No. 11-725

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 AMERICAN MEDICAL ASSOCIATION, AMERICAN SOCIETY OF HUMAN GENETICS, AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, AMERICAN OSTEOPATHIC ASSOCIATION, AMERICAN COLLEGE OF LEGAL MEDICINE, AMERICAN COLLEGE OF EMBRYOLOGY, AND THE MEDICAL SOCIETY OF THE STATE OF NEW YORK AS *AMICI CURIAE* IN SUPPORT OF PETITIONERS

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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 diagnosis and treatment and contravene this Court's long-standing precedents about the scope of patentable subject matter.

Amici are organizations of health care professionals. *Amici* are concerned about the effect on the practice of medicine of the Federal Circuit's decision that gene sequences are patentable subject matter. *Amici* routinely use patented inventions, such as pharmaceuticals and operating room tools. However, when a physician prescribes a medicine to a patient or uses a patented scalpel, he or she does not have to worry about patent infringement. The authorization and royalty are already built into the cost of the item. In contrast, when a physician seeks to find out information about a patient's genetic makeup, the physician must worry about whether he or she is infringing a patent that covers a gene sequence. Patient care is harmed when a physician

[1] No counsel for a party authored this brief in whole or in part, and no such counsel or a 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 the 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' letter granting *amici* consent to file has been filed with the Clerk of the Court.

must stop, mid-examination, and be compelled to access a patent database or call a patent lawyer to determine if his or her assessment of the patient's status infringes upon a patented gene sequence.

Amici urge the Court to grant the petitioners' writ of certiorari and establish clearly that isolated DNA and cDNA are products of nature and therefore not patentable subject matter.

Amicus Curiae **American Medical Association (AMA)** founded in 1847, is the largest professional association of physicians, residents and medical students in the United States. Additionally, through state and specialty medical societies and other physician groups seated in its House of Delegates, substantially all U.S. physicians, residents and medical students are represented in the AMA's policymaking process. The objectives of the AMA are promoting the science and art of medicine and improving public health.

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. The Litigation Center is a coalition of the AMA and the medical societies of every state and the District of Columbia.

Amicus Curiae **American Society of Human Genetics (ASHG)** is a non-profit, tax-exempt organization consisting of over 8,000 professionals in the field of human genetics including researchers, clinicians, academicians, ethicists, genetic counselors, and nurses whose work involves genetic testing. ASHG has studied the gene patent issue and found that patents on sequences interfere with research and medical care.

Amicus Curiae **American College of**

Obstetricians and Gynecologists is a private, non-profit, voluntary membership organization that consists of over 51,000 health care professionals dedicated to providing quality health care to women. More than ninety percent of Board-certified obstetricians and gynecologists in the U.S. are affiliated with the College. The patents at issue in this case interfere with the ability of the College's members to provide appropriate health care and undertake research.

Amicus Curiae **American Osteopathic Association (AOA)** founded in 1897, is the largest professional association of osteopathic physicians, residents, and medical students. The objectives of the AOA are to promote osteopathic medicine, a holistic approach to prevent, diagnose, and treat illness, disease, and injury. Osteopathic physicians use genetic information to diagnose and treat patients.

Amicus Curiae **American College of Legal Medicine** is the nation's most prominent professional society comprised of a majority of members holding degrees in both medicine and law. The society is influential in supporting medical and legal professionals, advising health policymakers, and recommending strategies for improving health care and promoting justice. The patents at issue in this case have significant implications for health policy and care.

Amicus Curiae **American College of Embryology** develops and maintains professional standards for embryologists. Its members offer a number of clinical services, including pre-implantation diagnosis—a technique used to test an embryo for genetic diseases before the embryo is

transferred into the uterus of a woman. Its members are also involved in research on innovative treatments, such as embryonic stem cell research. Patents on gene sequences have impeded embryologists' ability to study complex cellular and genetic interactions, such as those related to organ development.

***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. The patents at issue in this case interfere with the mission of MSSNY to provide high quality medical care to all people in the most economical manner.

SUMMARY OF THE ARGUMENT

This Court has granted certiorari in cases of great social importance and when there is a split among circuit courts. 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.

Genetic testing plays a central role in the diagnosis and treatment of human disease. Mutations in genetic sequences are an underlying cause or contributor to most diseases.

