2010-1406

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 OF AMICUS CURIAE BOSTON PATENT LAW ASSOCIATION IN SUPPORT OF DEFENDANTS-APPELLANTS AND REVERSAL OF SUMMARY JUDGMENT

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OCTOBER 29, 2010

CERTIFICATE OF INTEREST

Counsel for *amicus curiae*, Boston Patent Law Association, certifies the following:

1. The full name of every party or *amicus* represented by me is:
Boston Patent Law Association

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 me is: None

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 me are: None

4. [x] There is no such corporation as listed in Paragraph 3.

5. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

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THE BOSTON PATENT LAW ASSOCIATION'S INTEREST

The Boston Patent Law Association ("BPLA") is a nonprofit association of intellectual property attorneys and professionals who serve a broad range of clients that rely on the patent system, such as inventors, corporations, investors, universities, and research hospitals. These clients operate in an equally broad range of industries, including life sciences, high-tech, and traditional manufacturing.

The BPLA is concerned that denying patent eligibility to personalized medicine inventions, such as those at issue in this case, will hinder the development of better diagnostics and therapies, cripple the biotechnology industry, and discourage innovation generally.

Pursuant to F.R.A.P. 29(a), the BPLA has received the consent of all parties to file this *amicus* brief.[1]

INTRODUCTION

"But times change." These may be the three most important words in the Supreme Court's recent primer on § 101 patent eligibility, *Bilski v. Kappos*, 130 S. Ct. 3218, 3227 (2010). The Court's point is that the test for eligibility should not be stuck in the Industrial Age, when patent law had only to contend

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[1] This brief is solely the work of the BPLA and reflects its consensus view but not necessarily the view of any individual member or client. The BPLA's counsel in this matter, McCarter & English LLP, contributed its time in preparing this brief *pro bono*. No other entity funded or prepared this brief.

with machines made of iron, levers, gears, and springs. The personalized medicine inventions in this case--certain isolated DNA sequences and methods for using them--may have been unforeseen in the Industrial Age, but they are still worthy of patent protection today. Indeed, the Supreme Court reminds us that "Section 101 is a 'dynamic provision designed to encompass new and unforeseen inventions.'" *Id*. (citation omitted).

The popular media has portrayed this case, sensationally and incorrectly, as asking whether genes are patentable. The patents at issue, however, do not claim genes. Rather, the patents claim isolated DNA sequences, which are chemically distinct from what exists in nature and, unlike native genes, can be used as tools for diagnosing or treating disease. These human-made tools are not mere products of nature and thus are eligible for patent protection.

The district court's judgment to the contrary is faulty because it is based on a metaphor for the claimed invention rather than on the invention itself. The district court viewed isolated DNA as mere information--something akin to an unpatentable algorithm or code. But that view misconstrues isolated DNA, which is an engineered composition or manufacture. For sure, isolated DNA, like native DNA, carries information. But many other chemicals carry information, and yet nobody would view them as unpatentable. The district court's failure started with incorrect claim construction and spiraled from there.

Apart from the scientific and legal bases for patent eligibility, there is also an important policy reason for eligibility here. More than any other single factor, patents encourage innovation, competition, and access to new technologies. Limiting what can be patented will make patents less attractive, which in turn will deter innovation and commercialization of new products. Indeed, without Myriad's patents, doctors and patients would not benefit from the diagnostic tests at issue because no entity, let alone Myriad, would have taken the financial risk necessary to commercialize them. Denying patent eligibility here will weaken the patent system, weaken incentives for innovation, and thus weaken our national health and welfare.

ARGUMENT

I. THE CLAIMED INVENTIONS ARE PATENT ELIGIBLE

Reasoning that an isolated DNA sequence conveys the same information as the analogous native DNA sequence, the district court held that the claimed isolated DNA sequences are not "markedly different" from the native species and are thus unpatentable products of nature. *Ass'n for Molecular Pathology v. U.S. Patent and Trademark Office*, No. 09-Civ-4515, 2010 U.S. Dist. LEXIS 35418 at * 144-47 (S.D.N.Y. Apr. 5, 2010). To reach that result, the district court had to characterize DNA as merely a "physical embodiment of information." *Id*. at *135. Indeed, the district court distinguished DNA from

all other chemicals purely because it conveys information. *Id*. at *134 n.51. But that distinction confuses a lay person's metaphor for DNA with the scientific view, which sees DNA as a polymeric chemical structure. *Isolated* DNA is a human-engineered polymer that is chemically distinct from its native analog and, unlike native DNA, has many diagnostic and therapeutic uses.

A. Eligibility For Patent Protection Under Section 101 Is Broad

The first patent commissioner, Thomas Jefferson, believed that "ingenuity should receive a liberal encouragement." In keeping with this philosophy, the statute governing patent eligibility is worded broadly:

> Whoever invents or discovers <u>any</u> new and useful process, machine, manufacture, or composition of matter, or <u>any</u> new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

35 U.S.C. § 101 (emphasis added). "In choosing such expansive terms as 'manufacture' and 'composition of matter,' modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope." *Diamond v. Chakrabarty*, 447 U.S. 303, 308 (1980).

