA’s double-helical structure. A125-126. Shorter sequences of nucleotides within each chromosome form functional units called “genes.” A121.



National Human Genome Research Institute, *Chromosome*, http://www.accessexcellence.org/RC/VL/GG/nhgri_PDFs/chromosome.pdf.² Through a series of complex chemical interactions with enzymes in the body, genes participate in production of proteins that serve various biological functions. Watson 377-383, 457-458. Genes, however, contain some nucleotide stretches known as “introns” that do not contribute to protein production; nucleotide stretches that do contribute to protein production are called “exons.” A121-122.

Critically, at no point in the process of protein production—or at any other point in an organism’s natural life—are genes excised or uncoupled from the rest of the chromosome. That is, genes do not naturally exist as stand-alone molecules or separate chemical compounds.³

Isolated DNA molecules differ significantly from naturally-occurring, chromosomal DNA. Isolated DNA molecules are much smaller than chromosomal DNA, frequently corresponding only to a single gene. For example, the BRCA1 gene in its native form appears on human chromosome 17, which itself contains about 80 million base pairs. U.S. National Library of Medicine, *Chromosome 17*,

² All Internet sites were last visited on October 29, 2010.

³ The district court noted that certain chromosomal DNA can dissociate from certain *proteins* during particular cellular processes. A128. That does not mean, however, that genes exist separately from the much larger *chromosomes*. Rather, native DNA remains fixed in its chromosomal context and does not become a freestanding molecule. *See* Watson 135-36, 159.

<http://ghr.nlm.nih.gov/chromosome/17> (“*Chromosome 17*”). An isolated molecule of the BRCA1 gene, however, consists of only about 80,000 nucleotide pairs (*see id.*, *BRCA1*, <http://ghr.nlm.nih.gov/gene/BRCA1>) and exists and is usable outside of human cells (A588-619). Creation of an isolated BRCA1 DNA molecule requires identification of the gene among more than 20,000 genes that comprise the human genome and the 1200-1500 genes on the vast length of chromosome 17. *Chromosome 17*. The desired portion of chromosomal DNA is then excised from the rest of the chromosome by unbundling the chromosomal DNA from structural proteins and breaking particular covalent chemical bonds in the sugar-phosphate backbone of the chromosomal DNA. A127. The excised DNA molecule must typically be “amplified” (replicated million-fold through laboratory techniques to generate sufficient DNA for automated sequencing) and physically separated from other genomic DNA through a technique such as gel electrophoresis. *See* Watson 740-741, 751-757. This process yields a new and separate chemical compound that does not exist in nature.

The distinction between native chromosomal DNA and the artificial chemical compounds at issue is even starker in the case of so-called complementary DNA, or “cDNA.” cDNA molecules consist solely of exons, nucleotide stretches that contribute directly to the production of proteins. A133-134. cDNA does not occur naturally in the body; indeed, even the nucleotide

sequence of a cDNA molecule has no analogue in native chromosomal DNA, where the nucleotide sequences are interrupted by introns. A134. For example, the naturally-occurring BRCA1 and 2 genes each contain more than 70,000 nucleotides, while the exons that make up their corresponding cDNA molecules together have fewer than 16,000. A3656-3657. Thus, the structure of the claimed isolated cDNA molecules differs substantially from that of the natural BRCA genes.⁴

The district court notably did not rule that isolated genomic DNA molecules or cDNA were naturally-occurring substances. Rather, it framed the question as “whether or not claims directed to isolated DNA *containing naturally-occurring sequences* fall within the products of nature exception.” A195-196. Even leaving aside the dubious legal status of a “product[] of nature exception” as the court conceived it (*cf.* Appellants’ Br. 35, 41), the court erroneously compared the claimed molecules to naturally-occurring *nucleotide sequences*, rather than to naturally-occurring *DNA molecules*. Although they share the nucleotide sequence

⁴ The district court appeared to suggest that naturally-occurring “pseudogenes” within an organism’s chromosomal DNA necessarily contain identical nucleotide sequences to cDNA molecules corresponding to genes. A134, A222. The evidence the district court cited does not support that conclusion. One witness testified that nucleotide sequences in pseudogenes differed from cDNA sequences by at least 10%. A6974-6975. Another referenced an example where only a *portion* of BRCA1 cDNA was contained in the chromosomal DNA as a pseudogene. A7023. And in both examples, the pseudogene sequences—unlike cDNA—remain fixed portions of the larger chromosomal sequence, not freestanding molecules.

of some portion of chromosomal DNA, isolated genomic DNA molecules do *not* occur naturally because they are new and distinct molecules with different chemical structures from naturally-occurring DNA in a chromosome. The same is true *a fortiori* of cDNA, which does not even contain the same nucleotide sequence as any naturally-occurring gene in a chromosome. The USPTO has acknowledged the patentability of isolated DNA molecules for precisely these reasons. USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (2001) (“An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene ... is eligible for a patent as a composition of matter or as an article of manufacture because *that DNA molecule* does not occur in that isolated form in nature Like other chemical compounds, DNA molecules are eligible for patents when isolated from their natural state and purified[.]” (emphasis added)).