The patent claims at issue cover "isolated DNA" and "cDNA," which are described by their genetic sequences. The claims are extremely broad. Diagnosis and research cannot be undertaken on the most fundamental aspect of the human body, its genetic sequence, without isolating that DNA from the rest of the body. Patents granted on isolated DNA and cDNA by the U.S. Patent and Trademark Office (USPTO) have thus provided private companies with a monopoly over the use and study of the genetic sequences related to many diseases. The enforcement of these patents has impeded the provision of health care and inhibited research. This is a profound impediment to medical advances, of national importance.

The consequences of patents on genetic sequences for medicine and research are troubling in their own right, but these patents additionally conflict with over 150 years of this Court's precedents. Nature's handiwork is excluded from patentability. *Bilski v. Kappos*, 130 S. Ct. 3218, 3225

(2010). This Court has repeatedly held that products of nature and isolated products of nature that are not "markedly different" from what occurs in nature are not patentable subject matter. *See*, *e.g.*, *Diamond v. Chakrabarty*, 447 U.S. 303, 309-310 (1980); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948); *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 11-12 (1931); *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293, 311 (1884); *American Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. (23 Wall.) 566, 594 (1874); *O'Reilly v. Morse*, 56 U.S. 62, 112-121, 132 (1853); *Le Roy v. Tatham*, 55 U.S. 156, 175 (1852).

The Federal Circuit's decision in *Association for Molecular Pathology v. U.S. Patent and Trademark Office*, 653 F.3d 1329 (Fed. Cir. 2011), ignored this Court's guidance and concluded that an isolated product of nature was patentable. The decision was the result of a divided three-judge panel, which assigned undue weight to the U.S. Patent and Trademark Office's practice of granting patents on isolated DNA sequences.

The Court's consideration of the scope of patentable subject matter under 35 U.S.C. § 101 in *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*, 628 F.3d 1347 (Fed. Cir. 2010), *cert. granted*, 131 S. Ct. 3027 (Jun. 20, 2011), does not obviate the need to address the Federal Circuit's error in this case. *Prometheus* involves method claims challenged as invalid for claiming a law of nature and mental steps. The patents at issue in this case also include method claims, which both the district court and Federal Circuit have held to be invalid for claiming mental steps. However, the main challenge in this case is to composition of

matter claims which cover products of nature, which were not at issue in *Prometheus*. This Court has not examined the patentability of products of nature since 1980. Even if this Court decides that the *Prometheus* method claims are not patentable subject matter, health care and research will continue to be impeded by composition of matter patents covering genetic sequences. For these reasons, we respectfully request that the Court grant the petitioners' writ of certiorari.

ARGUMENT

I. Physicians' and Researchers' Access to Genetic Sequences for Diagnostic Testing and Research Is a Matter of National Importance.

Eighty-one percent of adults and 92% of children visit health care professionals annually, with an average of three visits a year. John R. Pleis, Brian W. Ward, and Jacqueline W. Lucas, *Summary Health Statistics for U.S. Adults: National Health Interview Survey, 2009*, 10 Vital and Health Statistics 13 (2010); Barbara Bloom, Robin A. Cohen, and Gulnur Freeman, *Summary Health Statistics for U.S. Children: National Health Interview Survey, 2010*, 10 Vital and Health Statistics, Table 14 (2011). In most of these nearly one billion health care visits per year, the patient's genetic make-up is potentially an issue. However, patents on genetic sequences have impeded health care professionals from gaining accurate information about their patients' genes.

The benefit of genetic testing is not limited to 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). Genes play a role in common chronic conditions including gastric ulcers, arthritis, mental retardation, and migraines. *Id*. 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.

Francis Collins, now director of the National Institutes of Health, said:

> By 2020, the impact of genetics on medicine will be even more widespread. The pharmacogenomics approach for predicting drug responsiveness will be standard practice for quite a number of disorders and drugs. . . . By 2020, it is likely that every tumor will have a precise molecular fingerprint determined, cataloging the genes that have gone awry, and therapy will be individually targeted to that fingerprint.

Francis S. Collins and Victor A. McKusick, *Implications of the Human Genome Project for Medical Science*, 285 Journal of the American Medical Association 540, 544 (2001). These important benefits will be diminished if the practice of patenting gene sequences continues.

