No. 12-398

IN THE

Supreme Court of the United States

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,
Petitioners,

v.

MYRIAD GENETICS, INC., ET AL.,
Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

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BRIEF OF *AMICI CURIAE* AMERICAN MEDICAL ASSOCIATION, AMERICAN SOCIETY OF HUMAN GENETICS, AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, AMERICAN OSTEOPATHIC ASSOCIATION, AMERICAN COLLEGE OF LEGAL MEDICINE, AND THE MEDICAL SOCIETY OF THE STATE OF NEW YORK IN SUPPORT OF PETITION FOR WRIT OF CERTIORARI

Professor Lori B. Andrews
Counsel of Record
Chicago-Kent College of Law
Illinois Institute of Technology
565 West Adams Street
Chicago, IL 60661
landrews@kentlaw.iit.edu
(312)906-5359

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STATEMENT OF INTEREST OF *AMICI CURIAE*[1]

Genetic information is integral to physicians' determination of which diseases a patient might be suffering from and which treatments might benefit or harm that patient. Patents on human genes interfere with physicians' ability to provide appropriate care to their patients. These patents inhibit, rather than encourage, scientific research and technological innovation. They also contravene this Court's long-standing precedents about the scope of patentable subject matter.

Amici are organizations of health care professionals. Their members number in the hundreds of thousands and they provide health care across the country. *Amici* are concerned about the effect that the Federal Circuit's decision will have on the practice of medicine and on medical research. *Amici* urge the Court to grant certiorari and establish clearly that isolated DNA and cDNA are products of nature and therefore are not patentable subject matter and that the correlation between a potential therapeutic and cellular growth rate is an unpatentable law of nature.

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[1] No counsel for a party authored this brief in whole or in part, and no such counsel or party made a monetary contribution intended to fund the preparation or submission of this brief. No party or entity other than *amici*, their members, or their counsel, made a monetary contribution to this brief's preparation or submission. Counsel of record received timely notice of the intent to file this brief under Supreme Court Rule 37. Petitioners have filed a letter with the Clerk of the Court granting consent to the filing of any and all *amicus curiae* briefs. Respondents' consent has been filed with the Clerk of the Court.

***Amicus Curiae* American Medical Association (AMA)**, a non-profit organization, is the largest professional association of physicians, residents, and medical students in the United States, with over 217,000 members. The AMA joins this brief on its own behalf and as a representative of the Litigation Center of the American Medical Association and the State Medical Societies.

***Amicus Curiae* American Society of Human Genetics (ASHG)** is a non-profit organization of over 8,000 professionals in the field of human genetics including researchers, clinicians, academicians, and counselors.

***Amicus Curiae* American College of Obstetricians and Gynecologists (ACOG)** is a non-profit organization of over 51,000 health care professionals dedicated to providing quality health care to women. Over 90% of Board-certified obstetricians and gynecologists in the U.S. are affiliated with ACOG.

***Amicus Curiae* American Osteopathic Association (AOA)**, with over 44,000 members, is the largest professional association of osteopathic physicians. The AOA promotes osteopathic medicine, a holistic approach to prevent, diagnose, and treat illness, disease, and injury.

***Amicus Curiae* American College of Legal Medicine (ACLM)** is the nation's most prominent professional society comprised primarily of members holding degrees in both medicine and law. The ACLM serves medical and legal professionals and advises health policymakers.

***Amicus Curiae* Medical Society of the State of New York (MSSNY)** is a voluntary association of approximately 24,000 licensed

physicians, residents, and medical students in all specialties in New York.

SUMMARY OF THE ARGUMENT

This Court has granted certiorari in cases of great social importance. Sup. Ct. R. 10. The question of whether genetic sequences are patent eligible is of far-reaching social importance—affecting patients, physicians, health care institutions, insurers, and researchers.

The patent claims at issue are of two types. Some cover "isolated DNA" and "cDNA," which are described by their genetic sequences, while others cover the correlation between potential therapeutics and cell growth. The enforcement of these patent claims impedes the provision of health care and shackles innovation.

Moreover, Myriad's patent claims conflict with this Court's jurisprudence on subject matter patent eligibility, which holds that "laws of nature, natural phenomena, and abstract ideas" are not patentable subject matter. *Mayo Collaborative Services v. Prometheus Labs,* 132 S. Ct. 1289, 1293 (2012).