The Supreme Court recently reaffirmed the broad scope and liberal purpose of § 101 by rejecting the "machine-or-transformation" test as the sole eligibility test for process claims because it was too limiting, especially in the Information Age, when inventions are no longer confined to mechanical products and processes. *Bilski v. Kappos*, 130 S. Ct. 3218, 3226-27 (2010). Of

course, the machine-or-transformation test can still be a "useful and important clue" to patent eligibility. *Id.* at 3227. But a "categorical rule" that would deny patent protection to inventions unforeseen in the Industrial Age "would frustrate the purposes of the patent law. *Id.* (citing *Chakrabarty*, 447 U.S. at 315). This inclusive nature of § 101 should inform this Court's analysis.

B. Myriad's "Isolated" DNA Claims Are Patentable

For purposes of § 101 eligibility, the claimed isolated DNA can be considered at least as a "manufacture." "Manufacture" means "the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery." *Chakrabarty*, 447 U.S. at 308 (citation omitted).

The *Chakrabarty* court ruled that a genetically-engineered bacterium was a "manufacture" eligible for a patent under § 101 because it was "markedly different" from natural bacteria and had "the potential for significant utility." *Id*. at 310. In support of this conclusion, the Court relied in part on a Congressional report discussing how a living thing, such as a new plant variety, could be distinguished from a product of nature and thus be eligible for a patent: "a plant discovery resulting from cultivation is unique, isolated, and is not repeated by nature, nor can it be reproduced by nature

unaided by man." *Id*. at 313 (citation omitted). Because the claimed bacterium was "the result of human ingenuity and research," it was patent eligible. *Id*.

As discussed below, the claimed isolated DNA molecules are manufactures eligible for patent protection because they result from cultivation and cannot be reproduced unaided by man. Put another way, and in keeping with the Supreme Court's definition of "manufacture," isolated DNA is the product of "raw" or native DNA that, through human ingenuity and labor, is physically transformed such that it has a new form, quality, or property. Isolated DNA has the potential for significant utility that the native DNA lacks.

1. The Correct Construction Of "Isolated" DNA Sequences

An essential first step in the assessment of patentability is a proper construction of the claims at issue. Claim terms must be given their ordinary meaning to a person of ordinary skill in the art. *Phillips v. AWH Corp.,* 415 F.3d 1303, 1313 (Fed. Cir. 2005) *(en banc*). If the patentee has defined the term in question, that definition controls. *Martek Biosciences Corp. v. Nutrinova, Inc.,* 579 F.3d 1363, 1380, 1382 (Fed. Cir. 2009). Here, the patentees have characterized the claimed inventions as chemical structures that have been "isolated" and then modified or refined through human ingenuity.

Claims 1, 2, and 5-7 of U.S. Pat. No. 5,747,282 ("the '282 patent") are drawn to an "*isolated*" DNA coding for a BRCA1 polypeptide, "*isolated*"

fragments thereof, and "*isolated*" mutants thereof. For example, Claim 1 is directed to "[a]n *isolated* DNA coding for a BRCA1 polypeptide having the amino acid sequence set forth in SEQ ID NO:2." The term "isolated" likewise appears in the claims of U.S. Pat. Nos. 5,837,492 and 5,693,473.

The patents define "isolated" to mean that the chemical structure has been engineered or, in a sense, cultivated or modified through human intervention:

> An "isolated" or "substantially pure" nucleic acid (e.g., an RNA, DNA or a mixed polymer) is one which is substantially separated from other cellular components. . . . The term embraces a nucleic acid sequence or protein which has been removed from its naturally occurring environment, and includes recombinant or cloned DNA isolates and chemically synthesized analogs or analogs biologically synthesized by heterologous systems.

'282 patent, col. 19, *ll*. 8-19 (emphasis added); *see also* '492 patent, col. 17, *l*. 62 -- col. 18, *l*. 5; '473 patent, col. 19, *ll*. 6-15.

The patents further recognize that the claimed isolated DNA sequences are chemical structures or compositions, not simply information:

> [t]he polynucleotide compositions of this invention include RNA, cDNA, genomic DNA, synthetic forms, and mixed polymers, both sense and antisense strands, and may be chemically or biochemically modified or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those skilled in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as uncharged linkages . . . and modified linkages (e.g., alpha anomeric nucleic acids, etc.).

'282 patent, col. 19, *ll*. 51-66; *see also* '492 patent, col. 18, *ll*. 36-51; '473 patent, col. 19, *ll*. 46-61.

Example 8 of the '282 patent details the extensive manipulation--or cultivation, if you will--of the naturally occurring BRCA1 gene that resulted in the isolation of the chemically distinct and human-made *isolated* BRCA1 sequences of the claims. S*ee* '282 patent, col. 52, *l*. 30 -- col. 58, *l*. 51.

