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

BRIEF FOR CANAVAN FOUNDATION, CLAIRE ALTMAN HEINE FOUNDATION, MARCH OF DIMES FOUNDATION, FACING OUR RISK OF CANCER EMPOWERED, NATIONAL ASSOCIATION FOR PSEUDOXANTHOMA ELASTICUM, AND OVARIAN CANCER NATIONAL ALLIANCE AS *AMICI CURIAE* IN SUPPORT OF PETITIONERS

John L. Hendricks
Counsel of Record
REED & SCARDINO LLP
301 Congress Ave.,
Suite 1250
Austin, Texas 78701
jhendricks@reedscardino.com
(512) 474-2449

Megan M. O'Laughlin
John T. Tower
HITCHCOCK EVERT LLP
750 North St. Paul
Street, Suite 1110
Dallas, Texas 75201
(214) 953-1111

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STATEMENT OF INTEREST OF *AMICI CURIAE*[1]

Each of the groups who submit this amicus brief represents a population of patients and their families who are adversely affected by the practice of patenting human DNA. Patents like Myriad's raise testing costs and simultaneously impede the development of more accurate and reliable diagnostic tools. The results are concretely and tragically experienced by patients and their families whose suffering might have been minimized or prevented altogether by more effective and less expensive means of testing for the genetic disposition to certain life threatening diseases.

Canavan Foundation is a non-profit organization with the mission to provide funding for research efforts to find an effective therapy for, raise awareness of, and to help avoid Canavan disease through carrier screening and prenatal testing. Despite efforts to sponsor low cost screening for potential carriers of Canavan disease,

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[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. 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.

a doctor and hospital who patented the relevant gene have prevented the group's efforts to provide free or inexpensive screening programs.

Claire Altman Heine Foundation (CAHF) is a non-profit organization dedicated to establishing pan-ethnic carrier screening for Spinal Muscular Atrophy (SMA)—the number one genetic killer of children under two. In CAHF's experience, the use of patent rights relating to the gene responsible for SMA has reduced access to SMA carrier screening.

Facing Our Risk of Cancer Empowered (FORCE) is a non-profit organization whose mission includes providing people with information and resources to determine whether they are at high risk for breast and ovarian cancer due to family history or genetic predisposition.

March of Dimes Foundation is a non-profit organization dedicated to improving the health of babies by preventing birth defects, premature birth and infant mortality. The March of Dimes Foundation has been in the forefront of supporting research on the genetic factors in diseases and the best methods of testing and treatment. March of Dimes' mission and research are adversely affected by patents on gene sequences.

National Association for Pseudoxanthoma Elasticum (NAPE) is a non-profit organization and the original Pseudoxanthoma Elasticum (PXE) patient support group in the United States, committed to providing education for afflicted

individuals and families. NAPE opposes gene patents because they interfere with research and development of diagnostic and therapeutic tools.

Ovarian Cancer National Alliance (OCNA) is a non-profit organization and the foremost advocate for women with ovarian cancer in the United States. OCNA opposes gene patents because such monopolies impede research on ovarian cancer and restrict access to genetic testing for the disease.

SUMMARY OF THE ARGUMENT

The issue before the Court is whether human genetic material, or a segment of the human genome, upon isolation and/or extraction from the body, constitutes patent eligible subject matter as defined in 35 U.S.C. § 101 . To be clear, the patents now at issue do not claim a means of isolating or extracting the gene; they claim the gene itself as invention. The U.S. District Court held that the genes as defined in the patent claims are "products of nature" and fall squarely within the judicially recognized exceptions to patentable subject matter. On appeal, the Federal Circuit panel affirmed the lower court's invalidation of all but one of Myriad's method claims but reversed its invalidation of composition claims, holding that the genetic sequences themselves were patent eligible. The panel was divided and produced three separate opinions, including one concurrence and one dissent. Writing for the majority, Judge Lourie concluded that the mere *isolation* of a gene sequence was alone sufficient to qualify the genetic material as a product of human invention, despite the fact that the nucleotide sequence of the gene had not been altered, added to, reduced, or manipulated in any way.