The district court also erroneously relied on two early Supreme Court cases that invalidated patents for *lack of novelty* because the claimed substances previously existed. A203-204. In *American Wood-Paper Co. v. Fiber Disintegrating Co.*, the Court ruled that a patent on wood pulp was “void for want of novelty” because “whatever may be said of their process for obtaining it, the product was in no sense new.” 90 U.S. (23 Wall.) 566, 595 (1874). Likewise, in *Cochrane v. Badische Anilin & Soda Fabrik*, the Court found a patent on “artificial alizarine” invalid because alizarine was not a “new composition of matter” but an

“old article.” 111 U.S. 293, 311 (1884). Neither opinion suggested, however, that a man-made molecule that did *not* previously exist was unpatentable subject matter.

Of course, the mere fact that isolated DNA molecules are patentable subject matter does not mean that every such molecule can be validly patented. Rather, patent eligibility is “only a threshold test”; a claimed invention must also be “novel, *see* §102, nonobvious, *see* §103, and fully and particularly described, *see* §112.” *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010). Accordingly, this Court has rejected claims to isolated DNA molecules on grounds of anticipation, obviousness, lack of utility, and failure to comply with the requirements of 35 U.S.C. §112. *E.g.*, *In re Gleave*, 560 F.3d 1331 (Fed. Cir. 2009) (patent to antisense DNA sequences denied as anticipated in light of prior art); *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009) (affirming USPTO’s obviousness rejection of a patent on a DNA molecule); *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) (claim to a vertebrate cDNA sequence encoding insulin held invalid for lack of written description); *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005) (rejecting claims to expressed sequence tags—short DNA molecules of unspecified cellular function—for lack of sufficient utility). None of these cases suggested that isolated DNA molecules were categorically unpatentable. Indeed,

this Court has frequently upheld patents to isolated DNA molecules without suggesting that the subject matter raised concerns under Section 101.⁵

Accordingly, the district court erred in assuming that isolated DNA molecules and cDNA are merely “purification[s]” of naturally-occurring substances. Rather, they are new compositions of matter that exist only when created by human ingenuity. That suffices to meet Section 101’s requirement of patentable subject matter. *See Chakrabarty*, 447 U.S. at 309 (upholding patentability of genetically-engineered bacterium that was a “nonnaturally occurring manufacture or composition of matter”).

B. Isolated DNA Molecules Are Chemical Compounds With New And Distinctive Properties And Uses Compared To Naturally-Occurring DNA

Even if the district court had been correct to treat isolated DNA molecules as purified products of nature, rather than as the new and distinct chemical compositions that they are, this Court should still reverse because isolated genomic DNA and cDNA molecules are man-made and exhibit new and distinctive “character” and “uses” compared to native DNA. Indeed, as discussed more fully in Part II below, the U.S. biotechnology industry was launched largely because of the possibility of using isolated DNA molecules for important medical applications

⁵ *E.g.*, *In re Deuel*, 51 F.3d 1552, 1560 (Fed. Cir. 1995); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991); *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993).

such as gene therapy and manufacture of therapeutic proteins, for which naturally-occurring DNA is useless. Thus, even accepting the district court's incorrect assumption that isolated DNA molecules are the "purification" of naturally-occurring substances, they are still patentable subject matter under governing precedent.

The United States has a long history of issuing patents covering purified substances (including substances derived from plants and other organic extracts) that acquire new and distinctive characteristics and properties through human ingenuity. In 1873, Louis Pasteur received U.S. Patent 141,072, which claimed "[y]east, free from organic germs of disease, as an article of manufacture." *See* USPTO Utility Examination Guidelines, 66 Fed. Reg. at 1093. A patent issued in 1900 claimed purified acetylsalicylic acid (aspirin), a naturally-occurring substance previously obtained only in impure form as a "product of coal tar."