2. Isolated DNA Markedly Differs From Native DNA

For at least a century, patents have been allowed for compositions isolated from nature or purified beyond their natural state. For example, Louis Pasteur obtained a valid U.S. patent claiming "[y]east, free from organic germs of disease, as an article of manufacture." U.S. Patent No. 141,072. In the early 1900s, Parke Davis & Co. obtained a patent for adrenaline, an otherwise naturally-occurring substance. In upholding the patent, the court ruled that adrenaline purified from a gland was patentable. The court reasoned that purified adrenaline differed "not in degree, but in kind" from native adrenaline and that, even if extraction did not change the substance chemically, extraction still resulted in "practical differences." The purified form "became for every practical purpose a new thing commercially and therapeutically . . . [and that] was a good ground for a patent." *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (S.D.N.Y. 1911), *aff'd*, 196 F. 496 (2d Cir. 1912).

This Court's predecessor has also upheld claims for purified or isolated compounds, observing that such compounds were not naturally occurring:

> Those compounds, as far as the record establishes, do not exist in nature in pure form, and appellants have neither merely discovered, nor claimed sufficiently broadly to encompass, what has previously existed in fact in nature's storehouse, albeit unknown, or what has previously been known to exist.

In re Bergstrom, 427 F.2d 1394, 1401 (C.C.P.A. 1970); *see also, e.g.*, *In re Kratz*, 592 F.2d 1169 (C.C.P.A. 1979) (purified compound found in strawberries was patentable); *Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958) (purified Vitamin B_{12} extracted from a micro-organism was patentable).

The key here, and what distinguishes Myriad's case from the extracted or modified products that were denied patent protection in cases on which the district court relied--such as *American Wood Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874) and *American Fruit Growers, Inc. v. Brodgex*, 283 U.S. 1 (1931)--is that the claimed nucleic acid molecules are markedly different from the naturally occurring genes. Similar to the purified compounds discussed above, the claimed nucleic acid (*e.g.,* DNA) molecules have, by virtue of their isolation, been transformed into new and useful manufactures with practical applications previously unavailable to humankind.

More specifically, the claimed nucleic acid molecules were separated (*i.e.*, "isolated") from other cellular components. There is no mechanism in the human body for the isolation of nucleic acid molecules. As basic procedures in recombinant DNA demonstrate, identifying, isolating, and purifying genes can be accomplished only through a series of complicated steps requiring human intervention. *See* James D. Watson *et al*., *Recombinant DNA* 99-133 (2d ed. 1992). Further, the DNA fragments and cDNA molecules claimed in the '282 patent do not exist naturally in the human body. Rather, they are "man made" compositions or manufactures.

Isolated nucleic acid molecules have new properties that allow them to perform new technological functions that could not have been performed using the naturally occurring genes. For example, unlike their naturally-occurring cousins, isolated nucleic acid molecules can be used in genetic tests to determine the presence of a specific DNA sequence that may be associated with a predisposition to a particular disease or responsiveness to a particular drug. *See* James D. Watson *et al*., *Recombinant DNA* 539 (2d ed. 1992).[2]

[2] Naturally occurring genes cannot be used in diagnostic applications because, among other things, (a) their sequences may be too long for practical hybridization to a patient's DNA and (b) they are not labeled and, thus, cannot be detected. *See, e.g*., M. Aquino de Muro, "Probe Design, Production, and Applications," Ch. 4 at 41-54 in *Molecular Biomethods Handbook* (J.M. Walker & R. Rapley, eds., 2d ed. 2008).

These isolated nucleic acid molecules may also be used to make DNA vaccines or to genetically engineer cells that can be grown in large scale cell cultures to produce, for example, large quantities of a therapeutic antibody or other proteins. *Id*. at 460. Isolated nucleic acid molecules may also be used to produce new agricultural products with improved properties like pest and disease resistance. *Id*. at 471-75. Thus, in the case of isolated nucleic acid molecules, human intervention has done much more than merely removing a natural product from its natural environment. Rather, scientists have produced a product with functions, properties, and characteristics that are different in kind from those of the naturally occurring molecules.

Other marked differences are also apparent. For example, the isolated DNA molecules of Claim 2 of the '282 patent and Claim 2 of the '492 patent are cDNA molecules. A cDNA molecule is a single-stranded DNA molecule "complementary" to a corresponding RNA molecule. *See* Benjamin Lewin, *Genes V* 164 (1994). cDNA is synthesized from an RNA template by reverse transcriptase, an enzyme that is not naturally present in a human cell and not encoded by a human gene but rather encoded by reverse-transcribing viruses. *Id*. at 164, 1237. cDNAs are either made by retroviruses or are synthetic molecules made from mRNA by enzymatic reactions carried out in the laboratory. Watson *et al*., *Recombinant DNA, supra* at 102-104. Thus, the

claimed cDNAs are not synthesized *in vivo* during regular cellular DNA replication or transcription of genes but rather can only be produced in the lab. *See* Lewin, *Genes V*, *supra* at 1237. [3]