On Plaintiffs' first Petition, this Court issued an order granting certiorari, vacating the Federal Circuit's decision and remanding this case to the

Federal Circuit for further proceedings in light of this Court's decision in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012). On remand, the same Federal Circuit panel affirmed its previous decision and issued a new set of opinions that are substantially the same as those issued previously. This result was unsurprising in view of the fact that the majority declared this Court's *Mayo* decision categorically irrelevant to composition of matter claims at issue in *Myriad*. According to the Federal Circuit's majority opinion, "*Mayo* does not control the question of patent-eligibility of such claims. They are claims to compositions of matter, expressly authorized as suitable patent-eligible subject matter in § 101." *Association for Molecular Pathology v. USPTO*, 689 F.3d 1303, 1325 (Fed. Cir. 2012). "[A] composition of matter is not a law of nature." *Id.* at 1331.

Petitioners again sought review by this Court, and on November 30, 2012, this Court granted petition for review on the single issue of whether human genes are patentable. Petitioners timely filed their brief in support of the district court's holding that human genetic sequences are not patentable subject matter. The Amici described herein now file their brief in support of petitioners.

Gene patents create a monopoly over information that is foundational for the biological and medical sciences. By authorizing such monopolies, the Federal Circuit's decision sets a precedent that impedes research and innovation in

the natural sciences. It is therefore inimical to the goals of innovation and growth for which the U.S. patent laws were designed.

In addition to its deviation from this Court's jurisprudence on fundamental issues affecting the scope and purpose of patent law, the Federal Circuit's decision authorizes patent practices that will severely compromise efforts in the U.S. to diagnose and treat chronic and life-threatening diseases. The adverse effects of gene patents on science and healthcare are profound and wide ranging.

As the patient groups who submit this brief are keenly aware, the Federal Circuit's decision not only subverts the constitutionally grounded purposes of the patent laws but ushers in a set of commercial practices that are injurious to the health and welfare of U.S. citizens. For these reasons, we urge the Court to reverse the Federal Circuit's decision and to uphold the decision of the district court below, finding that human genetic material is not patent eligible subject matter under § 101 of the U.S. Patent Act.

ARGUMENT

I. GENE PATENTS AFFORD A PRIVATE MONOPOLY OVER THE BASIC TOOLS AND SOURCES OF SCIENTIFIC KNOWLEDGE AND THEREBY UNDERMINE THE GOALS OF INNOVATION AND EXCHANGE FOR WHICH THE U.S. PATENT LAWS WERE DESIGNED

As this Court recognized in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012), the scope of patent-eligible subject matter is not limitless but instead reflects a balance of values. The patent offers a limited monopoly in exchange for information and does so to encourage innovation in the arts and sciences for the public good. The courts have recognized that just as insufficient patent protection fails to incentivize, too much patent protection obstructs the exchange of information necessary for innovation. Hence, for over 150 years, courts have disallowed patent claims that impede future innovation by preempting or broadly covering natural phenomena or natural laws: "The Court has repeatedly emphasized … a concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature." *Id.* at 1301; *see O'Reilly v. Morse*, 56 U.S. (15 How.) 62, 112-20 (1854).

Patents on natural phenomena undermine the patent system by allowing the patent holder to

control any and all uses of the claimed phenomena. The obstructive effects of patents that preempt natural laws were recognized early on in *Morse*, where the Court considered a series of claims for the use of electromagnetic force. *Id.* While upholding the validity of Morse's claims directed to specific applications, the Court invalidated Morse's eighth claim which broadly covered *any* use of electromagnetic force "for making or printing intelligible characters, signs or letters at a distance." *Id.* at 112. In rejecting this claim the Court explained:

> And if he can secure the exclusive use by his present patent he may vary it with every new discovery and development of the science, and need place no description of the new manner, process, or machinery, upon the records of the patent office … he claims an exclusive right to use a manner and process which he has not described and indeed had not invented, and therefore could not describe when he obtained his patent.