This Court vacated the original opinion of the Court of Appeals for the Federal Circuit in this case and remanded the case for consideration in light of *Mayo v. Prometheus*. *Association for Molecular Pathology v. Myriad Genetics*, *Inc.,* 132 S. Ct. 1794 (2012). On remand, the Federal Circuit refused to apply the *Mayo* holding to the genetic sequence claims, indicating that the *Mayo* decision is only relevant to the laws of nature exception and not to the products of nature exception. *Association for Molecular Pathology v. United States Patent and Trademark Office*, 689 F.3d 1303, 1325 (Fed. Cir. 2012). Yet the rationales for both exceptions are the same and the same test for patentability is employed

under both exceptions: whether a purported invention involves an inventive concept and is significantly different from nature. *Diamond v. Diehr*, 450 U.S. 175 (1981) (law of nature); *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) (product of nature); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948) (product of nature). Consequently, the *Mayo* holding is relevant to this case.

As a result of the Federal Circuit's refusal to properly analyze Myriad's patent claims in light of 35 U.S.C. § 101 and this Court's decision in *Mayo*, patient care and medical research will continue to be impeded to the detriment of patients and society. For these reasons, we respectfully request that the Court grant certiorari.

ARGUMENT

I. Physicians' and Researchers' Access to Genetic Sequences for Health Care and Research Is a Matter of National Importance and Urgency.

A person's genetic sequence holds a vast array of data relevant to his or her health. It can indicate a predisposition to disease, as well as provide guidance regarding what treatments might be beneficial (or risky) for that person. Genetic sequence information can mean the difference between life and death in the diagnosis and treatment of patients.

The benefits of genetic testing are not limited to people with rare diseases. Genetic factors contribute to the leading causes of death: cancers of all types, heart disease, hypertension, Alzheimer's, diabetes, susceptibility to infectious diseases (e.g. the flu), kidney disease, and asthma. Richard A. King, Jerome I. Rotter, and Arno G. Motulsky, The Genetic Basis of Common Diseases (2d ed. 2002). Even with respect to the narrow range of diseases that do not have a genetic component, genetic testing has a role in determining how well patients will metabolize and respond to proposed medications.

A. Patents Covering Genetic Sequences Interfere with Diagnosis and Treatment of Patients.

A patent on a genetic sequence grants the patent holder complete control over the use of that sequence. The holder can forbid health care providers from using even unpatented methods to

learn the sequence of a patient's gene. The patent holder can extract whatever royalty it wants from the person who wants to learn about his or her genetic sequence. Gene patent holders have prevented physicians and laboratories from offering genetic testing for medical conditions such as breast cancer, hearing loss, Alzheimer's, Long QT syndrome, Canavan disease, leukemia, hemochromatosis, and neurodegenerative disorders. Secretary [of Health and Human Services]'s Advisory Committee on Genetics, Health, and Society, *Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests*, 41-42 (2010) [hereinafter "SACGHS"]; Debra G.B. Leonard, *Medical Practice and Gene Patents: A Personal Perspective*, 77 Academic Medicine 1388 (Dec. 2002).

In this case, because Myriad has exclusive use of the BRCA1 and BRCA2 gene sequences, no woman can get an independent second opinion about her condition before deciding to have her healthy breasts or ovaries removed in order to avoid cancer. As a result, women may have their breasts or ovaries removed unnecessarily when they receive a false positive result on a BRCA1 or BRCA2 test because they do not have access to an independent confirmatory test. *See, e.g.*, Judy Peres, *Genetic Testing Can Save Lives – But Errors Leave Scars*, Chicago Tribune, September 26, 1999, at 1. Myriad's exclusive control of the BRCA1 and BRCA2 gene sequences also restrict men's access to diagnostic testing. Although BRCA mutations are rarer in men, a mutation does increase the risk of male breast cancer as well as prostate and pancreatic cancer.