Farbenfabriken of Elberfeld Co. v. Kuehmsted, 171 F. 887, 890 (C.C.N.D. Ill. 1909) (upholding patent against invalidity challenge, noting that the inventor "took a comparatively worthless substance and changed it into a valuable one"). And in 1911, Judge Learned Hand, sitting as a district judge, ruled that the utility of purified adrenaline extracted from animal glands rendered it patentable:

[E]ven if it were merely an extracted product without change, there is no rule that such products are not patentable. [The inventor] 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.

Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 103 (C.C.S.D.N.Y. 1911), *aff'd in relevant part*, 196 F. 496 (2d Cir. 1912).⁶

The Supreme Court has similarly indicated that a preexisting product (whether sourced naturally or otherwise) that undergoes a “transformation” producing a “new and different article” with “a distinctive name, character, or use” is a patentable “manufacture.” *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 12-13 (1931) (quoting *Hartranft v. Wiegmann*, 121 U.S. 609, 613, 615 (1887)) (ruling a borax-coated orange patent-ineligible because it “remains a fresh orange, fit only for the same beneficial uses as theretofore”).⁷ Other courts considering whether purified substances were patentable over preexisting impure extracts have likewise pointed to new and beneficial uses of the claimed invention

⁶ Contrary to the district court’s reasoning (A209-210), Judge Hand’s observation that a purification that produces “a new thing” with a new use renders the resulting product patent-eligible is consistent with the Supreme Court’s decisions, as discussed below.

⁷ It is far from clear that *American Fruit Growers* imposed a general rule of patentability, as opposed to a characteristic of a “manufacture,” and the decision has been criticized even on its own terms. *See, e.g., Chisum on Patents* §1.02[3][a] (2010) (noting that a borax-coated orange that proved mold resistant would have a distinctive quality or property). Nonetheless, even assuming that Section 101 requires that a patentable product have a “new or distinctive form, quality or property” compared to a naturally-occurring item, the isolated DNA molecules at issue here plainly satisfy that test.

as the defining criterion. *E.g.*, *In re Merz*, 97 F.2d 599, 601 (C.C.P.A. 1938) (“[I]f the process produces an article of such purity that it differs not only in degree but in kind[,] it may be patentable. If it differs in kind, it may have a new utility in which invention may rest.”); *see also Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156, 164-165 (4th Cir. 1958) (upholding claims to vitamin B12 compositions because, even if viewed as “purification of the active principle in natural fermentates,” the claimed compositions possessed significant utility compared to the “quite useless” natural fermentates, such that the “new products are not the same as the old”); *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379, 1389 n.6 (N.D. Cal. 1987) (noting that purified Factor VIII:C, a natural blood clotting protein, is patent-eligible).⁸

Isolated DNA and cDNA molecules have a significantly different “character” and “use” compared to genes within their native setting, *i.e.*, within a large and complex chromosomal DNA molecule. In their natural form, human genes are trapped in the midst of other chromosomes and all the hundreds of other

⁸ Contrary to the district court’s apparent belief (A212 n.48), *Chakrabarty* did not adopt an additional requirement that a claimed purified substance have “markedly different characteristics” from the natural substance. The Court’s observation that the claimed strain of bacteria had “markedly different characteristics from any found in nature and one having the potential for significant utility,” *Chakrabarty*, 447 U.S. at 311, merely confirmed that the claimed strain had a “distinctive name, character, or use,” *Hartranft*, 121 U.S. at 615 (cited in *Chakrabarty*, 447 U.S. at 309-310). In any event, as shown in text, isolated DNA molecules *do* possess “markedly different characteristics” from naturally-occurring chromosomal DNA.

components of a cell; they are essentially inaccessible and under the control of the physiology of the organism in which they reside. A125-126. Native DNA serves its natural purpose within a cell, but it cannot be used in virtually any practical diagnostic, therapeutic, or industrial application. In this respect, it resembles the therapeutically useless “product of coal tar.” *Farbenfabriken*, 171 F. at 887.

Isolating a DNA molecule, in addition to creating a whole new chemical composition that does not exist in nature (*see supra* §I.A), imparts new utilities and functions unavailable from native DNA. For example, one of the patents-in-suit contemplates gene therapy using isolated DNA molecules that can be copied many times over and then introduced into patients’ cells to replace missing, mutated, cancer-inducing, or otherwise malfunctioning genes. A603 (32:34-33:20).

Isolated DNA molecules can also be introduced into bacterial, yeast, or mammalian host cell expression systems to produce proteins (such as tumor suppressing proteins) in mass quantities and with a quality that natural sources cannot produce, thereby permitting therapeutic uses. A604 (34:39-63).