Morse, 56 U.S. at 113. Morse's eighth claim was found to be so broad that it would cover virtually every use of electromagnetism for printed communication. The claim would have tied up a field of basic knowledge and prevented others from using it to make valuable contributions. Patent claims on human genetic sequences have had the

same effect in the medical sciences. Myriad's patents have allowed it to stifle and/or control a huge amount of data on the nature and significance of variants in the BRCA1 and BRCA2 genes. Myriad has no reason to identify or disclose additional variations in the BRCA1 and BRCA2 genes when they have patent claims covering practically all variations thereof. *See e.g.*, Myriad's Patent No. 5,837,492, claim 6 (covering mutations of a BRCA2 polypeptide which correlate with an increased risk of cancer); Myriad's Patent No. 5,747,282, claims 5 and 6 (covering DNA sequences with "at least 15 nucleotides" of an identified sequence). The vast data that Myriad does collect from its testing, it has refused to disclose with the scientific community. Andrew Pollack, *Despite Gene Patent Victory, Myriad Genetics Faces Challenges*, N.Y. Times, Aug. 24, 2011.

Advocates of gene patenting, such as Myriad, argue that prohibiting gene patents would impede innovation and compromise medical diagnosis and treatment. But there is no factual support for those assertions. To the contrary, unless the Federal Circuit's decision is reversed, the result will be less research, inferior diagnostic testing, and worse outcomes for patients. The negative impact of gene patents on medical research, diagnostic procedures, and patient outcomes is no longer speculative; there is ample empirical evidence of their detrimental effects.

A. *Specific Consequences of Myriad's Patents*

As a consequence of its patents, Myriad gained the exclusive right to perform genetic testing and research on the BRCA1 and BRCA2 genes in the United States. When one party such as Myriad controls all testing of a gene sequence, it has no incentive to develop further knowledge of gene mutations affecting the risk of breast cancer or improve the quality of testing. Indeed there are multiple scientific studies that demonstrate the significant limitations of Myriad's test.[2] According to one study published in 2006, the test Myriad employs to detect breast cancer risk does not take into account significant possible mutations of the gene that correlate with a susceptibility to breast cancer. Tom Walsh et al., *Spectrum of Mutations in BRCA1, BRCA2, CHEK2, and TP53 in Families at High Risk of Breast Cancer*, 295 J. Am. Med. Ass'n 1379, 1379-1388 (2006). In the study, researchers sampled DNA from 300 members of high-risk families that had received negative test

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[2] *See* Maurizia Dalla Palma et al., *The Relative Contribution of Point Mutations and Genomic Rearrangements in BRCA1 and BRCA2 in High-Risk Breast Cancer Families*, 68 Cancer Research 7006, 7011 (2008) (finding 8% of non-Ashkenazi Jewish test subjects carried a BRCA mutation not detectable by Myriad's standard test); Allison W. Kurian et al., *Performance of BRCA1/2 Mutation Prediction Models in Asian Americans*, 26 J. Clinical Oncology 4752, 4754-56 (2008) (finding that the models used by Myriad underestimate the prevalence of BRCA1/2 mutations among Asian American women by a full 50%).

results from Myriad. *Id.* The researchers used six methods to search DNA for breast cancer gene mutations, and found that 12% of the patients studied carried rearrangements of BRCA1 or BRCA2 that were not included in Myriad's array. *Id.*[3] Despite this and other empirical evidence that Myriad's test is deficient and often produces ambiguous results even with the mutations it checks, Myriad, as a result of its DNA sequence patents, remains in sole control of how or whether any new research on the BRCA genes will be conducted and/or incorporated into the tests that it offers.

Furthermore, Myriad's patent monopoly severely restricts the availability of second opinions from medical experts. Although Myriad argues that multiple laboratories provide second opinions for BRCA1 and BRCA1 test results (Myriad Brief in Opposition to Petition for Writ of Certiorari at 16 (S. Ct. Oct. 31, 2012)), these laboratories use the same exclusive test offered by Myriad. The only available option for a woman seeking a second opinion is the same test, which will not find mistakes inherent in the test, such as the exclusion of cancer causing mutations in the testing protocol.

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[3] The number of missed mutations may be even higher. According to Institute Curie geneticist Dr. Dominique Stoppa-Lyonett, Myriad's test may miss up to 20% of the expected BRCA1 mutations. Steve Benowitz, *French Challenge to BRCA1 Patent Underlies European Discontent*, 94 J. Nat'l Cancer Inst. 80, 80 (2002).