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

Patents on genetic sequences grant the patent holder complete control over the use of a gene sequence. Gene patent holders have prevented physicians and laboratories from offering genetic testing for medical conditions such as breast cancer, hearing loss, Alzheimers, Long QT syndrome,

Canavan disease, leukemia, hemochromatosis, cystic fibrosis, 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"]; Gina Shaw, *Does the Gene Patenting Stampede Threaten Science?*, 9 AAMC Reporter (2000); Debra G.B. Leonard, *Medical Practice and Gene Patents: A Personal Perspective*, 77 Academic Medicine 1388 (Dec. 2002).

Patents on genetic sequences have even led to patients' deaths, 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 gene associated with Long QT was patented and assigned to the University of Utah Research Foundation. U.S. Patent No. 6,207,383. The company with the exclusive license to the Long QT sequence went through corporate upheavals. For a two-year period, the licensee did not offer diagnostic testing for Long QT syndrome. Other laboratories had the capability and willingness to offer the test, but were forbidden to do so by the patent licensee. During this period at least one patient, a 10-year-old girl, died from her undiagnosed Long QT syndrome. Her death could have been prevented had the gene 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 gene sequence to determine whether a treatment might be helpful or deadly—has also been undermined by the patenting of gene 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*, Wall Street Journal, June 18, 2001, at B1. While such information is crucial to physicians and patients, the use of the sequence to identify people who would not benefit from the drug would diminish the market for the drug.

Patents on genetic sequences are also interfering with the deployment of multiplex testing, where the sequences of several genes are tested at once. SACGHS at 49. For example, as many as 43 different genes can predispose people to diabetes;[2] as many as 80 genes predispose people 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 those genetic sequences could be analyzed in one test. But genetic sequence patents mean that a single test cannot be used. The 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

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[2] This figure is based on a search of the USPTO database. See, e.g., U.S. Patent No. 6,902,888.

of a person's entire genome of approximately 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 the 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 cost over $37 million. Applying even a seemingly modest royalty of $100 per gene would total an unaffordable $2 million per test. If the Federal Circuit's decision is upheld, physicians will be unable to provide whole-genome sequencing.

B. Patents Covering Genetic Sequences Prevent the Improvement of the Accuracy of Genetic Diagnostic Testing.

Generally, a physician has other options if a consultant or laboratory makes a mistake. This is not the case for genetic testing in areas where a single company—in this case, Myriad—holds exclusive rights over testing a genetic sequence. Where there is only one test provider for a medical condition, such as for breast and ovarian cancer, muscular dystrophy, neurologic disorders, and Long QT syndrome, physicians have raised concerns about

the lack of quality and accuracy of the genetic tests. SACGHS at 46-47. The SACGHS concluded that the best way to ensure quality of genetic testing is to allow laboratories to independently verify results and to promote competition among laboratories. *Id.* at 48. Neither of these options for ensuring quality is available under the Federal Circuit's ruling because it allows patent holders to prevent other physicians and laboratories from using patented gene sequences. *Id*.

Because of Myriad's patents on the BRCA1 and BRCA2 sequences, no other physician or laboratory can perform diagnostic testing on women. This is a tragedy because the way Myriad performs its test is prone to errors. As a result of those errors, some women's mutations have been missed, condemning them to undiagnosed breast cancer. Other women have been given the misimpression that they have a relevant mutation, and may have had their breasts and ovaries removed unnecessarily. The result of Myriad's exclusive control over the use of the BRCA1 and BRCA2 sequences has led to the misdiagnosis of patients and has precluded the deployment of improved genetic tests. Ledbetter Decl. ¶¶ 14-16; Ostrer Decl. ¶6; Tom Walsh et al., *Spectrum of Mutations in BRCA1, BRCA2, CHEK2, and TP53 in Families at High Risk of Breast Cancer*, 295 Journal of the American Medical Association 1379, 1386 (2006) (12% of the 300 people examined from high risk families had mutations that the Myriad tests missed).

There are alternative testing methods for testing for BRCA1 and BRCA2 that are less expensive and identify more mutations in the breast cancer gene than the method Myriad uses, but they

are not available in countries covered by Myriad's patents. In France, for example, a physician found a breast cancer gene mutation in an American family that the Myriad test had missed. Sophie Gad et al., *Identification of a Large Rearrangement of the BRCA1 Gene Using Colour Bar Code on Combed DNA in an American Breast/Ovarian Cancer Family Previously Studied by Direct Sequencing*, 38 Journal of Medical Genetics 388, 389 (2001). Similarly, in countries where the Alzheimer gene sequence and the hemochromatosis gene sequences were *not* patented, researchers found previously unknown mutations. *Gene Patents and Other Genomic Inventions: Hearings Before the Subcommittee on Courts and Intellectual Property of the House Committee of the Judiciary*, 106th Congress, 121-127 (2000) (statement of Dr. Jon F. Merz). If Myriad's patent claims over the BRCA1 and BRCA2 genes are invalidated, competition from other laboratories would allow the development of a more comprehensive test. Swisher Decl. ¶¶ 24-26.

