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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 subm ission. Petitioner s 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

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 TH E BASIC TOOLS AND SOURCES OF SCIENT IFIC KNOWLEDGE AND THEREBY UNDERMINE THE GOALS OF INNOVATION AND EXCHANGE FOR WHICH THE U.S. PATENT LA

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*

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

[2] *See* Maurizia Dalla Palma et al., *The Relative Contribution of Point Mutations and Genomic Rearrangements in BRCA1*

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 te st, 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 pati ent 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.

(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 convin ced 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 su ed 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).

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

Bros., both of which relied heavily on a consideration of the function al 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

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]

[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

nothing to alter what is useful and beneficial about them; their utility rests primarily, if not entirely, on their natural encoding propeifaes. Like the strains of bt <eria at issue in *Funk Bros.*, the coding portions of a nucleotide sequence "serve the ends nature originally provided and t <tquite 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 diffe rences 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 Sequ ence 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

> 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,

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