No. 12-398

IN THE

Supreme Court of the United States

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,

Petitioners,

—v.—

MYRIAD GENETICS, INC., ET AL.,

Respondents.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

REPLY BRIEF FOR PETITIONERS

Daniel B. Ravicher
Sabrina Y. Hassan
Public Patent Foundation (PUBPAT)
Benjamin N. Cardozo School of Law
55 Fifth Avenue, Suite 928
New York, NY 10003
(212) 545-5337

Christopher A. Hansen
Counsel of Record
Steven R. Shapiro
Sandra S. Park
Aden J. Fine
Lenora M. Lapidus
American Civil Liberties Union Foundation
125 Broad Street
New York, NY 10004
(212) 549-2500
chansen@aclu.org

Attorneys for Petitioners

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

OTHER AUTHORITIES

INTRODUCTION

This Court has taken a balanced and nuanced view in distinguishing unpatentable compositions and methods that cover laws or products of nature from genuine, patentable inventions. *See, e.g.*, *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012); *Diamond v. Chakrabarty*, 447 U.S. 303 (1980); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948). The Federal Circuit, by contrast, has strained to minimize the product/law of nature doctrine in order to find virtually everything patentable. *See, e.g.*, *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347 (Fed. Cir. 2010), *rev'd sub nom. Mayo*, 132 S. Ct. 1289; App. at 8a-96a; Pet. at 18 (listing cases). This case presents the simple question of whether removing a human gene from the body and cell makes it patentable.

Respondents Myriad Genetics *et al.* (Myriad) argue that because the Circuit paid lip service to *Chakrabarty* and *Mayo*, its opinion is consistent with this Court's approach and the law is settled. Br. in Opp'n at 19-20 ("BIO"). But even a cursory reading of the majority opinions reveals the degree to which they diverged. Myriad also argues that its patents are valid because they are beneficial, not completely preemptive, and justified by industry reliance on PTO practice. BIO at 2-7. These arguments do not comport with *Mayo* and are, in any event, contradicted by the facts. *See infra* Section I.

Myriad attempts to avoid the undisputed facts about the stunning nature and scope of its patent claims by ignoring the claim language. *E.g.*, BIO at 1-4; *see infra* Section II. Its final argument that this case presents a poor vehicle for review is also

fundamentally flawed. BIO at 31-36. As the first opportunity in thirty years to clarify the Court's product of nature doctrine, this case is the appropriate vehicle for such a review. BIO at 31-36; *see infra* Section III.

I. THE FEDERAL CIRCUIT CREATED NEW LEGAL RULES THAT DIVERGED FROM THIS COURT'S PRECEDENTS.

Despite Myriad's claim that the law applied by the Circuit is settled, it is clear that the Circuit created new legal standards in upholding these patents, while simultaneously rejecting those articulated in this Court's Section 101 precedents.

Myriad distorts the Circuit's opinion beyond recognition. For example, Myriad describes Judge Lourie's opinion as faithfully applying the "distinctive name, character, and use" standard. BIO at 11-12. Of course, this Court has applied other standards in analyzing patent eligibility, including whether the invention has "markedly different characteristics from any found in nature." *Chakrabarty*, 447 U.S. at 310. And contrary to Myriad's contention, Judge Lourie never referred to a different "name" for the genes, which are called the same thing whether in or out of the body. He explicitly rejected the idea that any different function or use of the gene when "isolated" was even relevant to the Section 101 question. App. at 52a, 55a. And when discussing structure (or character), he referred to only one factor, breaking of a covalent bond, *id.* at 53a-55a, which Myriad remarkably tries to bolster by suggesting isolated DNA is "free-standing" and shorter. BIO at 12-14; *but see* App. at 102a-13a.

Myriad describes Judge Moore as holding that claims to longer segments of DNA are "patent-eligible, given their structural differences from native DNA." BIO at 13. But she quite clearly says the opposite, upholding the patents based on industry reliance in spite of her view that "isolated" full-length genes may not be markedly different from genes in the body. App. at 85a-86a.