C. Patents Covering Genetic Sequences Impede Innovation and Research.

Gene patents impede innovation. There is no way to "design around" gene patents. Because an isolated gene sequence is identical to the sequence of a gene in the body, a patent holder can prevent scientists and clinicians from undertaking any genetic research related to that disease. 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.

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). Similarly, 49% of the members of the American Society of Human Genetics had to limit their research due to gene patents. Isaac Rabino, *How Human Geneticists in U.S. View Commercialization of the Human Genome Project*, 29 Nature Genetics 15 (2001). 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.

There is no exception to patent infringement liability for research involving gene sequences by scientists other than the patent holder. Under current Federal Circuit doctrine, the very narrow research exception that exists is "for all practical purposes a nullity." Janice M. Mueller, *The Evanescent Experimental Use Exemption from United States Patent Infringement Liability: Implications for University and Nonprofit Research and Development*, 56 Baylor Law Review 917 (2004); *Madey v. Duke Univ.*, 307 F.3d 1351, 1362 (Fed. Cir. 2002).

D. The Issue Is Also of Major 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., Joseph Henry Press, 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 of taxpayer money 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 2-10, n. 52. 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, a grant 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 Institutes of Environmental Health Sciences (also paid with taxpayer money) and researchers from other institutions. Rachel Nowak, *NIH in Danger of Losing Out on BRCA1 Patent*, 266 Science 209 (1994).

Unlike other areas of invention, 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 it.

II. The Federal Circuit Issued a Decision That Conflicts with Over 150 Years of This Court's Precedents and the Federal Circuit Needs Guidance on the Patentability of Products of Nature.

This Court has granted certiorari in cases of great social importance and when there is a split among circuit courts. Sup. Ct. R. 10. Because the Federal Circuit is the only circuit court that hears patent appeals, there will never be a split among circuit courts. However, there is an analogous situation in this case—there is disagreement among the deciding judges over the appropriate test to determine whether gene sequences are products of nature falling outside of patentable subject matter under § 101. The Federal Circuit's majority opinion that isolated DNA sequences and cDNA are not products of nature conflicts with this Court's long-standing precedents.

A. The Federal Circuit Judges Who Decided the Appeal Are in Disagreement About Whether Isolated Genetic Sequences Are Products of Nature.

Numerous *amicus* briefs and declarations were filed in the district court leading to a 58-page decision holding that isolated DNA sequences and cDNA are not patentable subject matter because they are not "markedly different" from products of nature under the *Chakrabarty* standard. *Association for Molecular Pathology v. U.S. Patent and Trademark Office*, 702 F. Supp. 2d 181 (S.D.N.Y. 2010). On

appeal, each judge of the three-judge panel wrote a separate opinion and each used a different test to determine whether Myriad's claimed gene sequences were "markedly different" from the naturally occurring gene sequence. Judge Lourie relied on what he perceived to be physical structural differences in holding that isolated DNA sequences and cDNA are "markedly different" from naturally occurring gene sequences. *Association for Molecular Pathology*, 653 F.3d at 1351-1352. Judge Moore relied on a concept of utility to find gene fragments, but not larger isolated DNA sequences, "markedly different." *Id*. at 1365 (Moore, J., concurring-in-part). Judge Bryson considered both physical similarities and similarities in utility in his analysis in finding isolated DNA sequences not to be patentable. *Id*. at 1378. (Bryson, J., concurring-in-part and dissenting-in-part) ("the test employed by the Supreme Court in *Chakrabarty* requires us to focus on two things: (1) the similarity in structure between what is claimed and what is found in nature and (2) the similarity in utility between what is claimed and what is found in nature.")