Native DNA simply cannot be used in these therapeutic applications. Rather, it is only when a new, isolated DNA molecule is produced independently from a chromosome that these uses become possible. Accordingly, this is not a situation in which natural substances “serve the ends nature originally provided and act quite independently of any effort of the patentee.” *Funk Bros. Seed Co. v.*

Kalo Inoculant Co., 333 U.S. 127, 131 (1948). Rather, isolated DNA molecules serve ends that nature never contemplated and that would be impossible without the intervening effort of the patentee. They are accordingly “new and different article[s]” that have distinctive “character” and “use” compared to native DNA. *American Fruit Growers*, 283 U.S. at 12-13 (quoting *Hartranft*, 121 U.S. at 615).

The district court dismissed the utility of isolated DNA molecules as “*primarily* a function of the nucleotide sequence identity between native and isolated BRCA1/2 DNA.” A224 (emphasis added). But the utility of isolated DNA is no more attributable to its similarity to native DNA than the utilities of insulin, penicillin, vitamin B12, adrenaline, or other drug preparations are due to their similarity to their naturally-occurring counterparts. The district court’s observation could be made about essentially any biotechnology product. An inquiry into *why* isolated DNA is useful, however, cannot detract from the fact that it *is* useful. Its utility depends on the fact of isolation: the isolated molecule’s chemical separation from other genomic material in the chromosome and its resulting amenability to use as a therapeutic, diagnostic, or industrial tool. It is not as though native DNA can be used in those applications or that isolated molecules are effective to a greater degree; rather, native DNA cannot be used for such purposes *at all*. That is the “character” and “use” that distinguishes isolated DNA molecules from native DNA for purposes of patentability.

C. The District Court Improperly Treated DNA Molecules As “Different” From Every Other Chemical Compound, Incorrectly Treating DNA As Mere Information

The district court’s ruling also rested on its fundamentally erroneous decision to ignore “the chemical nature of DNA” and instead treat DNA as “a physical embodiment of *information*.” A217 (emphasis added). The court often employed this metaphor, likening DNA’s nucleotide sequence to “information”—whether in a chromosome within the human body or in isolated molecules in a laboratory. *E.g.*, A95-96 (“DNA represents the physical embodiment of biological information, distinct in its essential characteristics from any other chemical found in nature.”); A121 (each gene “contains the information used by the body to produce those proteins”); A123 (“Gene sequences constitute biological information insofar as they describe the structural and chemical properties of a particular DNA molecule and serve as the cellular ‘blueprint’ for the production of proteins.”).

DNA sequences are often analogized to “information,” in that the sequence of particular nucleotides in a gene can be said to “tell” which protein is produced. But the various “informational” metaphors used in nomenclature for chemical processes associated with DNA—transcription, translation, editing, codes—are just that: metaphors. DNA itself is a chemical, and proteins are produced through

chemical reactions.⁹ The description of those reactions as a relaying of “information” may be useful as a pedagogical tool, but it does not differentiate DNA from any other chemical compound. In the presence of appropriate enzymes and reactants, under appropriate conditions, DNA participates in a series of chemical reactions that form proteins, just as other enzymatically-driven chemical reactions take place to form various products.

To be sure, DNA plays an important role in biology. But the proposition that *native* DNA has “unique properties ... that distinguish it from all other chemicals and biological molecules found in nature” (A216 n.51) is not a reason to treat *man-made, isolated* DNA molecules differently under Section 101 from other man-made chemical compounds. The statute does not justify a one-off exception for isolated DNA molecules merely because DNA can be metaphorically described as “information” (A136, A217), as “fundamental to biological thought” (A216), or as our “common heritage” (A119). Isolated DNA and cDNA molecules are chemical compounds. That they possess characteristics that can be compared to information or language does not change their fundamental nature as “compositions of matter” that are patentable under Section 101.

⁹ Specifically, enzymes interacting with a gene’s nucleotide sequence catalyze the formation of mRNA, another type of molecule also comprised of nucleotides but that excludes introns. Other enzymes, in turn, interact with the mRNA molecules to catalyze the formation of strings of amino acids or “polypeptides,” which eventually become the proteins that serve the body’s various biological functions.