B. *Adverse Effects of Gene Patenting Generally*

Myriad's patents provide but one example of the adverse effects of patents that preempt natural phenomena. In April 2010, the U.S. Department of Health and Human Services issued the 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 (2010) [hereinafter "SACGHS"]. The SACGHS report found that research in the field of genetics has already begun to suffer as a consequence of gene patents. "Patents are already hindering the development of multiplex tests. Laboratories utilizing multiplex tests are already choosing not to report medically significant results that pertain to patented genes for fear of liability." *Id.* at 3. As a consequence of their chilling effects on genetic research, the existence and enforcement of gene patents discourage the development of better quality testing methods. "Neither sample sharing nor competition is possible when an exclusive-rights holder prevents others providing testing. As a result, significant concerns about the quality of a genetic test arise when it is provided by a patent-protected sole provider." *Id.* at 4.

Perhaps most directly and immediately of concern to the groups who submit this brief, the practice of patenting human genetic material has already proven to increase the costs of diagnostic procedures, restrict patient access to existing

genetic testing, and preclude the availability of better tests and of second opinions of the often ambiguous results of current testing methods. *See Id.* at 1-6.

C. *Salient Cases of Individual Hardship Attributable to Genetic Patents*

There can be no doubt that patents on human genes worsen patient outcomes. The harm that results from patenting human genes is dramatically illustrated in the case of a young girl named Abigail who lost her life to a disease called familial Long QT syndrome (LQTS). LQTS is a disorder of the heart's electrical system that affects 1 in 3,000 newborns and can result in sudden death. Misha Angrist, et al, *Impact of Patents and Licensing Practices on Access to Genetic Testing for Long QT Syndrome*, SACGHS at Appendix A, F-1. The disease has been correlated to mutations within three particular genetic sequences. The company that obtained a patent and exclusive license to the mutated genes developed a diagnostic test, but did not offer it for two years because the exclusively-licensed laboratory went into bankruptcy. During that time, the company nevertheless sought to enforce the patent against other parties who could have provided genetic testing for LQTS. *Stifling or Stimulating – The Role of Gene Patents in Research and Genetic Testing: Hearing Before the Subcomm. on Courts, the Internet and Intellectual Property of the H. Comm. on the Judiciary*, 110th Congress 35, 40

(2007) (statement of Dr. Marc Grodman). In the case of at least one patient, a ten year-old girl named Abigail who presented with an arrhythmia, death was preventable. *Id.* If the patent holder had made testing available, the cause of Abigail's arrhythmia would have been readily identified as LQTS, and the appropriate therapies (beta-blocker drugs, implantable cardioverter-defibrillators, and avoidance of certain arrhythmia triggers) could have been prescribed. *Id.*; Angrist, SACGHS at Appendix A, F-1.

In addition to such adverse effects on the availability and affordability of quality testing, individual patients and their families have been abused by physicians and hospitals who are incentivized to patent genes for commercial gain. No case illustrates this problem better than the history of the discovery of genetic factors for Canavan disease. Beginning in the early 1990s, Ashkenazi Jewish families of children with Canavan disease provided tissue and money for over a decade to a research physician so that he could sequence the genetic mutation that caused this devastating neurological disease. The Greenbergs—whose two children were afflicted with and died from Canavan disease—rallied other Canavan's families and together they freely gave blood and tissue samples from their dying children. Their purpose was to provide a low cost screening and prenatal testing program to identify potential carriers of the disease. Soon after the research

physician (a long-time personal physician of the Greenbergs) identified the relevant gene sequence for carriers of the mutation, he and his hospital patented it without the knowledge or consent of the tissue sources. *See Greenberg v. Miami Children's Hosp. Research Inst., Inc.*, 264 F. Supp. 2d 1064 (S.D. Fla. 2003). When the Canavan Foundation and its constituents convinced medical providers to offer Canavan gene testing for free, the hospital threatened to enforce its patents and shut down the free testing.