When a genetic sequence is isolated from its natural state in the chromosome, the ends of the sequence are no longer chemically bonded to the next sequence on the chromosome. According to Judge Lourie, who wrote the majority opinion, the breaking of the covalent bonds (itself a natural process that occurs in and out of the body) makes the gene sequence markedly different and therefore patentable subject matter. *Id.* at 1351; Wolf-Deitrich Heyer, Kirk T. Ehmsen, and Jachen A. Solinger, *Holliday Junctions in the Eukaryotic Nucleus: Resolution in Sight*, 28 Trends in Biochemical

Sciences 548 (2003). Yet any "isolation" of a product of nature from its environment (a mineral from the ground, the plant from the wild) will change its ends. Cutting a strand of hair from the head will change its ends—they will fray and no longer be in continuous contact with the fibers of the hair; yet, like an isolated DNA strand, the isolated hair will retain all of its other characteristics.

Both Judge Moore and Judge Bryson disagreed with Judge Lourie that the structural differences resulting from breaking the covalent bonds make the isolated DNA sequences "markedly different"—finding the differences alone to be too insignificant. *Association for Molecular Pathology*, 653 F.3d at 1364-1365 (Moore, J., concurring-in-part) ("although the different chemical structure does suggest that claimed DNA is not a product of nature, I do not think this difference alone necessarily makes isolated DNA so 'markedly different'"); *Id.* at 1378 (Bryson, J., concurring-in-part and dissenting-in-part) ("What is claimed in the BRCA genes is the genetic coding material, and that material is the same, structurally and functionally, in both the native gene and the isolated form of the gene.").

B. Judge Lourie's Reliance on Purely Structural Differences in Holding Isolated DNA Sequences Patentable Subject Matter Is in Conflict with This Court's Precedents.

The Federal Circuit's majority opinion by Judge Lourie that the breaking of covalent bonds made the composition of matter "markedly different" from its naturally occurring counterpart conflicts

with over 150 years of this Court's precedents. This Court has stated 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.*, 90 U.S. at 594), nor are synthetic products that are not markedly different from what is found in nature (*Cochrane*, 111 U.S. at 311).

According to this Court, "a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter." *Chakrabarty*, 447 U.S. at 309. Yet Judge Lourie's reasoning would mean that a mineral taken out of the ground would be patentable if a chemical bond were broken, as in the case of lithium, where ionic bonds must be broken to isolate it from nature. *Association for Molecular Pathology*, 653 F.3d at 1376 (Bryson, J., concurring-in-part and dissenting-in-part).

The Federal Circuit also ignored this Court's precedents in finding cDNA to be "markedly different" than DNA in nature and thus to be patentable. cDNA is useful in the laboratory because it has the same nucleotide sequence and contains the same information as found in the exons of naturally occurring DNA and can perform the same functions as a full nucleotide sequence or DNA molecule. Bruce Alberts et al., Molecular Biology of the Cell 469-546 (4th ed. 2002).

cDNA exists in the body, making up about 17% of the human genome. International Human Genome Sequencing Consortium, *Initial Sequencing and Analysis of the Human Genome,* 409 Nature 860, 880 (2001). But even if cDNA could only be synthesized in a lab, it still would not be patentable subject matter. In *Cochrane v. Badische Anilin & Soda Fabrik*, this Court held that a patentee who

made a synthetic version of a naturally occurring dye (alizarine)—but having a brighter hue—did not claim a patent eligible invention but only an ineligible product of nature. 111 U.S. 293, 311 (1884). "Calling it artificial alizarine *did not make it a new composition of matter, and patentable as such, by reason of its having been prepared artificially*." *Id.* (emphasis added). Thus, the Federal Circuit erred in finding cDNA to be "markedly different" from the sequence as it occurs within the chromosome and finding Myriad's cDNA claims to be patentable subject matter.

C. The Federal Circuit Gave Undue Deference to the USPTO in Determining Isolated Genetic Sequences to Be Patentable Subject Matter.

Despite stating that the structural differences between isolated DNA and naturally occurring DNA do not make the isolated DNA markedly different and recognizing that large segments of isolated DNA have no new utility, Judge Moore ultimately concluded that isolated DNA that contained most of or all of a gene was patentable subject matter, in light of "settled expectations" due to the USPTO's decades-long practice of granting patents on isolated DNA. *Association for Molecular Pathology*, 653 F.3d at 1366-1367 (Moore, J., concurring-in-part) ("If I were deciding this case on a blank canvas, I might conclude that an isolated DNA sequence that includes most or all of a gene is not patentable subject matter. . ..").