Patents on genetic sequences have even led to the death of patients, as in the case of Long QT

syndrome, a disorder of the heart's electrical system that is characterized by irregular heart rhythms and a risk of sudden death. The disease can be treated with an implanted defibrillator. A genetic sequence associated with Long QT was patented and assigned to the University of Utah Research Foundation. U.S. Patent No. 6,207,383. For a two-year period, the exclusive licensee did not offer diagnostic testing for Long QT syndrome. Other laboratories had the capability and willingness to assess whether patients had a potentially fatal mutation of the Long QT gene, but were prevented from doing so due to the patent on the genetic sequence. During this period at least one patient, a 10-year-old girl, died from undiagnosed Long QT syndrome. Her death could have been prevented had the isolated genetic sequence not been patented. *Stifling or Stimulating – The Role of Gene Patents in Research and Genetic Testing: Hearing Before the Subcommittee on Courts, the Internet and Intellectual Property of the House Judicary Committee*, 110th Congress 40 (2007) (statement of Dr. Marc Grodman).

The promise of pharmacogenomics—the ability to test a patient's genetic sequence to determine whether a treatment might be helpful or deadly—has also been undermined by the patenting of genetic sequences. A company filed for patent protection on a genetic sequence that indicates whether patients will benefit from its asthma drug. For the 20-year term of the patent, the company will not allow anyone to use the sequence to determine whether its drug will help or harm patients. Geeta Anand, *Big Drug Makers Try to Postpone Custom Regimens*, The Wall Street Journal, June 18, 2001, at B1. Even though such information is crucial to physicians and

patients, the use of the sequence to identify people who would not benefit from a drug would diminish the market for the drug.

Patents on genetic sequences also interfere with multiplex testing, where the sequences of several genes (or even a person's entire genome) are tested at once. SACGHS at 49. For example, as many as 80 genes can indicate a predisposition to asthma. G. Malerba and P.F. Pignatti, *A Review of Asthma Genetics: Gene Expression Studies and Recent Candidates*, 46 Journal of Applied Genetics 93 (2005). For a complete diagnosis, all the relevant genetic sequences could be analyzed in one test. But genetic sequence patents preclude a single test from being used. Because some genetic sequence patents are exclusively licensed, a patient's tissue sample must be sent to multiple laboratories, increasing costs and introducing additional chances of error.

The technology exists to allow the sequencing of a person's entire genome, approximately three billion base pairs, including 20,000 genes, at an affordable rate. "The goal of completely sequencing a human genome for $1,000 is in sight." W. Gregory Feero, Alan E. Guttmacher, and Francis S. Collins, *Genomic Medicine – An Updated Primer*, 362 New England Journal of Medicine 2001, 2008 (2010). Whole genome sequencing offers the possibility of personalized medicine, where a patient can take preventive measures to minimize his or her risk for a wide range of genetic diseases. However, patents on genetic sequences impede the deployment of a whole genome analysis for patients. Sulston Decl. ¶ 38; Ledbetter Decl. ¶ 24. Testing all 20,000 of a person's genes at the Myriad BRCA rate would convert a test that could be done for $1000 to one that cost over $37

million. Applying even a seemingly modest royalty of $100 per gene would total an unaffordable $2 million per test. If the decision of the Court of Appeals for the Federal Circuit is upheld, physicians will be unable to provide meaningful results and comprehensive information from whole genome sequencing.

B. Patents Covering Genetic Sequences Impede Innovation.

Patents on "isolated" genetic sequences impede innovation. There is no way to "design around" these patents. Any research or diagnosis done on a gene from a patient's body is controlled by the patent holder because no research or diagnosis can be done without "isolating" the DNA from the body. Myriad has stopped research involving BRCA1 and BRCA2 at major universities such as Yale. Kimberly Blanton, *Corporate Takeover Exploiting the US Patent System,* Boston Globe Magazine, Feb. 24, 2002, at 10.

Myriad argues that patents are necessary to encourage innovation (such as the discovery and isolation of genetic sequences). Myriad Supp. Br. at 16-18 (Fed. Cir., June 15, 2012). But the majority of geneticists are willing to undertake the research to discover genes and develop genetic tests without the possibility of a patent. In fact, in a study of ASHG members, 61% of those in industry, 78% of those in government, and 77% of academic scientists stated that they disapproved of patenting DNA. Isaac Rabino, *How Human Geneticists in U.S. View Commercialization of the Human Genome Project*, 29 Nature Genetics 15 (2001).

Gene sequence patents are not necessary to incentivize the discovery of genes and the development of genetic tests. SACGHS, *supra*, at 30. "[P]atents were not needed to develop genetic tests for hearing loss, SCA [spinocerebellar atrophy], breast cancer, LQTS [long-QT syndrome], Canavan disease, and HH [hereditary hemochromatosis]. Indeed, all of these tests were on the market before the test offered by the relevant patent-rights holder." *Id*. at 31.