D. *The Practice of Gene Patenting Discourages Patient Participation and Thereby Limits the Fundamental Resource for Genetic Research*

Patient concern over the ultimate use of their personal tissue samples and genetic information has become a serious issue in genetic research. Patients have sued to stop use of their biological and genetic material in light of patent-holders' financial gain, undisclosed later uses, and restrictive licensing practices. *See Moore v. Regents of the Univ. of Cal.*, 793 P.2d 479 (Cal. 1990); *Greenberg*, 264 F. Supp. 2d 1064 ; *Washington Univ. v. Catalona*, 490 F.3d 667 (2007). Ignoring the role of patients in genetic research and innovation discourages patient participation, "the only irreplaceable, critical resource … in the discovery of [a] gene." Jon Merz, *Discoveries: Are There Limits on What May Be Patented?*, Who Owns Life? (2002).

The Canadian College of Medical Geneticists' official statement on gene patents addresses the needs of patients and other research participants who donate their time and personal biological samples "altruistically with a motivation to promote better care for others." Julie Richer et al., *CCMG statement on gene patents*, 82 Clin. Genet. 405-407 (2012). Granting a patent to a single individual or entity in effect "fails to recognize the essential public investment in this process of collaboration and discovery . . . [and] fails to respect the wishes of patients who generously contribute with the hope of helping others," an oversight that "may have damaging effects on the future of genetic medicine by limiting the willingness of our patients to participate in future research endeavors." *Id.*

Indeed, as the role of personalized medicine and whole-genome sequencing rapidly expands, some geneticists support transparency between researchers and patients as not only a moral and ethical imperative but also in the best interest of researchers and innovation. Misha Angrist, *You never call, you never write: why return of 'omic' results to research participants is both a good idea and a moral imperative*, 8(6) PMC 651-657 (Dec. 2011).

II. UNDER THIS COURT'S JURISPRUDENCE, ISOLATED GENE SEQUENCES ARE NOT PATENTABLE SUBJECT MATTER

Despite the broad language set forth in 35 U.S.C. § 101, the scope of what is eligible for patent protection is not limitless. This Court consistently recognizes boundaries of eligibility for patent protection by identifying general areas and subjects that are off limits to private monopolization. These subjects for exclusion are often described in terms including "natural phenomena," "laws of nature" and "abstract ideas." *See Diamond v. Diehr*, 450 U.S. 175 (1981); *Parker v. Flook*, 437 U.S. 584 (1978). But the Court has used other phrases such as "products of nature,"[4] "physical phenomena"[5] and "forces of nature"[6] interchangeably with "natural phenomena" and "laws of nature."

The rationale behind such exceptions is rooted in the idea that innovation requires unfettered access to a strata of basic concepts and natural phenomena that are prerequisite to and foundational of any advances in science and commerce. In *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948), the Court

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[4] *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 130 (2001); *Diamond v. Chakrabarty*, 447 U.S. 303, 311 (1980).

[5] *Bilski v. Kappos*, 130 S. Ct. 3218, 3221 (2010); *Chakrabarty*, 447 U.S. at 309.

[6] *Dolbear v. Am. Bell Tel. Co.*, 126 U.S. 1, 532 (1888).

explained that "patents cannot issue for the discovery of the phenomena of nature ... The qualities of [nature] ... are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none." *Id.* at 130.

In *Mayo*, this Court reaffirmed that patent eligible subject matter under § 101 is limited by exclusions for natural phenomena, laws of nature, and abstract ideas, and reiterated the rationale for these exclusions:

> "Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." And monopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it.

Mayo, 132 S. Ct. at 1293 (quoting *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)).

With these fundamental concerns in mind, this Court held *Mayo's* patent claims invalid because they effectively did nothing more than describe natural phenomena, *i.e.* correlations governed by natural laws. Steps such as administering an amount of the drug, determining the metabolite concentration, and inferring the need for a change in dosage contributed nothing

inventive to the correlations governed by nature that lay at the core of the claimed invention. "[A] process that focuses upon the use of a natural law [must] also contain other elements or a combination of elements, sometimes referred to as an 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Id.* at 1294 (citing *Flook*, 437 U.S. at 594). Focusing on the absence of an "inventive concept," this Court concluded that well-known procedures for administering and determining contributed nothing of ingenuity to the claims.