Both the Federal Circuit and Myriad pay only brief lip service to *Mayo* and prior opinions, gutting them of content to justify patenting a law/product of nature. The majority did not see *Mayo* as relevant to composition claims, App. at 58a, even though these claims preempt use of laws of nature as well as products of nature. For example, claim 6 of patent '492, claims *any* "isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide… associated with a susceptibility to cancer." App. at 427a. The claim broadly preempts using any person's DNA to investigate the correlation between BRCA2 mutations and one or more cancers, without specifying or disclosing either the clinically significant mutations or the cancers for which patients may be susceptible. This and the other isolated DNA claims challenged here preempt scientific inquiry, disproportionately tying up both products and laws of nature. *See Mayo*, 132 S. Ct. at 1301.

Myriad asserted its patents to stop every other laboratory in the U.S. from offering clinical sequencing of these genes and providing patients with their own genetic information. App. at 37a. Myriad exercised its rights to threaten laboratories that were using different testing methods from

Myriad's, such as the University of Pennsylvania laboratory run by petitioners Arupa Ganguly and Haig Kazazian and that was sued by Myriad. App. at 34a. Because clinical genetic testing provided to patients in the U.S. relies on isolated DNA, these patents are of huge concern to the medical and scientific communities and patients, both those with hereditary conditions or disease predisposition and those who might benefit from treatments tailored to their genome. *See, e.g.*, Br. of Amici Curiae Am. Med. Ass'n *et al.*, Oct. 30, 2012; Br. for Canavan Foundation *et al.* as Amici Curiae, Oct. 30, 2012; Amici Curiae Br. for Academics in Law, Medicine, Health Policy and Clinical Genetics, Oct. 30, 2012 ("Academic *Amici* Brief"); App. at 4a-7a.

Myriad attempts to dispute how its patents monopolize the BRCA genes by pointing to other potential testing methods it contends would not violate its patents. Its flawed argument inadvertently establishes the preemptive effect of its patents. First, some of the tests mentioned do not sequence DNA at all; instead, they measure other biological phenomena, such as gene expression and proteins. They do not involve the natural phenomena at issue here – a person's genetic sequence – and their existence is irrelevant to whether the product and law of nature at issue – the DNA – is preempted. And because these tests measure different biological phenomena, they are not at all appropriate alternatives to DNA sequencing. That Myriad would resort to distracting the Court with references to these methods illustrates the deeply problematic and preemptive effect of its patents. Second, other methods cited by Myriad would violate the patent claims as defined by the

Circuit. For example, whole genome sequencing involves the breaking of DNA's covalent bonds, which Judge Lourie found to be key to defining isolated DNA. Myriad for the first time suggests otherwise, but the plain claim language belies its suggestion. *See* App. at 116a-17a. In the guise of explaining the scope of its claims, Myriad actually is rejecting the interpretation of the claims set out by the district court and Circuit. But for a patentee to assert that it would not enforce its rights against certain activities simply does not diminish their preemptive effect. The patents give Myriad the power to determine what testing can or cannot be done relating to patented genes and chill scientific work and innovation that could be pursued by the medical community.

Allowing the Circuit's opinion to stand would undo core holdings of *Funk Brothers*, recently cited by the Court in *Mayo*, 132 S. Ct. at 1293-94, and introduce a new legal standard for Section 101 eligibility – permitting a patent on a composition whenever it is removed from its natural environment and has some increased utility. Myriad emphasizes that the Circuit found that isolated DNA is patentable because it is DNA removed from its natural environment. BIO at 1. Yet, under *Funk Brothers*, removal of something from its natural environment is not sufficient to render it patentable. The patented strains of bacteria in *Funk Brothers* were "isolated," removed from their natural environment, and aggregated so as to more efficiently fix nitrogen without inhibiting each other. 333 U.S. at 129-30. They still could not be patented. *Id.* at 132. Moreover, the concurring opinion in this case held that claims covering short DNA segments