Rather than encourage innovation, genetic sequence patents stifle it. A survey of directors of laboratories that perform DNA-based genetic tests indicated that over half (53%) had been impeded from developing tests due to gene patents. Cho Decl. ¶ 10; Mildred K. Cho et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 Journal of Molecular Diagnostics 3 (2003).

C. The Issue Is Also of National Importance Because of the Substantial Public Investment in the Discovery of Genetic Sequences.

"The Human Genome Project could easily be the most important organized scientific effort in the history of mankind." M. R. C. Greenwood and Rachel E. Levinson, *Expanding the Horizons of Biotechnology in the Twenty-first Century*, *in* Biotechnology: Science, Engineering, and Ethical Challenges for the Twenty-first Century 233-245 (Frederick B. Rudolph and Larry V. McIntire eds., 1996). The entire foundation of the Human Genome Project was built on taxpayer money, which was awarded to researchers to sequence genes. Over $1.8

billion was spent by the U.S. government and non-profit institutions on genomics in the year 2000 alone. Lori B. Andrews, *Harnessing the Benefits of Biobanks*, 33 Journal of Law, Medicine and Ethics 22, 30 n. 52 (2007).

Myriad did not "invent" the BRCA genes nor did it alone discover them. Its researchers were part of an international publicly-funded consortium sequencing the breast cancer gene. Myriad used over $5,000,000 of taxpayer money from the National Institutes of Health. Bryn Williams Jones, *History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing*, 10 Health Law Journal 123, 131 (2002). Myriad also relied on the work of federal researchers from the National Institute of Environmental Health Sciences (also funded with taxpayer money) and researchers from other institutions. Rachel Nowak, *NIH in Danger of Losing Out on BRCA1 Patent*, 266 Science 208, 209 (1994).

Unlike other areas of innovation, the discovery of genetic sequences has been primarily funded by taxpayer funds. That alone gives this case major social importance. Everyone in this country has a stake in the outcome.

II. Myriad's Claims Are Invalid Under Section 101 Jurisprudence.

Nature's handiwork is excluded from patentability. *Mayo Collaborative Services v. Prometheus Labs,* 132 S. Ct. 1289, 1293 (2012); *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010). "'Laws of nature, natural phenomena, and abstract ideas' are

not patentable." *Mayo*, 132 S. Ct. at 1293 (2012) (citations omitted). "[A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter." *Mayo*, 132 S. Ct. at 1293; *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)). Rather, a newly discovered natural phenomenon must be "treated as though it were a familiar part of the prior art." *Parker v. Flook*, 437 U.S. 584, 591-92 (1978); *See also Bilski*, 130 S. Ct. at 3230.

For over 150 years, this Court has held that products of nature are not patentable (*Chakrabarty*, 447 U.S. at 309), nor are isolated or purified products of nature (*American Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. (23 Wall.) 566, 594 (1874)), nor are synthetic products that are not markedly different from what is found in nature (*Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293, 311 (1884)).[2]

Even when a newly-discovered law of nature or product of nature is novel, nonobvious, and useful, it is still unpatentable under Section 101. *Mayo*, 132 S. Ct. at 1304. Newton's law of gravity was novel and nonobvious when it was discovered. It has been

[2] The Federal Circuit tries to undermine these precedents by characterizing them as having invalidated the patent claims due to novelty concerns (now codified as §102 concerns) rather than patent eligible subject matter concerns (now codified as §101 concerns). *Association for Molecular Pathology*, 689 F.3d 1326 n. 10. However, these cases were decided under the Patent Act of 1836, Ch. 357, 5. Stat. 117 (July 4, 1836), before either §101 or §102 existed. In fact, these are the precedents, along with cases like *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1 (1931), that led to the creation of §101 in the 1952 Patent Act.

useful in understanding our physical universe and has informed our engineering disciplines. Gold mined from the earth has uses ranging from ornamentation to medicine. Even though such discoveries may meet other criteria for patentability, Section 101 prohibits their patenting. Laws of nature and products of nature must be "free to all men" so as to encourage innovation and to reward only actual inventors. *Funk Bros.*, 333 U.S. at 130.