A. *The Federal Circuit's Misapplication of This Court's Precedents*

The Federal Circuit majority has now twice concluded that Myriad's isolated DNA claims were patentable subject matter by virtue of being "isolated" from their natural environment of the human genome. *Association for Molecular Pathology v. USPTO*, 689 F.3d 1303 (Fed. Cir. 2012). According to the majority's opinion, isolation requires the breaking of covalent bonds at each end of a gene segment and thereby results in a composition having "markedly different characteristics" from the characteristics of the same sequence of nucleotides occurring in the larger genome. *Id.* at 1328. Although the Federal Circuit relied on the language of *Chakrabarty*, it deviated significantly from the analytic approach taken by *Chakrabarty* and its predecessor, *Funk*

Bros., both of which relied heavily on a consideration of the functional properties of organic compositions.

In *Funk Bros.*, this Court acknowledged that the claimed composition of bacteria was new and useful, but concluded that "[i]t is no more than the discovery of some handiwork of nature and hence is not patentable." *Id.* at 131. Significantly, the Court did not address the structural characteristics of the composition in determining whether it was a product of nature as opposed to a human manufacture. Instead, the Court observed:

> The bacteria *perform* in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee.

Id. (emphasis added). Under a similar analysis, this Court in *Chakrabarty* held that patent claims for a genetically-enhanced bacterium capable of decomposing oil more effectively was a human manufacture and therefore fell within subject matter patentable under § 101. In reaching this decision, the Court said nothing about chemical or structural differences in explaining how the claimed bacteria were markedly changed. Instead, it differentiated the claimed subject matter by observing that it had a petroleum degrading

capability "which is possessed by no naturally occurring bacteria." *Chakrabarty*, 447 U.S. at 305.

The analysis in both *Funk Bros.* and *Chakrabarty* turned on an assessment of whether the claimed invention described any performance advantages beyond those inherent in the natural components. The claimed invention in *Funk Bros.* was not patentable because it described nothing more than a new means of packaging natural components whose natural tendencies remained unaltered. In contrast, the new bacterium in *Chakrabarty* fell on the side of human manufacture because its utility and suitability for claimed purposes derived from a property that did not occur in any bacteria naturally.

Judged against this analytic framework Myriad's composition claims are more similar to those considered in *Funk Bros.* Isolated human gene sequences, regardless of the packaging, whether extracted from cells or extracted and further purified into cDNA, are structurally and functionally identical to human gene sequences as they naturally occur. The characteristics and function of a gene reside in the gene sequence—that is, the A's, C's, G's, and T's that code for the expression of a specific protein. These characteristics and functions (the active portion of the gene sequence) have not been changed in "isolated" DNA. The person claiming ownership of an isolated gene is seeking a monopoly on its natural functions—the ability of a gene sequence to

anneal to its complementary strand (which allows diagnosis) and the ability to produce proteins. Just as the utility of the claimed invention in *Funk Bros.* was reducible to the natural behavior in each of the components, the claimed utility of isolated gene sequences resides in the natural order and behavioral properties of the nucleotide sequences and depends upon those properties remaining substantially unchanged.

The Federal Circuit majority essentially reduces the "markedly different characteristics" analysis of *Chakrabarty* to a test of whether *any* human intervention has left *any* chemical change at the molecular level. Moreover, it appears Judge Lourie would apply this test regardless of the description used in the claims of the asserted invention and regardless of what field of art or science is at issue. In fact, with a simple statement Judge Lourie dismissed the relevance of the field of genetics and functional properties of the "isolated DNA":

> We recognize that biologists may think of molecules in terms of their uses, but genes are in fact materials having a chemical nature and, as such, are best described in patents by their structures rather than by their functions.

Ass'n for Molecular Pathology, 689 F.3d at 1330. There is nothing in *Chakrabarty* or *Funk Bros.* to

support or even to suggest Judge Lourie's approach to the interpretation of composition claims or to support his selection of covalent bonds as the principal and defining feature of any organic compound.