II. INVALIDATING PATENTS ON ISOLATED DNA MOLECULES WOULD DISCOURAGE, NOT PROMOTE, INNOVATION

A. Patents On Isolated DNA Molecules Promote Innovation

Patents on isolated DNA molecules have featured prominently in a number of biotechnology success stories. For example, Amgen's pioneering work with erythropoietin revolutionized the treatment of anemia. Patients with renal failure frequently suffered from anemia due to insufficient erythropoietin; a full 25% of renal patients on dialysis required regular blood transfusions before Amgen isolated the DNA that codes for erythropoietin and made it therapeutically available. Jelkmann, *Molecular Biology of Erythropoietin*, 43 Internal Medicine 649, 649 (2004). Amgen's development and marketing of its therapeutic, Epogen[®], virtually eliminated the need for such transfusions. Amgen's patent on the isolated DNA molecule for erythropoietin, U.S. Patent No. 4,703,008, has been critical in protecting this breakthrough. *E.g., Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991).

Another prominent success story involves Chiron Corporation, which now operates as Novartis Vaccines & Diagnostics. For decades, patients receiving blood transfusions were at serious risk of contracting a deadly form of Hepatitis formerly known as "Non-A, Non-B Hepatitis." After nearly a decade of research, Chiron scientists identified, isolated, characterized, and cloned the Hepatitis C Virus (HCV) genome. Chiron's patenting of certain isolated HCV DNA molecules

helped attract the investment and licensing revenue that allowed it to develop screening methods that dramatically changed blood testing. Screening for HCV nucleic acids using Chiron's patented discoveries has reduced the incidence of contracting Hepatitis C during a blood transfusion from an alarming 1:25 chance in 1989 to near zero today. Alter & Houghton, *Hepatitis C Virus and Eliminating Post-Transfusion Hepatitis*, 6 *Nature Medicine* 1082, 1083 fig. 2 (2000).

Patents on isolated DNA molecules have been critical in developing other important technologies:

Therapeutic Proteins. DNA-based therapeutics are used to treat many diseases and conditions, including cancer, diabetes, growth deficiency, rheumatoid arthritis, hemophilia, and hepatitis. Although recombinant DNA and cell cultures are generally used to produce therapeutic replacement proteins and monoclonal antibodies, patents on isolated DNA encourage foundational research and facilitate the disclosure and additional investment needed to bring DNA-based therapeutics to market.

Gene Therapy. Replacement gene therapy can treat diseases caused by the lack of a particular protein, such as hemophilia or severe combined immunodeficiency disease (SCID). BIO, *Guide to Biotechnology* 34 (2008), available at <http://www.bio.org/speeches/pubs/er/BiotechGuide2008.pdf> ("*Guide to Biotechnology*"). Transient gene therapy has been tested for the treatment of

various cancers, autoimmune diseases, chronic heart failure, nervous system disorders, and AIDS. *Id.* One study found that gene therapy restored the vision of dogs afflicted by Leber congenital amaurosis, a previously-untreatable condition that causes almost complete blindness. Subsequent phase I trials in humans showed a statistically significant increase in visual sensitivity in three human subjects 30 days after treatment. Cideciyan et al., *Human Gene Therapy for RPE65 Isomerase Deficiency Activates the Retinoid Cycle of Vision But With Slow Rod Kinetics*, 105 Proc. Nat'l Acad. Sci. 15112, 15113-15114 (2008).

Vaccination. By using DNA that encodes only certain proteins from the surface of a virus or bacteria, biotechnology innovators have been able to manufacture vaccines carrying a lower risk of infection. Vaccines that use small pieces of DNA to trigger antibody production also have the potential to provide immunization against microbes for which no vaccine is currently available. *Guide to Biotechnology* 34.

Genetic Testing. As with screening for HCV, patents on isolated DNA molecules help attract investment that allows researchers to develop genetic tests to identify hereditary diseases, test a patient's genetic predisposition to a particular disease, or screen for pathogens. This testing promises to usher in an era of "personalized medicine"—also known as targeted therapy—in which knowledge about an individual patient's genome can help identify optimal treatments and

dosages. Between 1993 and 2009, the number of diseases for which genetic testing is available increased from just over 100 to more than 1,800. *See* GeneTests, *Growth of Laboratory Directory* (2000), <http://www.ncbi.nlm.nih.gov/projects/GeneTests/static/whatsnew/labdirgrowth.shtml>. The current Director of the National Institutes of Health has observed that “personalized medicine remains one of the most compelling opportunities we have to improve the odds of staying healthy.” Collins, *Personalized Medicine*, Boston Globe, July 17, 2005, at E12.