In a patentability analysis, Section 101 is a separate and threshold analysis. *Mayo* 132 S. Ct. at 1304. To be valid, a claim involving a law of nature must have an "inventive concept" that makes the claim "significantly more" than the law of nature. *Id.* at 1294 (citing *Flook*, 437 U.S. at 594; *Bilski*, 130 S. Ct. at 3230). Similarly, a claim involving a product of nature must have an inventive concept that involves significantly more than describing the product of nature. The claimed invention must be "markedly different" from what occurs in nature. *Chakrabarty*, 447 U.S. at 310. *See also Funk Bros.*, 333 U.S. at 130 (1948); *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 11-12 (1931); *Cochrane*, 111 U.S. at 311; *American Wood-Paper Co.*, 90 U.S. (23 Wall.) at 594.[3]

Section 101 assures that innovators in our society—including physicians and scientists—have access to the raw materials for innovation. Laws of

[3] This test is no more difficult to apply than any other analysis of patentability. If an inventor patents one type of mousetrap and another inventor files for a patent on another type of mousetrap, a judgment must be made about whether the second mousetrap involved an inventive concept and was markedly different from the prior art (the first mousetrap). In the application of Section 101, a similar analysis is made. But in that case the prior art is the product of nature itself.

nature and products of nature are the "basic tools of scientific and technological work." *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972). Innovation is enhanced when all researchers have access to these basic tools.

The patent claims at issue in this case, covering isolated DNA and cDNA, which are described by their genetic sequences, are invalid because they are patents on products of nature without an inventive concept and because isolated DNA and cDNA are not markedly different from what occurs in nature in every human being. Similarly, correlations between treatments and cell growth are unpatentable laws of nature. If gene discoverers want to exempt themselves from the application of Section 101, their remedy is with Congress, not the courts.

A. Isolated DNA Is an Unpatentable Product of Nature.

Myriad's isolated genetic sequence claims do not involve an "inventive concept" and are not "markedly different" from the genetic sequence as it occurs in nature. The term "isolated" adds nothing of significance to the genetic sequence claims because isolation of genetic sequences is a well-understood conventional activity engaged in by geneticists. *See Mayo*, 132 S. Ct. at 1298.

When Myriad's counsel was pressed to identify its inventive concept at oral argument on remand, Myriad's main argument was that the decision of the scientist about where to "cut" the gene sequence to remove it from the chromosome was the inventive concept. Fed. Cir. Oral Arg. on Remand Trans. at

42:48 (July 20, 2012). Under such logic, the first surgeon who successfully removed a kidney for transplant, because he decided where to cut, could obtain a composition of matter patent covering all kidneys later removed by anyone else.

Nor does the breaking of covalent bonds make isolated DNA patentable. The change in chemical bonds is insignificant because the isolated genetic sequence is the same string of nucleotides that exists in the cell. In fact, the sequences patented by Myriad would be of no use in diagnosis or treatment if they were different from the sequences that occur naturally in the human body. Additionally, because the claims are written in terms of the genetic sequences, patentability should be determined by an analysis of the genetic sequence, not by the chemical structure.

B. cDNA Is an Unpatentable Product of Nature.

cDNA is useful in the laboratory because it has the same nucleotide sequence and contains the same information as the coding regions of naturally occurring genes and can perform the same functions as a full genetic sequence or DNA molecule. Bruce Alberts et al., Molecular Biology of the Cell 469-546 (4th ed. 2002).

Myriad's use of routine chemical tools to synthesize cDNA lacks the inventive concept necessary for patentable subject matter. cDNA is not "markedly different" from the sequence as it occurs within the chromosome. As this Court held in *Cochrane* with regard to a synthetic version of a dye, "[c]alling it artificial alizarine *did not make it a new*

composition of matter, and patentable as such, by reason of its having been prepared artificially." 111 U.S. at 311 (emphasis added).

Once the gene's naturally occurring DNA sequence—an unpatentable product of nature—is known, synthesis of cDNA is a routine mainstay of the art of biologists and chemists. Allowing a patent on cDNA would be a disproportionate reward in relation to what the alleged inventor contributed.