Notably, the Federal Circuit majority was divided in its rationale for upholding the validity of Myriad's composition patents. Writing for the court, Judge Lourie relied on the premise that slight structural changes incidental to the process of isolation were alone sufficient to qualify the gene sequence as a product of human invention. In a concurring opinion, Judge Moore disagreed with this premise stating: "To the extent the majority rests its conclusion on the chemical differences between genomic and isolated DNA (breaking the covalent bonds), I cannot agree that this is sufficient to hold that the claims to human genes are directed to patentable subject matter." *Ass'n for Molecular Pathology*, 689 F.3d at 1341 (J. Moore concurring). Despite her reasonable rejection of Judge Lourie's premise, Judge Moore errs in her subsequent suggestion that short isolated sequences of nucleotides might be patentable by virtue of their new utility in the field of genetics.[7]

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[7] Judge Moore's concurrence in holding that isolated gene sequences are patentable subject matter appears to rest on an argument that deference is due to the USPTO's long history of allowing such patents and the settled expectations of patent holders who have relied upon such administrative guidelines. As Judge Bryson's dissent aptly points out, the USPTO does

Although Judge Moore's appeal to new utility is not misplaced, her argument fails to connect the new utility of an isolated gene segment with any contribution of human ingenuity. The only human intervention at issue in this case is the *process* of isolation. If the process of isolating genes was innovative, the process may be patent eligible, but it does nothing to transform the nucleotide sequence into something new. In the present case, however, there is nothing innovative in the isolation process and the only consequence of human intervention is a particular segment of what usually (but not always) occurs as part of a longer sequence.

Judge Moore's reasoning implausibly treats size as a defining property of isolated DNA that in turn confers patentability on an otherwise entirely natural composition. Apart from its potentially absurd consequences, this argument fails to acknowledge what the Court in *Funk Bros.* and *Chakrabarty* emphasized, namely, that classification of an organic composition as a product of human manufacture must show how its properties and utility depend upon a contribution of human ingenuity. Isolated gene sequences, no matter how short, are not patent eligible products of human manufacture because isolation does

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not have lawmaking authority and whatever expectations it may create or reliance it may have induced do not justify a continuation of practices which are contrary to legal precedent and subversive of the goals of the patent laws.

nothing to alter what is useful and beneficial about them; their utility rests primarily, if not entirely, on their natural encoding properties. Like the strains of bacteria at issue in *Funk Bros.*, the coding portions of a nucleotide sequence "serve the ends nature originally provided and act quite independently of any effort of the patentee" regardless of how they are formatted. *Funk Bros.*, 333 U.S. at 131.

B. *Application of* Mayo Collaborative Servs. v. Prometheus Labs., Inc., *to the Issue of Genetic Sequence Patents*

If *Funk Bros*. and *Chakrabarty* guide away from a narrow concern with structural chemical differences in assessing patent eligibility of biological technology, this Court's decision in *Mayo* addresses the question of how much change or difference is "marked" and sufficient to qualify as a transformation from nature to human contrivance.

In *Mayo*, this Court posed the question of whether: "the patent claims add *enough* to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws?" *Mayo*, 132 S. Ct. at 1297. The correlative question in this case is whether the process of isolating DNA and the attendant changes that occur as a consequence of isolation make it different *enough* to *transform* it in any defining way. Based on this Court's reasoning

in *Funk Bros.*, *Chakrabarty*, and now *Mayo*, the answer is clearly no.

Myriad's claims are directed to the natural genomic sequence which has been isolated through a routine process into a conventional format or package. In *Mayo*, this Court clarified that it is not *enough* to base patent eligibility on elements that "add nothing specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field." *Mayo*, 132 S. Ct. at 1299.

Isolating a natural substance is not an inventive step but rather a routine and conventional process. As the Federal Circuit recognized in *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293 (Fed. Cir. 2007), "isolation 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 Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007)).

Even if the process or method of isolation itself were not routine but somehow inventive, this would not imply a transformation in the claimed subject matter of a nucleotide sequence. As the Court in *Funk Bros.* made clear, the act of repackaging organic compositions without changing their natural tendencies and functional properties is not sufficient to establish a patent claim for the

natural components themselves. In the present case, the structural changes that occur as a consequence of isolation—breaking covalent bonds—have no bearing on what DNA is or does. Such changes do not alter defining *properties* of DNA as described in the patent or as interpreted by a person of skill in the art of genetics.