Agriculture. Researchers continue to work on ways to feed more people at lower cost and with less environmental impact by identifying and using genetic markers associated with natural resistance to insects and diseases, resistance to environmental stresses such as drought and temperature fluctuations, and improved characteristics such as lower nutrient use and higher yield. Substantial investment is still required to unlock the full potential of DNA-based agriculture. Important genomes, such as the cow and chicken genomes, were not sequenced until 2004. *Guide to Biotechnology* 49. The corn genome, only the third of any major crop to be sequenced, was not completed until 2008. *Id.* at 14. Private investment will play a critical role in encouraging further research and translating it into important new products that will change the way food is grown around the world.

Food Safety. The importance of DNA-based inventions to the food supply does not end on the farm. DNA probes can detect harmful or lethal

microorganisms in the food supply. When a problem is detected, DNA fingerprinting can be used to trace products back to their source and enable appropriate remedial steps.

Industrial and Environmental Biotechnology. Patents on isolated DNA molecules are also important for industrial, energy, and environmental applications. DNA-encoded biocatalysts, such as enzymes, can decrease energy use, replace harsh chemicals in industrial processing, and produce biofuels and green plastics without the use of petroleum, helping to reduce dependence on “dirty” energy sources and mitigate global climate change.

Unforeseeable Discoveries. Just as important as DNA-based research already in progress are the unforeseen discoveries that the right incentives will enable. As of 2008, less than one percent of the world’s microorganisms had been cultured and characterized. *Guide to Biotechnology* 64. A stable patent system that rewards the discovery, characterization, and isolation of useful DNA molecules is critical to encouraging the private investment that will help bring future discoveries to fruition.

B. A Decision That Isolated DNA Molecules Are Not Patent-Eligible Would Have Far-Reaching Negative Consequences

Unless reversed, the decision below promises to cause serious harm to U.S. biotechnological innovation. The biotechnology industry depends heavily on patent protection to encourage the investment of time and capital necessary to

develop inventions—including those discovered industrially or in-licensed from world-class universities in support of further academic research—into real-life products. Biotechnological investment is substantial: 2008 saw more than \$30 billion in biotechnology-related research and development investment in the United States alone. Ernst & Young, *Beyond Borders: Global Biotechnology Report* 34 (2009). The average cost of bringing a single biotechnology-related therapeutic to market, including basic research, clinical trials, and post-approval testing, exceeds \$1.2 billion. Grabowski, *Follow-On Biologics*, 7 *Nature Reviews Drug Discovery* 479, 482 (2008). For every successful product, many more are abandoned, often only after large investments have been made. *E.g., id.* at 481 (only 30% of biological therapeutics that make it as far as human trials succeed).

In light of the high risk and difficulty involved, patents are critical to reassuring investors that they will earn a reasonable financial return on products that actually make it to market. This is particularly true for biotechnology companies, most of which are emerging firms with 50 or fewer employees working on products that can take 15 years or more to produce. *Guide to Biotechnology* 2, 77. Because such entities cannot fund their work on revenue from product sales, they rely on investor capital for survival. *Id.* at 2.

The stage in the corporate lifecycle after the point of basic discovery but before proof of concept has been described as the “valley of death”—a time when

companies struggle to raise the hundreds of millions of dollars needed to take their inventions to the next stage of development. Patents—including those on isolated DNA molecules—play a critical role in sustaining innovative companies during this period and beyond. Patents “are typically the only assets those firms possess that are sufficiently stable and valuable to attract the large amounts of capital they need to exploit promising research toward new drugs and diagnostics.” Barfield & Calfee, *Biotechnology and the Patent System* 27 (2007); see also Grabowski et al., *The Market for Follow-On Biologics*, 25 *Health Affairs* 1291, 1299 (2006) (“Intellectual property has been an important factor for biotech start-ups in securing venture funding and partnerships with larger firms.”). Such intellectual property is often in-licensed from universities, which recognize that the costs and risks of product development cannot be borne by public or non-profit entities. *E.g.*, AUTM, *University Technology Transfer*, http://www.autm.net/AM/Template.cfm?Section=White_Papers&Template=/CM/ContentDisplay.cfm&ContentID=1895 (describing development of human insulin).

A ruling that isolated DNA molecules are categorically ineligible for patent protection would shake investor confidence and interfere with the ability of biotechnology companies, particularly small companies, to attract the capital needed to fund further research and development. A limited preview of what might happen came in March 2000 when investors mistakenly interpreted a

statement by President Clinton and British Prime Minister Blair as announcing an intent to narrow patent protection for gene-based innovations. Even though the statement was quickly clarified, leading American biotechnology companies lost \$50 billion in aggregate shareholder value over the following two weeks. Davies, *Cracking the Genome* 205-207 (2001).