were acceptable under *Funk Bros.* because they had new utility as primers and probes. App. at 82a-83a. The claims here are not limited to uses of isolated DNA as primers or probes; but even if they were, increased utility does not by itself cross the Section 101 threshold. The court of appeals in *Funk Brothers* "thought that Bond did much more than discover a law of nature, since he made an new and different composition of non-inhibitive strains which contributed utility and economy to the manufacture and distribution of commercial inoculants." 333 U.S. at 130-31. But the Court found that despite this, Section 101 was not satisfied: "[T]here is no invention here unless the discovery that certain strains of the several species of these bacteria are non-inhibitive and may thus be safely mixed is invention. But we cannot so hold without allowing a patent to issue on one of the ancient secrets of nature now disclosed." *Id.* at 132. Nevertheless, the Circuit concurrence would uphold patents whenever the composition has increased utility – even utilities undescribed in the patent claims at issue, App. at 83a-85a – while the majority found utility irrelevant, App. at 55a. Both undermined central holdings of *Funk Brothers* and *Chakrabarty*. Finally, Myriad goes so far to suggest, as it argued in the proceedings below, that *Funk Brothers* is not relevant to Section 101 but instead to Section 103, BIO at 27, despite this Court's repeated reliance on *Funk Brothers* in its Section 101 decisions. *Mayo,* 132 S. Ct. at 1293-94; *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010), *Chakrabarty,* 447 U.S. at 309; *Parker v. Flook,* 437 U.S. 584, 591 (1978); *Gottschalk v. Benson,* 409 U.S. 63, 67 (1972).

The Circuit's decision distorts the Section 101 analysis in other crucial ways that will impact future cases. The Circuit ignored this Court's clear instruction in *Mayo* that the Section 101 question should be decided irrespective of whether patentees have substantial reliance interests. *Mayo,* 132 S.Ct. at 1304-05. For the concurrence in this case, these interests were the decisive factor in upholding patents on full-length genes, App. at 86a, and Myriad similarly reiterates the importance of the industry's interests. This reasoning cannot be reconciled with this Court's precedents, such as *Mayo*, *Bilski*, *Chakrabarty*, *Flook*, *Benson*, *Funk Brothers*, and *American Fruit Growers v. Brogdex Co.*, 283 U.S. 1 (1931), where patents were found invalid based on the legal principles laid out by this Court without regard to reliance interests or PTO practice. In *Mayo*, this Court admonished against providing enhanced protection for specific fields. *Mayo*, 132 S.Ct. at 1305; Pet. at 23-24. Yet in this case, the majority held as a matter of law that it was improper to consider the biology of genes since the only relevant question was one of chemistry. App. at 55a. *See also* Academic *Amici* Brief at 18-22 (explaining how the Circuit committed a fundamental error in construing the claims based on chemistry, rather than biology).

II. THE PATENT CLAIMS REACH PRODUCTS/LAWS OF NATURE AND NOT INVENTIONS.

Petitioners have already explained the nature of the claims and the reasons why they reach products/laws of nature. *E.g.*, Pet. at 6-7.

Respondents' only real response is to misrepresent the claim language.

Myriad's first argument is to emphasize that they have only patented "isolated" DNA, not DNA in the body. *E.g.*, BIO at 1. But, Myriad concedes that "isolation" means nothing more than "substantially separated from other cellular components" and "removed from its naturally occurring environment." *Id.* In other words, they patented the human genes simply pulled out of the body. Myriad argues it altered the DNA from the composition it has in the body. *E.g.*, BIO at 15. Petitioners already addressed this. *E.g.*, Pet. at 24-25, 28-29; *see also* App. at 102a-05a, 333a-44a. If the genes outside the body were so different from that inside the body, Myriad's testing of the "isolated" genes would be diagnostically useless. Pet. at 5. Three of the four judges who have written in this case determined there were no structural changes that alone qualify isolated DNA as an invention. App. at 81a-82a, 86a, 102a, 333a. Moreover, while removing the DNA from its natural environment allows the gene to be examined by scientists, the properties of DNA that the majority of the Circuit and Myriad point to are the product of the routine process of isolation, not of any "invention" by Myriad. *See* App. at 51a, 82a-85a (describing qualities of the patented DNA, that would describe any gene that is isolated). Had Myriad been the first to isolate a gene, it could have patented the method. But it cannot now claim that any characteristics of DNA incidental to isolation justify its patents. Isolated genes simply cannot be said to have "markedly different characteristics from any found in nature."

Myriad's second argument is that they identified the region of the overall human chromosome that correlated with an increased risk of breast and ovarian cancer. BIO at 3-4. Of course, many other scientists laid the foundation for these discoveries, including Dr. Mary-Claire King, who identified the locus of the BRCA1 gene. App. at 99a, 273a-77a. Even giving due credit to Myriad for its contribution, it is hard to imagine a more perfect definition of "we identified a law of nature." Myriad also makes repeated self-serving arguments, largely unsupported by the record, about the difficulty of identifying the relevant gene and making it available for testing. *E.g.*, BIO at 4. Yet, patents are not a reward for effort. The difficulty and complexity of uncovering $E=mc^2$ cannot be overemphasized, but that law of nature is clearly not patentable.