C. The Method Described in Claim 20 Is Unpatentable Subject Matter.

Claim 20 of U.S. Patent No. 5,747,282, like the invalid claims in *Mayo*, 132 S. Ct. at 1290-1291, consists of (1) an "administering" step (where a cell containing an altered BRCA1 gene causing cancer is grown in the presence of a potential therapeutic compound); (2) a "determining" step (where the growth of the cell with the potentially therapeutic compound is compared to the growth of a control cell); and (3) a "wherein" step (describing that a slower growth of the cell in the presence of a compound indicates a cancer therapeutic).

The "administering" step in claim 20, like the administering step in *Mayo*, only serves to identify who would be interested in the correlation: physicians. The "determining" step in *Mayo* tells the physician to measure the patient's metabolite levels using routine methods. *Id.* Similarly, the "determining" step in claim 20 tells the physician or researcher to measure the growth of the cells—a routine activity for physicians and scientists in the field. The "wherein" step in both instances simply tells the physician or researcher about the relevant

law of nature. For the same reason that the claims in *Mayo* were invalid as claiming a law of nature, this Court should grant certiorari and hold that claim 20 is invalid.

D. Myriad's Contributions Do Not Justify the Threat to Innovation.

In a Section 101 analysis, courts need to weigh "how much future innovation is foreclosed relative to the contribution of the inventor." *Mayo*, 132 S. Ct. at 1303. Indeed, "[t]he reason for the exclusion is that sometimes *too much* patent protection can impede rather than 'promote the Progress of Science and useful Arts,'" *Laboratory Corp. of America Holdings v. Metabolite Labs., Inc.*, 126 S. Ct. 2921, 2922 (2006) (J. Breyer, dissenting). In *O'Reilly v. Morse*, this Court held that by patenting all uses of electromagnetism to produce characters at a distance, "while he shuts the door against inventions of other persons, the patentee would be able to avail himself of new discoveries in the properties and powers of electro-magnetism which scientific men might bring to light." 56 U.S. (15 How.) 62, 113 (1853). In this case, Myriad can improperly avail itself of all later discoveries related to human breast cancer genetic diagnosis and treatments, disproportionate to its efforts.

Myriad's contribution to the sequencing and identification of the BRCA1 and BRCA2 genes was minor in comparison to what its patents foreclose. Myriad used common techniques to isolate, sequence, and clone the BRCA1 and BRCA2 genes. Further, Myriad did not identify the sequences on its own.

Myriad had significant scientific aid and financial support, including from taxpayer funds.

Myriad not only patented the entire genetic sequence of BRCA1 and of BRCA2, but also every sequence of 15 nucleotides that appears in the BRCA1 genetic sequence. *See* claims 5 and 6 of '282 patent. These sequences appear hundreds of thousands of times in the 3 billion base pairs of the human genome. Myriad now can demand a royalty for the use of numerous genetic tests that have nothing to do with breast cancer because those sequences of 15 nucleotides occur in so many places in the genome. There are 340,000 infringing sequences on Chromosome 1 alone. Thomas Kepler, Colin Crossman, Robert Cook-Deegan, *Metastasizing Patent Claims on BRCA1*, Genomics (2010). Since those 15 nucleotide sequences occur an average of 14 times per gene, Myriad could ask for a royalty on every test done on any gene. Myriad could hold the deployment of whole genome sequence testing hostage by threatening to pursue an infringement action for every instance one of those 15 nucleotide segments is sequenced.

E. The Federal Circuit Did Not Adequately Apply This Court's Precedents.

On remand, the Federal Circuit failed to adequately consider Section 101 and *Mayo*.[4] This

[4] On remand, the Federal Circuit issued an opinion nearly identical to its original opinion in reasoning, wording and length. A track change comparison shows how little deference the court gave to *Mayo* and how little the Federal Circuit's second decision differed from its first decision. John Conley and

Court has repeatedly stated that "laws of nature, natural phenomena, and abstract ideas" are excluded from patentability and has treated all three exceptions in the same manner. *Mayo*, 132 S. Ct. at 1293 (citing Diamond *v. Diehr*, 450 U.S. 175, 185 (1981)). Yet, Judge Lourie, writing for the majority, held that since a gene sequence is not a "law of nature," the teachings of *Mayo* do not apply. *Association for Molecular Pathology*, 689 F.3d at 1325, 1333. The Federal Circuit's approach is inconsistent with this Court's precedents which apply Section 101 to both laws of nature and products of nature. *Diehr*, 450 U.S. 175 (law of nature); *Funk Bros.*, 333 U.S. 127 (product of nature); *Chakrabarty*, 447 U.S. 303 (product of nature). Judge Lourie failed to realize that the law of nature exception is identical to the products of nature exception and thus the teachings of *Mayo* are relevant to this case.