The decision below has even greater potential to disrupt the willingness of investors to fund research and development. Although the district court purported to limit its decision to isolated DNA molecules (A216 n.51), its distinction between nucleic acids and other compositions of matter is questionable for the reasons discussed in Part I. The decision therefore potentially casts doubt on patent protection for a wide variety of natural substances that have been isolated and purified (*see supra* §I.B), to the detriment of the biotechnology industry and the public.

III. CLAIMS TO ISOLATED DNA MOLECULES DO NOT HARM PATIENTS OR IMPEDE THE PROGRESS OF SCIENCE

Plaintiffs have claimed that patents on isolated DNA molecules harm patients and stifle research. Such contentions do not withstand scrutiny. As a *Nature* editorial recently summarized, opponents of DNA patenting initially

worried that patents would make it harder to develop new genetic diagnostic tests; that corporate monopolies would hamper patients' access to the tests; and that thickets of interlinked intellectual property rights would scare off those interested in researching and improving the tests.... But for all the fuss, few, if any, of the initial concerns have been borne out.

Property Rights: The Granting of Patents on Human Genes Has So Far Not Been the Disaster It Was Predicted To Be, 458 Nature 386 (2009). Summarizing empirical research, the Federal Trade Commission likewise noted that “concern previously centered on the belief that biotechnology patent protection was too strong” and “would actually obstruct commercialization of new products, thereby hindering follow-on innovation. This problem has yet to materialize.” FTC, *Emerging Health Care Issues* 32 (2009) (footnote omitted).

A. Patents On Isolated DNA Molecules Benefit Rather Than Harm The Public

The stories of the individual Plaintiffs in this case help explain why BIO members have pushed so hard to encourage insurance companies with restrictive reimbursement policies to pay for important therapeutics and diagnostics and to establish company-sponsored plans that provide products and services to patients who cannot afford them. A106-107, A149-150 (discussing patients whose insurance companies would not pay for genetic testing). Plaintiffs’ effort to abolish patents on isolated DNA molecules, however, is misdirected and short-sighted. It mistakes problems in the insurance system for problems in the patent system and will harm rather than help patients in the long run.

It is easy to argue after an invention has already been discovered and disclosed that the public would be better off if it were not patented. It is just as easy to single out a particular invention and argue with the benefit of hindsight that

patent protection was not necessary for its discovery and development. Such facile arguments ignore the long-term benefits that the public derives from providing patent protection in exchange for the disclosure of new and useful discoveries. *See, e.g., Eli Lilly & Co. v. Premo Pharm. Labs., Inc.*, 630 F.2d 120, 138 (3d Cir. 1980) (“Congress has determined that it is better for the nation in the long-run to afford the inventors of novel, useful, and nonobvious products short-term monopolies on such products[.]”).

The advances made by the U.S. biotechnology industry under current law were not inevitable, and the industry’s future success depends on the ability to continue attracting private investors willing to shoulder the substantial risk of financing research and development. In the life sciences, early-stage companies hold roughly two-thirds of the future clinical pipeline. Boston Consulting Group, *Rising to the Productivity Challenge* 6 & Ex. 4 (2004). Without patent protection for isolated DNA molecules, many companies would be unable to see those projects through to completion. The list of potentially life-enhancing therapeutics and diagnostics that die in the pipeline as a result might never be known. But their absence would be acutely felt by patients.

B. Patents On Isolated DNA Molecules Do Not Impede The Progress Of Science

Plaintiffs and their amici argued below that patents on “upstream” inventions, such as isolated DNA molecules, stifle basic research. But this often-

repeated claim is largely based on speculation and a few high-profile anecdotes rather than solid evidence. See Caulfield et al., *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 *Nature Biotech.* 1091 (2006). “[E]mpirical research suggests that the fears of widespread anticommons effects that block the use of upstream discoveries have largely not materialized.” *Id.* at 1093; see also Adelman & DeAngelis, *Patent Metrics*, 85 *Tex. L. Rev.* 1677, 1681 (2007) (“The existing empirical studies find few clear signs that the patenting of biotechnology inventions is adversely affecting biomedical innovation.”).

For example, a 2006 report by the National Research Council of the National Academies found that

the number of projects abandoned or delayed as a result of technology access difficulties is reported to be small, as is the number of occasions in which investigators revise their protocols to avoid intellectual property complications or pay high costs to obtain access to intellectual property. Thus, for the time being, it appears that access to patents or information inputs into biomedical research rarely imposes a significant burden for academic biomedical researchers.

National Research Council, *Reaping the Benefits of Genomic and Proteomic Research* 134 (2006).