Myriad argues repeatedly that it was simply patenting a "molecule." *E.g.*, BIO at 14. Again, that is irrelevant. If nature made the molecule, as it did, it is not patentable. Myriad did not invent the length, composition, or function of the BRCA1 or BRCA2 molecules; human biology determined these qualities of the two genes. App. at 106a-07a, 339a, 342a-44a. Moreover, Myriad did not patent "a" molecule but literally hundreds of millions of molecules, many of which Myriad has never described and never seen and all of which make up naturally-occurring BRCA1 and BRCA2 genes. Pet. at 6-7. Thus, Myriad claims *any* DNA that codes for a particular protein or *any* part of that protein. It claims the full-length BRCA genes and *any* segments of them as short as 15 nucleotides. It claims not only the wild-type or normal genes, but *any* mutations of the genes, known and unknown. Thus, it claims the

molecules that are the BRCA1 and BRCA2 genes of every one of the more than 300 million people in the United States and almost innumerable small segments. *E.g.*, App. at 105a-06a (one claim alone includes an "almost incalculably large number of new molecules"); Pet. at 7.

In other words, Myriad's claims are not inventions; they represent products and laws of nature and the fundamentally erroneous conclusion of the Circuit to the contrary merits review.

III. THIS CASE IS THE PROPER VEHICLE TO REVIEW THESE ISSUES.

Myriad proposes various weak arguments that this case is not an appropriate vehicle for review. The opposite is true. First, Myriad argues that the petitioners will not be able to test for harmful mutations in the BRCA genes if these claims are declared invalid because other claims would also preclude examination of the genes. BIO at 33. Myriad made this argument to the Circuit, which properly and unanimously rejected it. App. at 39a-40a.

Second, the record is sufficient for review free of factual disagreement. Myriad itself moved for summary judgment based on this record, which included dozens of declarations. App. at 237a. In addition, a large number of *amicus* briefs, virtually all from organizations with expertise, have acknowledged there is no fundamental dispute on the facts.

Third, Myriad hints that this Court should await a further *en banc* Federal Circuit argument on the law relating to method claims. BIO at 34-35.

But, this case is about composition claims as well as method claims and there is no vehicle of which petitioners are aware that will resolve the lower court confusion on this doctrine except through the granting of the petition.

Patent claims like the ones at issue will continue to be relevant for many years to come. Even setting aside the broader issue of the product of nature doctrine, the USPTO continues to issue new patents on human genes. *See, e.g.*, U.S. Patent 7,928,212 (filed June 16, 2010). Moreover, Myriad has control over patents on isolated BRCA DNA that will not expire for more than another decade, allowing it to continue to exclude the medical and scientific community from undertaking important clinical work relating to these genes. *See, e.g.*, U.S. Patent No. 7,250,497 (filed June 9, 2003) (titled "Large Deletions in Human BRCA1 Gene and Use Thereof" and expiring June 9, 2023).

Finally, Myriad once again trots out its argument that none of the plaintiffs has standing. BIO at 31-33. The Circuit unanimously rejected this argument on three occasions. App. at 25a, n.6. In addition, Myriad made this same argument to this Court in opposing the prior petition, yet the Court granted the petition. App. at 1a. That Myriad continues to advance the argument highlights the narrow standing rules applied by the Federal Circuit, which are inconsistent with this Court's holding in *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118 (2007), and which led the Federal Circuit to improperly deny standing to the other plaintiffs in this case. *See* Pet. at 32-35. If anything, therefore, Myriad's standing argument simply reinforces the

need for this Court to grant Question 3 presented by the Petition.

CONCLUSION

For all these reasons, petitioners respectfully ask that the petition be granted.

Respectfully submitted,

Christopher A. Hansen
Counsel of Record
Sandra S. Park
Aden J. Fine
Lenora M. Lapidus
Steven R. Shapiro
American Civil Liberties Union Foundation
125 Broad Street
New York, N.Y., 10004
(212) 549-2500
chansen@aclu.org

Daniel B. Ravicher
Sabrina Y. Hassan
Public Patent Foundation (PUBPAT)
Benjamin N. Cardozo School of Law
55 Fifth Avenue, Suite 928
New York, NY 10003

Dated: November 9, 2012