Moreover, the Federal Circuit ignored its own precedents in holding that genetic sequences are patentable. The Federal Circuit elsewhere has correctly recognized that a patent cannot be granted to an applicant who has discovered a natural attribute of an entity. *In re Cruciferous Sprout Litigation*, 301 F.3d 1343 (Fed. Cir. 2002). In that case, the Federal Circuit stated, "[T]he glucosinolate content and Phase 2 enzyme-inducing potential of sprouts necessarily have existed as long as sprouts themselves, which is certainly more than one year before the date of application . . . ." *Id.* at 1350. Here,

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Dan Vorhaus, *Applying Mayo to Myriad: Latest Decision Brings No New News*, Genomics Law Report, Aug. 17, 2012, http://www.genomicslawreport.com/index.php/2012/08/17/applying-mayo-to-myriad-latest-decision-brings-no-new-news/#more-6807.

the valuable attributes of a gene sequence—the ability to anneal to a complementary strand for diagnosis and to produce proteins—are inherent in the sequence itself and are not caused by anything the supposed inventor did.

In *Aventis Pharma Deutschland GMBH v. Lupin, Ltd.*, 499 F.3d 1293 (Fed. Cir. 2007), the Federal Circuit found patent claims to an isolated chemical compound with therapeutic properties to be invalid, holding that "[i]solation of interesting compounds is a mainstay of the chemist's art," and that "[i]f it is known how to perform such an isolation doing so 'is likely the product not of innovation but of ordinary skill and common sense.'" *Id.* at 1302 (citing *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007)). Yet in the case at bar, the Federal Circuit held that Myriad's patents on isolated gene sequences were valid, despite the isolation of gene sequences being the mainstay of the biologist's art.

Under the Federal Circuit's analysis, even the elements of the periodic table would be patentable. Indeed, Myriad's Counsel at oral argument admitted that the element lithium would be patentable if Myriad's view of the products of nature doctrine prevailed. Fed. Cir. Oral Arg. Trans. at 1:07:28 (Apr. 4, 2011). Such a travesty would conflict with past precedents that hold that the elements of the periodic table are not patentable. *General Electric Co. v. DeForest Radio Co.*, 28 F.2d 641 (3rd Cir. 1928), *cert. denied*, 278 U.S. 656 (1929)(isolated tungsten); *In re Marden* (Marden I), 47 F.2d 957 (C.C.P.A. 1931)(isolated uranium); *In re Marden* (Marden II), 47 F.2d 958 (C.C.P.A. 1931)(isolated vanadium).

III. The United States Patent and Trademark Office Erred in Granting Genetic Sequence Patents and Its Erroneous Decision Should Not Be Given Deference.

The United States Patent and Trademark Office (USPTO) ignored this Court's precedents and applied flawed reasoning to permit patents on genetic sequences. Consequently, that reasoning should not be accorded deference. The USPTO relied on the 1873 grant of a patent to Louis Pasteur for a purified yeast and on a 1911 lower court decision upholding a patent for isolated and purified adrenaline. *Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001); *Parke-Davis & Co. v. H. K. Mulford Co.*, 189 F. 95 (S.D.N.Y. 1911), *affirmed*, 196 F. 496 (2d Cir. 1912). However, the Pasteur patent and *Parke-Davis* preceded this Court's decision in *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1 (1931). That decision elaborated on the products of nature doctrine in a way that calls into question the grant of the yeast patent and adrenaline patent. Indeed, no less an authority than Pasquale J. Federico (later Commissioner of Patents and principal drafter of the 1952 Patent Act, which includes Section 101) stated that in light of *American Fruit Growers*, a claim like Pasteur's "would now probably be refused by the examiner, since it may be doubted that the subject-matter is capable of being patented." Pasquale J. Federico, *Louis Pasteur's Patents*, 86 Science 327 (1937).[5] Thus, the USPTO

[5] The Pasteur patent might not even have been valid according to the law at the time it was issued. Since Pasteur never enforced his patent, there was no judicial assessment of whether the patent was valid. Maurice Cassier, *Louis Pasteur's*

erred when it began granting patents on genetic sequences.