By definition, isolated DNA or cDNA molecules are also different from naturally-occurring genes, even if they carry or convey the same information. Those of ordinary skill in the art view DNA as a chemical composition. *See, e.g.*, D. Voet & J.G. Voet, *Biochemistry* 848-914 (2d ed. 1995) (chapter entitled "Nucleic Acid Structures and Manipulation"). This Court has also viewed DNA as a chemical. *See Regents of the Univ. of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997) (treating claims for rat insulin cDNA as a chemical structure for purposes of the written description analysis). The USPTO also views DNA as a chemical, not as merely a living software code. *See* USPTO Utility Examination Guidelines, 66 Fed. Reg. No. 4, 1093 (Jan. 2001) ("Like other chemical compounds, DNA molecules are eligible for

[3] While mRNAs result from regular cellular gene expression *in vivo*, they are chemically distinct from cDNAs. They contain different sugars and otherwise differ in composition. *See* Watson *et al*., *Recombinant DNA, supra* at 14, 37-38. The sugar present in DNA is deoxyribose, while the sugar present in RNA is ribose. *Id*. at 14. The base compositions of RNAs and DNAs also differ. DNA contains thymine, whereas RNA contains uracil. The difference in the type of sugar present causes RNA to be less chemically stable. Voet & Voet, *Biochemistry*, *supra*, at 850. In addition, because of the difference in sugar structures, the three-dimensional structure of double-stranded forms of DNA typically differs from that of double-stranded RNA or RNA-DNA hybrids. L. Stryer, *Biochemistry* 788-790 (4th ed. 1995).

patents when isolated from their natural state and purified or when synthesized in a laboratory from chemical starting materials") (emphasis added). Thus, contrary to the district court's use of a metaphor to characterize DNA, the claimed nucleic acid molecules must be viewed as chemical compositions or manufactures that are chemically and functionally distinct from naturally occurring DNA.[4]

Moreover, naturally occurring genes are composed of "exons" and "introns." Unlike naturally-occurring genes, cDNA molecules contain no introns. Lewin, *Genes V, supra* at 150 and Figure 6.18 (showing that introns are removed from precursor RNA when exons are spliced together). Thus, cDNA molecules (such as those claimed in the '282 and '492 patents) have chemical structures that differ completely from naturally-occurring genes.

[4] Distinguishing DNA from all other chemicals or matter, as the district court did, fundamentally misunderstands chemistry and biology. Many other chemicals convey information and yet they would not be subject to the same scrutiny or controversy as in this case. For example, prion proteins carry information that allows them to adopt an extremely stable 3-D conformation (the disease form) that can itself convert other normal pre-prion proteins to the disease form. A. Aguzzi, "Unraveling prion strains with cell biology and organic chemistry," *Proceedings of the National Academy of Sciences of the United States of America* 105 (1): 11–2 (2008). Fullerenes, a class of molecules composed entirely of carbon, also carry information that allows them to self-assemble into various structures. *See*, *e.g.*, Fullerene, Encyclopedia Britannica on-line (www.britannica.com) and U.S. Pat. No. 7,132,572, entitled "Fullerine compounds."

Contrary to the district court's analysis, it does not matter that the claimed isolated DNA sequences convey the same information as their naturally-occurring *in vivo* analogs. The point of *Parke-Davis* and similar cases is not that the isolated or purified matter had a different function from the naturally-occurring version. Indeed, as taught by the underlying patent in *Parke-Davis*, purified adrenaline has the same biological function as adrenaline produced in the body--namely "hemostatic, blood-pressure-raising, and astringent properties." *See* U.S. Pat. No. 730,176. Rather, the point is that isolation or purification "renders available for use the above-mentioned properties of the suprarenal glands in a stable, pure, and concentrated form." *Id*. at col. 1, *ll*. 44-50. In the same way, the claimed nucleic acid molecules in this case have, by virtue of their isolation, been rendered available for use. Neither naturally occurring genes nor the proteins they create in the cells of the body are available for use. *See, e.g.*, T. Strachen & A.P. Read, *Human Molecular Genetics* 401-426 and 515-543 (2d ed. 1999).

That being said, isolated nucleic acid molecules provide and enable various entirely new technological functions that are different from the functions of the naturally occurring genes present in the body. For example, as seen above, isolated nucleic acid molecules may be used to diagnose diseases, but naturally occurring genes cannot be so used. Isolated nucleic acid

molecules may also be used to make DNA vaccines or to produce large quantities of a therapeutic antibody--again, functions that the naturally occurring genes cannot perform.

In short, the claimed isolated DNA molecules have markedly different structural and functional characteristics as compared with naturally occurring genes, and they enable new and valuable applications previously unknown and unavailable to man.