A 2005 survey of scientists involved in biomedical research found that “patenting does not seem to limit research activity significantly, particularly among those doing basic research.” Walsh et al., *Patents, Material Transfers and Access to Research Inputs in Biomedical Research* 3 (Sept. 20, 2005), available at

<http://www2.druid.dk/conferences/viewpaper.php?id=776&cf=8> (“Walsh, *Patents & Access*”). Only one percent of a random sample of 381 academic scientists reported a project delay of more than a month due to patents on materials necessary for their research, and *none* reported abandoning a research project due to the existence of patents. *Id.* at 17; *see also* Walsh et al., *View from the Bench*, 309 *Science* 2002 (2005).

An earlier study found that patents “rarely precluded the pursuit of worthwhile projects.” Walsh et al., *Working Through the Patent Problem*, 299 *Science* 1021, 1021 (2003). It noted that “for a given project, usually fewer than a dozen outside patents require serious consideration, and the number of licenses required is much fewer, often none.” *Id.* When requested, licenses were often available at minimal or no cost. Walsh, *Patents & Access*, at 17. “Thus, not only are barriers or delays rare, but costs of access for research purposes are negligible.” *Id.*

Anecdotes regarding specific instances of patent enforcement, such as those involving Myriad (*e.g.*, A152-155), fall far short of demonstrating that patents on isolated DNA impede research. As an initial matter, it is important not to confuse the ordinary assertion of patent rights against *commercial competitors* with limits on basic research. “Myriad appears to have never asserted its patents based on genetic testing research, but only against substantial direct commercial

competitors.” Holman, *The Impact of Human Gene Patents on Innovation and Access*, 76 UMKC L. Rev. 295, 347 (2007). Indeed, a vast amount of BRCA-related clinical and experimental research has been conducted since Myriad’s patents issued. *See* A5570-5575; *see also* Huys et al., *Legal Uncertainty in the Area of Genetic Diagnostic Testing*, 27 *Nature Biotech.* 903, 909 (2009) (“[T]he present analysis and accompanying observations do not point to the existence of a wide patent thicket in genetic diagnostic testing.”). Arguments about stifling research also ignore the protection provided to researchers under 35 U.S.C. §271(e)(1), *see Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005), and the common law research exception, *see Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (Story, J.).

More fundamentally, anecdotes about a single company or single field of use hardly provide a sound basis for eliminating all patents on isolated DNA molecules. The public has been well served by the USPTO’s position that isolated DNA molecules are patent-eligible subject matter and its reliance on other, more carefully tailored doctrines to block patents that should not issue. *See supra* p. 10. If a different balance is to be struck, it should be struck by Congress based on sound evidence and with due regard to the reliance interest of existing patent-holders, rather than by the courts based on anecdotal evidence about one particular patent-holder.

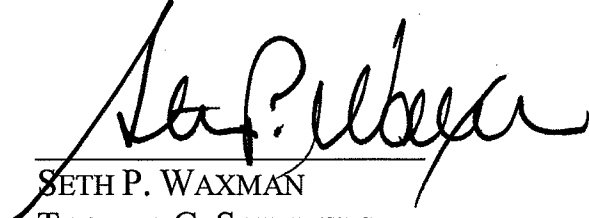
CONCLUSION

The judgment of the district court should be reversed.

Dated: October 29, 2010

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CERTIFICATE OF SERVICE

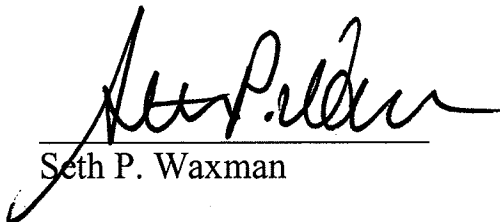
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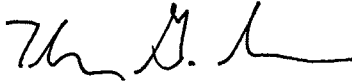
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CERTIFICATE OF COMPLIANCE

Counsel for Amici Curiae Biotechnology Industry Organization and Association of University Technology Managers hereby certifies that:

1. The brief complies with the type-volume limitation of Federal Rules of Appellate Procedure 29(d) and 32(a)(7)(B)(i) because exclusive of the exempted portions it contains 6,998 words as counted by the word processing program used to prepare the brief; and
2. The brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type-style requirements of Federal Rule of Appellate Procedure 32(a)(6) because it has been prepared using Microsoft Office Word 2003 in a proportionally spaced typeface: Times New Roman, font size 14.

Dated: October 29, 2010



Thomas G. Saunders