Judge Moore gave too much deference to the

USPTO's practice of granting patents on isolated DNA. The USPTO's rulemaking power "authorizes the Commissioner to promulgate regulations directed only to 'the conduct of proceedings in the [PTO]'; it does not give the Commissioner the authority to issue substantive rules." *Merck & Co. v. Kessler*, 80 F.3d 1543, 1550 (Fed. Cir. 1996). The USPTO's practice of issuing patents on isolated gene sequences is only owed deference based on the "thoroughness of its consideration and the validity of its reasoning." *Id.* The comments issued by the USPTO in response to arguments that isolated DNA is not patentable subject matter were "perfunctory" and "do not reflect thorough consideration and study of the issue." *Association for Molecular Pathology*, 653 F.3d at 1380 (Bryson, J., concurring-in-part and dissenting-in-part) (citation omitted).

The USPTO ignored this Court's precedents and applied invalid reasoning to grant patents on genetic sequences. To justify its grant of genetic sequence patents, the USPTO relied on the 1873 grant of a patent to Louis Pasteur for a purified yeast and on a 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, Pasteur never enforced his patent, so there was no judicial assessment of whether the patent was valid. Maurice Cassier, *Louis Pasteur's Patents: Agri-Food Biotechnologies, Industry and Public Good*, *in* Living Properties, 39 (Jean-Paul Gaudillière, Daniel J. Kevles, and Hans-Jörg Rheinberger eds., 2009). Moreover, the Pasteur patent and *Parke-Davis* preceded this Court's

decision in *American Fruit Growers*. As noted shortly thereafter by Pasquale J. Federico (later Commissioner of Patents and principal drafter of the 1952 Patent Act), in light of this Court's decision in *American Fruit Growers*, a claim like Pasteur's "would now probably be refused by the examiner, since it may now be doubted that the subject-matter is capable of being patented." Pasquale J. Federico, *Louis Pasteur's Patents,* 86 Science 327 (1937). Thus, the USPTO acted in error when it began granting patents on gene sequences.

Further, 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.).

> 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. *Id.*

Had Judge Moore based her decision on whether isolated DNA is a product of nature, instead of deferring to the USPTO's practice, the Federal Circuit likely would have agreed 2-1 that Myriad's claims to isolated DNA are invalid. Yet, the Federal Circuit held otherwise.

III. This Case Raises Crucial Patent Eligibility Issues of National Importance Not Present in *Prometheus Laboratories, Inc. v. Mayo Collaborative Services.*

This Court has granted certiorari in *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*—a case that presents issues of 35 U.S.C. § 101 subject matter patentability for method claims. However, *Prometheus* will not provide guidance on the central issue raised here: the patentability of compositions of matter.

This is not the first time the Federal Circuit has failed to appropriately apply this Court's precedents. *See, e.g., KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 415 (2007). In this case, the failure to apply this Courts' precedents will cause clear harm. Physicians will be denied use of gene sequences to diagnose patients. Patients will be denied testing and prevented from receiving second opinions, and researchers will be prevented from furthering our understanding of the underlying causes of human disease.

Further harms to innovation—beyond the harms from gene patents—will result if this Court does not hear this case. Patents will be granted by the USPTO and upheld by lower courts because of minor differences between the claimed invention and a product of nature or because a covalent bond is broken when a product of nature is extracted. These patents will impede innovation by allowing patents on products of nature that would have been excluded prior to the Federal Circuit's decision. 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 on the same grounds that gene sequences are patentable. Fed. Cir. Oral Arg. at 1:07:28-1:08:31 *available at* http://www.cafc.uscourts.gov/oral-argument-recordings/2010-1406/all. Such a travesty would conflict with past precedents 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.3d 958 (C.C.P.A. 1931)(isolated vanadium). In fact, allowing the Federal Circuit decision to stand could lead to patents on minerals from the ground.

CONCLUSION

The record below demonstrates the social importance of this issue. Dozens of *amici* file briefs and hundreds of declarations were filed at the trial court level alone. Because this is a matter of great social importance, with a split in opinion among the judges who have considered the matter, we respectfully request the Court to grant certiorari, articulate the proper standard for determining patentable subject matter of composition claims directed to products of nature, and hold that isolated human genes, DNA sequences and cDNA are ineligible for patenting under 35 U.S.C. § 101. It is crucial to patient care and to medical research that the Court hear this case and ensure that natural biological materials removed from the body and the

basic scientific information that Myriad has sought to propertize be freely shared, used, and analyzed.

Respectfully submitted,

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