C. Myriad's Claimed Methods Are Patentable

Even though laws of nature, natural phenomena, and abstract ideas may not be patentable, it is well-established that "an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection." *Diamond v. Diehr,* 450 U.S. 175, 187 (1981); *accord*, *Bilski v. Kappos*, 130 S. Ct. 3218, 3230 (2010). Here, Myriad has found new applications for isolated DNA. Thus, the method claims are patent eligible independent of the isolated DNA product claims.

This Court has held that a method for calibrating drug dosages by measuring metabolites in patients is patent-eligible because determining levels of the metabolite in the patient "necessarily involves a transformation, for those levels cannot be determined by mere inspection," and the determining step is central to the method. *Prometheus Labs. v. Mayo Collaborative Servs.,* 581

F.3d 1336, 1347 (Fed. Cir. 2009). Although the claim did not recite a specific means for determining the metabolite level, it was understood that such determining step involved transforming the blood sample by means of "[s]ome form of manipulation, such as high pressure liquid chromatography." *Id*.[5]

Likewise, Myriad's diagnostic method claims--such as those found in the '999, '001, '441, and '857 patents--satisfy § 101 because each requires the transformation of a patient sample to isolate the patient's DNA and analyze it. For example, the "comparing" step in these claims encompasses at least hybridization of a probe to RNA isolated from the patient's sample and detection of a hybridization product (*see*, *e.g.*, Claim 4 of the '441 patent and Claim 4 of the '001 patent). At the end of this process, the patient's sample is no longer the same--it has been chemically and physically altered or changed.

Detecting a difference between the germline sequence of a *BRCA* gene in a patient's tissue sample with the germline sequence of the wild-type *BRCA* gene requires testing of a sample that has been derived from the subject.

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[5] The Supreme Court has vacated *Prometheus* and has remanded the case for further consideration in the wake of the *Bilski* opinion. Previously, this Court affirmed that the claimed diagnostic methods in *Prometheus* were patent eligible because they satisfied the machine-or-transformation test. Although the Supreme Court held that the machine-or-transformation test is no longer *the* exclusive test, it also held that it could still be used as *a* test. Accordingly, the BPLA believes that this Court's *Prometheus* holding is unaffected by *Bilski* and should be reaffirmed and followed in this case.

Testing the sample entails transforming the sample such that detection of the gene alteration can be made possible. For example, nucleic acid sequences may be extracted from the sample and, subsequently, the sample can be contacted with a labeled probe that is able to hybridize to the germline sequence within the sample and detect it. *See* Lewin, *Genes V*, *supra* at 645-47. Methods for extracting and detecting the nucleic acid sequences entail transforming the sample. *See, e.g.,* Watson *et al*., *Recombinant DNA*, *supra* at 129-130. Moreover, this transformation is central to the purpose of the underlying diagnostic or screening methods because this step is not only "a significant part" of these claims as required by *Prometheus*, 581 F.3d at 1347, but is the essence of these claims. Thus, claims directed to such methods are eligible under §101.

II. PATENTS PROMOTE INNOVATION AND BENEFIT SOCIETY

The historian and author William Rosen argues that the "single most powerful idea in the world"--which led first to the invention of the steam engine, then to the Industrial Revolution and its culture of sustained invention, and finally to America's dominant, prosperous, and innovative economy--was not the discovery of some physical law or the invention of a particular gadget, but rather the idea that ideas themselves can be property subject to exclusive rights--i.e., the patent. William Rosen, *The Most Powerful Idea in the World*

324 (2010). In his book, Rosen asks why the Industrial Revolution started in England and then expanded, exponentially, in the United States during the 18th and 19th centuries, rather than in some other place and time, such as ancient Greece or Renaissance Italy. The answer is that England and then the U.S. had an organized, legally-mandated patent system conducive not just to invention but also to disclosure and commercialization of inventions. President Lincoln, who is the only U.S. president awarded a patent (No. 6469, entitled, "Buoying Vessels Over Shoals"), explained how the patent system itself is an innovation:

> The advantageous use of Steam-power is, unquestionably, a modern discovery. And yet, as much as two thousand years ago, the power of steam was not only observed, but an ingenious toy was actually made and put in motion by it, at Alexandria in Egypt. What appears strange is that neither the inventor of the toy, nor any one else, for so long a time afterwards, should perceive that steam would move useful machinery as well as a toy . . . in the day before Edward Coke's original Statute on Monopolies [the first patent law, enacted in 1624], any man could instantly use what another had invented; so that the inventor had no special advantage from his own invention. . . . The patent system changed this; secured to the inventor, for a limited time, the exclusive use of his inventions; and thereby added the fuel of interest to the fire of genius, in the discovery and production of new and useful things.

From President Lincoln's speech entitled, "Discoveries, Inventions, and Improvements," as quoted in *The Most Powerful Idea in the World* at 323-24 (emphasis added); *see also, e.g.*, David Silverstein, *Patents, Science and Innovation: Historical Linkages and Implications for Global Technological*

Competitiveness, 17 Rutgers Computer & Tech. L.J. 261, 263 (1991) ("the U.S. patent system has played a significant role in both stimulating innovation and promoting the commercialization of new technologies").