Specifically, the patents at issue do not teach the importance or value of the terminal points of the isolated DNA. The irrelevance of these granular changes to the claimed invention is further underscored by the fact that some claims cover numerous compositions which differ one from another in the molecular structure of their terminal points. For example, claim 6 of the Patent No. 5,747,282 for "an isolated DNA having at least 15 nucleotides of the [nucleotide sequence set forth in SEQ ID NO:1]" covers over 17 million compositions at least 15 nucleotides long within the 5,914 nucleotide sequence of SEQ ID NO:1. The 17 million compositions are claimed irrespective of variation in the molecular structure of their terminal ends. Such differences are irrelevant to the patent claims and the properties of the nucleotide sequence or coding function that defines DNA. Moreover, such differences are irrelevant to the purported utility of the claimed subject matter.

In sum, *Mayo* teaches that identifying de minimis molecular differences in the ends of a complex polymer chain is not *enough* to merit patent protection if such differences bear no

relationship to any change in the properties claimed or any inventive concept or solution to a problem. *Mayo* read in conjunction with *Funk Bros.* and *Chakrabarty* compels the conclusion that merely isolating a natural sequence of nucleotides from the human genome by a routine process into a scientifically conventional format does not sufficiently alter the natural properties of DNA to qualify "isolated DNA" as patentable subject matter.

C. *The Intellectual Labor Required to Discover and Isolate a Genetic Sequence Does Not Justify Patent Protection for the Genetic Sequence*

Myriad has placed great emphasis on its research on genetics and the complexities of identifying useful genetic sequences. However, these are irrelevant to a determination of whether genetic sequences are patent eligible subject matter. Regardless of the intellectual labor required for discovery of natural laws and useful products of nature, such discoveries must remain accessible to assure their use in future science and innovation. Justice Breyer's statements in dissent in *Laboratory Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124 (2006) further elaborate on the reasons for recognizing the exceptions to patentable subject matter regardless of the effort, cost or value of the discovery:

> The justification for the principle does not lie in any claim that "laws of

> nature" are obvious, or that their discovery is easy, or that they are not useful. To the contrary, research into such matters may be costly and time-consuming; monetary incentives may matter; and the fruits of those incentives and that research may prove of great benefit to the human race. Rather, the reason for the exclusion is that sometimes too much patent protection can impede rather than "promote the Progress of Science and useful Arts," the constitutional objective of patent and copyright protection.

Id. at 136 (Breyer, J., dissenting).

Regardless of the human ingenuity and labor required to isolate, extract or purify a segment of human DNA, the sequence of nucleotides remain a product of nature. As stated by this Court over a century ago:

> There are many things well known and valuable in medicine or in the arts which may be extracted from ... substances. But the extract is the same, no matter from what it has been taken. A process to obtain it from a subject from which it has never been taken may be the creature of invention, but the thing itself when

> obtained cannot be called a new manufacture.

American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 593-94 (1874).[8]

[8] *See also Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884) (finding artificial alizarine derived from a precursor substance and having the same properties as those found in natural alizarine was not patentable); *Ex parte Latimer*, 1889 Dec. Comm'r Pat. 123 (finding purified pine needle fiber not patentable).

CONCLUSION

This case, more than any other, illustrates why the building blocks of human knowledge, including the human genome, should not be subject to monopoly through patent law. Extending patent protection to human genes results in less, not more, innovation in a sphere of research activity where innovation and freedom from monopoly are vital to the prevention and treatment of life threatening diseases. For the reasons herein, Amici respectfully request that this Court reverse the Federal Circuit's decision.

Respectfully submitted,

John L. Hendricks
REED & SCARDINO LLP
301 Congress Ave., Suite 1250
Austin, Texas 78701
(512) 474-2449
jhendricks@reedscardino.com

Attorney for Amici Curiae
Canavan Foundation
Claire Altman Heine Foundation
March of Dimes Foundation
Facing Our Risk of Cancer
Empowered
National Association for
Pseudoxanthoma Elasticum and
Ovarian Cancer National Alliance

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