The Federal Circuit compounded this error by looking to *Parke-Davis* in assessing the genetic sequence claims. *Association for Molecular Pathology*, 689 F.3d at 1329; *see also id.* at 1339 (Moore, J., concurring-in-part). Judge Moore additionally cited the discredited Pasteur patent as precedent. *Id.* at 1344 (Moore, J., concurring-in-part).

The Federal Circuit also held that the USPTO's actions created "settled expectations" that prohibited the Federal Circuit from holding genetic sequence claims invalid. *Id.* at 1332; *see also*, *id.* at 1366-1367 (Moore, J., concurring-in-part). However, allowing settled expectations to dictate the validity of a patent would lead to absurd results. The examiners at the USPTO are not infallible. Sometimes whole categories of claims have been erroneously included or excluded from patentability. In fact, in a study of challenges to patent validity, 46% of challenged patents were found to be invalid. John R. Allison, Mark A. Lemley, *Empirical Evidence on the Validity of Litigated Patents*, 26 QIPLA Q.J. 185 (Summer 1998).

If the USPTO were owed the level of deference that the Federal Circuit proposes, there would be no recourse to challenge invalid patents. Anytime a court reviews a patent there is a chance to change settled expectations. In *State Street Bank & Trust Co v. Signature Financial Group, Inc.*, 149 F.3d 1368 (Fed. Cir. 1998), the Federal Circuit changed the

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Patents: Agri-Food Biotechnologies, Industry and Public Good, *in* Living Properties, 39 (Jean-Paul Gaudillière, *et al.*, eds., 2009).

settled expectation of business owners who had previously felt free to use business methods without concern for patent infringement. As is clear in *Mayo*, settled expectations do not provide an adequate reason for courts to uphold otherwise invalid patents.

Furthermore, the U.S. Government asked the Federal Circuit not to give deference to the USPTO's practice of granting patents on isolated DNA. The Department of Justice submitted an *amicus* brief in the Federal Circuit arguing that isolated DNA is a product of nature and not patentable subject matter. Brief for the United States as *Amicus Curiae* in Support of Neither Party 11, *Association for Molecular Pathology* (Fed. Cir., Oct. 29, 2010).

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

IV. Invalidation of Myriad's Patent Claims Is Not Only Required by Section 101, It Is Consistent with Scientific and Medical Ethics Codes.

Scientists have long-standing, historically recognized duties to freely disseminate their discoveries of products of nature and laws of nature and not to subject those discoveries to private property rights. *See, e.g.*, Robert K. Merton, On the Shoulders of Giants: A Shandean Postscript (1985).

Medical professionals, too, recognize the ethical duty to share scientific knowledge rather than to patent it.

As *Amicus* AMA's Ethics Opinion 9.095 states, "The use of patents, trade secrets, confidentiality agreements, or other means to limit the availability of medical procedures places significant limitation on the dissemination of medical knowledge, and is therefore unethical." American Medical Association, Opinion 9.095 – The Use of Patents and Other Means to Limit Availability of Medical Procedures (adopted June 1995), www.ama-assn.org/ama/ pub/physician-resources/medical-ethics/code-medical-ethics/opinion 9095.shtml. Similarly, *Amicus* ACOG's ethics opinion finds medical and surgical patents to be unethical and urges that genetic sequence patents not be granted. The American College of Obstetricians and Gynecologists, *ACOG Committee Opinion Number 364: Patents, Medicine, and the Interests of Patients*, 109 Obstetrics & Gynecology 1249, 1252 (2007, reaffirmed 2009).

Just as patent law recognizes that discoveries of nature must be widely shared to promote innovation, physicians' and scientists' ethical duties recognize that laws of nature and products of nature must be treated as prior art and shared to benefit the public and to encourage innovation.

CONCLUSION

An assessment of the validity of the patent claims at issue in the case is of great social importance. Patents on genetic sequences and patents on correlations between therapeutics and cell growth thwart patient care and hinder innovation. They also are invalid under Section 101. For these

reasons, this Court should grant certiorari.

Respectfully submitted,

Lori B. Andrews
Counsel of Record
Chicago-Kent College of Law
Illinois Institute of Technology
565 West Adams Street
Chicago, IL 60661

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