Patents promote innovation and commercialization of new products and processes in many ways. For example, companies will not invest in research and development unless they can be assured of some market exclusivity. Patent law provides the necessary exclusivity and thus fosters investment in innovation. *See Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480 (1974) ("The patent laws promote this progress by offering a right of exclusion for a limited period as an incentive to inventors to risk the often enormous costs in terms of time, research, and development"); *Patlex Corp. v. Mossinghoff*, 758 F.2d 594, 599 (Fed. Cir.) ("encouragement of investment-based risk is the fundamental purpose of the patent grant, and is based directly on the right to exclude"), *modified*, 771 F.2d 480 (Fed. Cir. 1985).

The BPLA views this case not just as a narrow question about whether certain isolated DNA claims are patentable but more broadly as an attack on the patent system itself. One of Plaintiffs-Appellees' themes in the underlying case, which has been repeated in the popular media, is that Myriad's patents stifle competition and unfairly limit research in and access to important technologies for diagnosing and treating breast and ovarian cancers. But this

argument fundamentally misunderstands the role and nature of patents. Patents promote innovation and actually increase research in and access to personalized medicine and other life-saving technologies. Without patents, no women would have access to the breast and ovarian cancer tests at issue because no company would risk the huge investment to commercialize them.

A. Biotechnology Inventions Are Costly To Develop; Patents Protect Investment In Such Inventions

The biotechnology industry is an important and growing sector of the economy that not only generates new life-saving drugs and diagnostics but also jobs and tax revenues. For example, in the BPLA's home state of Massachusetts, there are over 430 biotechnology companies employing an estimated 45,000 people, with payrolls totaling over $4 billion. These companies have more than 2,200 drugs in development (about 8% of the global pipeline of drugs) and account for over $4 billion in exports.[6]

Strong patent protection for biotechnology products will ensure that this sector of the economy remains vibrant and innovative. *Cf. Kewanee Oil Co.* 416 U.S. at 480 ("The productive effort thereby fostered [by patents] will have a positive effect on society through the introduction of new products and

[6] These estimated figures were provided to the authors of this brief by the Massachusetts Biotechnology Council.

processes of manufacture in the economy, and the emanations by way of increased employment and better lives for our citizens").

More specifically, biotechnology inventions are costly to develop. A Tufts University study estimates that the cost of discovering, developing, and then commercializing a new biotechnology product averages $1.2 billion. *See* Tufts Center for the Study of Drug Development, Press Release: *Average Cost to Develop a New Biotechnology Product is $1.2 Billion* (November 9, 2006), *available at* http://csdd.tufts.edu/NewsEvents/NewsArticle.asp?newsid=690. Another study, conducted by researchers from the Federal Trade Commission's Bureau of Economics, calculates that development costs range from about $500 million to as much as $2 billion. *See* Christopher P. Adams & Van V. Brantner, *Estimating the Cost of New Drug Development: Is it Really $802 Million?*, 25 Health Affairs 420 (March/April 2006); Joseph D. DiMasi *et al.*, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. Health Econ. 151, 166 (2003).[7]

Adding to this cost is the time involved in product development. From the start of clinical trials to FDA approval averages 90.3 months (7.5 years).

[7] The dollar figures reported above reflect "capitalized" costs, which factor in the cost of capital and other accounting factors. The actual out-of pocket costs are lower but still significant. For example, according to the Tufts study cited above, out-of-pocket costs for pre-clinical product development average $198 million and $361 million for clinical trials.

See DiMasi *et al*., 22 J. Health Econ. at 164-165 (2003). From initial drug discovery to the start of human testing averages 52 months (4.33 years). *Id*. at 166. Thus, getting a new product to market can take twelve years or more. *See also* Henry Grabowski, *Patents, Innovation and Access to New Pharmaceuticals*, 5 J. Int'l Econ. L. 849, 851 (2002) (drugs take "several hundred million dollars to discover, develop, and gain regulatory approval," and the process can "take more than a decade to complete").

New product development is also risky. Most product candidates never make it to market. Either they fail to make it out of the lab, to emerge from clinical trials, or to gain FDA approval. According to the Tufts study cited above, only one in three biotechnology products that begins clinical trials ever emerges with FDA approval. The success rate for conventional drugs is even less. *See* Grabowski, 5 J. Int'l Econ. L. at 851 (fewer than 1% of new compounds make it to clinical trials, and only 22% of compounds in clinical trials receive FDA approval).

Given these high costs, time lags, and risks, it is no wonder that patents have become so important to the biotech industry. Companies and investors would not fund such risky research and development projects absent strong patent protection. *See* Dan L. Burk, *Biotechnology and Patent Law: Fitting Innovation to the Procrustean Bed*, 17 Rutgers Computer & Tech. L.J. 1, 22

(1991) ("one concrete fact is clear: patents are critical to the growth and competitiveness of American biotechnology because patents are something that investors expect"); F. Scott. Kieff, *Facilitating Scientific Research: Intellectual Property Rights and the Norms of Science--A Response to Rai and Eisenberg*, 95 Nw. U. L. Rev. 691, 704 (2001) (the ability of patents to attract investment has been the "critical factor in the great success the [biological research] community has enjoyed since 1980"); Grabowski, 5 J. Int'l Econ. L. at 851-52 (same); Yusing Ko, *An Economic Analysis of Biotechnology Patent Protection*, 102 Yale L.J. 777, 800 (1992) (same).

B. Patents Spur Creativity And Competition

Patents foster innovation and competition in at least three ways. First, the *quid pro quo* of the patent grant is disclosure. Without patents, inventors would tend to keep their inventions secret for fear of misappropriation. Giles S. Rich, *The Relation between Patent Practices and the Anti-Monopoly Laws*, 24 J. Pat. Off. Soc'y 159, 177-180 (1942). Newcomers can thus build on the store of knowledge created by earlier patent disclosures. *Id*. at 180. Indeed, rather than inhibiting the exchange of information, as some fear, patents actually facilitate full disclosure. Kieff, 95 Nw. U. L. Rev. at 701 (the patent system "is in fact a time-tested way to assure broad and ready access to proprietary information") (citation omitted).

Second, patents make the exchange of information--and thus the invention process itself--more efficient. *See* Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J. L. & Econ. 265, 276-77 (1977). For example, upon review of another company's patent, a competitor can avoid duplicating the patentee's effort and can allocate R&D resources to a different project. Alternatively, the competitor can avoid the mistakes of the first inventor. That is, many patents never result in commercial products. Later innovators, however, can learn from the failures of the earlier patentees without having to reinvent the proverbial wheel. Without a patent system, these failures would more likely remain unknown. *Id*. at 267-71; *see also* Giles S. Rich, *The Principles of Patentability*, 42 J. Pat. Off. Soc'y 75, 83 (1960) ("It should never be forgotten that *patented* inventions are published. . . . *Patents* on inventions that have failed can promote progress").

Third, patents force competitors to "design around," meaning to invent new solutions that do not infringe the patent. The threat of patent enforcement thus stimulates research and prompts competitors to develop new, perhaps superior products that might otherwise have gone undeveloped. *See Yarway Corp. v. Eur-Control USA, Inc*., 775 F.2d 268, 277 (Fed. Cir. 1985) ("This court has indicated that the incentive to 'design around' patents is a positive result of the patent system"). The end result of this tension between patent

owners and would-be copyists is that patents actually stimulate, rather than hinder, innovation and competition:

> Thus, paradoxically, monopoly may evoke competition: The threat from patent monopolies in the hands of such "outsiders" may create a sort of competition—a David versus Goliath competition—which reduces the inertia of some huge industrial aggregations that might otherwise be sluggish [in developing new products].

Picard v. United Aircraft Corp., 128 F.2d 632, 642-43 (2d Cir. 1942) (Frank, J., concurring); *see also* Mark Blaxill & Ralph Eckardt, *The Invisible Edge: Taking Your Strategy to the Next Level Using Intellectual Property* 57 (2009) (patents allow smaller companies to compete with larger or better funded ones).

C. Patents Prevent Free Riders And Encourage Wider Availability And Distribution Of New Products

Inventors may or may not be motivated by economic gain. Some may invent for glory. Some out of academic curiosity. And some for altruistic reasons. The great insight of the patent system, however, is that even if a given inventor does not care about economic gain, the company that would commercialize the invention most certainly does. An individual inventor may not be an industrialist with the resources to manufacture or promote his or her invention. A patent, however, allows the inventor to put the invention into the hands of an entrepreneur or company that can. *Picard,* 128 F.2d at 642-43

("But if we never needed, or do not now need, patents as bait for inventors, we may still need them, in some instances, as a lure to investors").

Without patents, inventors may not risk disclosure for fear of misappropriation. Correspondingly, investors would not fund innovation and industrialists would not commercialize the invention absent the exclusive rights needed to prevent free-riding. In short, free riders (not patents) stifle innovation and the free-flow of information between inventors and producers. *See* Erik S. Maurer, Note, *An Economic Justification for a Broad Interpretation of Patentable Subject Matter*, 95 Nw. U. L. Rev. 1057, 1060-63 (2001); Ko, 102 Yale L.J. at 799; Rich, 24 J. Pat. Off. Soc'y at 177-180.

Many inventions will not make it into the hands of consumers at all absent strong patent protection. *See, e.g.,* Ko, 102 Yale L.J. at 799 ("A monopoly secured through patent protection could thus increase, rather than restrict, the use of an invention. . . ."). This principle is particularly true in the biotechnology industry, which requires such a large investment to commercialize a new product. *Id*. at 800.

Judge Rich provided a good illustration of this concept. He recounts the plight of Mr. Spencer, who invented an improved wheelchair. Spencer neglected to patent his invention, however, preferring instead to donate his wheelchair to society. The problem was that because the invention lacked

patent protection, no company would risk manufacturing it because competitors could too easily copy it. As a result, the wheelchair never made it to market and could not benefit society. Rich, 24 J. Pat. Off. Soc'y at 179.

Accordingly, invalidating the patents at issue will allow others a free ride on the efforts of the inventors and the expenditures that Myriad made to commercialize and promote its tests. Seeing this, other companies will curtail research and development efforts, and innovation will decrease significantly.

D. The Criticism Of Gene-Related Patents Is Overstated

In the district court, Plaintiffs-Appellees argued that Myriad's patents stifle research. But this argument was based on limited anecdotal evidence and ignored the big picture. Studies indicate that biotechnology patents "do not seem to have a substantial impact upon academic research . . . and only about 1% of the random sample of academics reported experiencing a delay or modification in their research due to patents." John P. Walsh *et al*., *Patents, Material Transfers and Access to Research Inputs in Biomedical Research*, Final Report to the National Academy of Sciences' Committee on Intellectual Property Rights in Genomic and Protein-Related Inventions, 37 (2005); s*ee also* Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, 76 UMKC L. Rev. 295, 299-300 (2007) ("the paucity of documented examples in which

the fears surrounding gene patents have manifested themselves is striking . . . the case against gene patents is attenuated to the extent it relies on anecdotal evidence and unsubstantiated assumptions") and at 352 (". . . a patentability bar specifically targeting genes or DNA seems unwarranted at the current time").

If anything, patents promote research by providing a mechanism (*e.g.*, royalties from patent licensing) to fund it. Kieff, 95 Nw. U. L. Rev. at 704.

E. Without Strong Patents, Innovation Will Decline

Without strong patent protection, new product development throughout the economy, but particularly in the life sciences field, will decline sharply. *See, e.g.*, Grabowski, 5 J. Int'l Econ. L. at 851 n.6 (60% of new pharmaceuticals would not have been developed without patent protection") and 853 ("Without a well-structured system of patent protection, neither the research pharmaceutical industry nor the generic industry would be able to grow and prosper, and the rate of new product introductions and patent expirations would decline significantly").

The link between healthy patents and a healthy economy is strong. For example, the 1970s is generally seen as a decade of economic stagnation in which the U.S. lost its edge to foreign competition. Toyota and BMW began to compete with GM and Ford. Sony color TVs quickly outsold those of RCA. Scholars explain that during that decade, government policies and academic

theories tended to view patents suspiciously. Likewise, courts in the 1970s tended to invalidate patents more frequently and otherwise issued rulings that weakened patent protection. These policies, court rulings, and academic theories made patents less attractive to American businesses. As a result, patent applications by U.S. companies declined sharply. R&D spending and technological innovation likewise declined. Foreign companies were soon able to outpace American innovation or--just as often--were able to buy up devalued American patents and inventions at bargain rates. *See* Blaxill & Eckardt, *The Invisible Edge, supra*, at 66-69 and 232-38 (2009); Silverstein, 17 Rutgers Computer & Tech. L.J. at 268-70 and 302-315.

Beginning in the 1980s, however, with some pro-patent rulings by this (newly-formed) Court and a pro-patent shift in government policies and academic philosophy, patents came back into fashion. An improved economy and a boom in technological innovation--including the blossoming of the biotechnology industry--soon followed. *Id*. Indeed, according to economic studies, biotechnology innovation and growth in the United States since 1980 is largely due to a revived patent system. Kieff, 95 Nw. U. L. Rev. at 701 (citing studies by the National Research Council and others). This Court, therefore, should support innovation by viewing the DNA inventions at issue as eligible for patent protection.

CONCLUSION

The BPLA respectfully urges this Court to consider the setbacks to innovation and the economy that a narrow reading of § 101 will have in this case. Affirming the district court will weaken the biotechnology industry and our economy generally. Accordingly, this Court should reverse the district court and hold that the patent claims at issue are eligible for patent protection.

Dated: October 29, 2010

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ASSOCIATION FOR MOLECULAR V PTO, 2010-1406

DECLARATION OF AUTHORITY PURSUANT TO 28 U.S.C. § 1746 AND FEDERAL CIRCUIT RULE 47.3(d)

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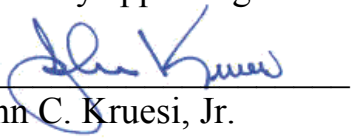
October 29, 2010



John C. Kruesi, Jr.

United States Court of Appeals
for the Federal Circuit

ASSOCIATION FOR MOLECULAR V PTO, 2010-1406

CERTIFICATE OF SERVICE

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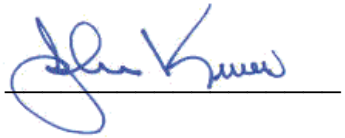

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I certify that this brief complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B) and this Court's Local Rule 32(b). According to the word-count feature of the word processing program used in preparing this brief (Microsoft Word 2002), this brief contains **6,912** words, excluding the parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii) and this Court's Local Rule 32(b).

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