No. 2010-1406

IN THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, THE AMERICAN COLLEGE OF MEDICAL GENETICS, THE AMERICAN SOCIETY FOR CLINICAL PATHOLOGY, THE COLLEGE OF AMERICAN PATHOLOGISTS, HAIG KAZAZIAN, MD, ARUPA GANGULY, Ph.D, WENDY CHUNG, MD, Ph.D, HARRY OSTRER, MD, DAVID LEDBETTER, Ph.D, STEPHEN WARREN, Ph.D, ELLEN MATLOFF, M.S., ELSA REICH, M.S., BREAST CANCER ACTION, BOSTON WOMEN'S HEALTH BOOK COLLECTIVE, LISBETH CERIANI, RUNI LIMARY, GENAE GIRARD, PATRICE FORTUNE, VICKY THOMASON, and KATHLEEN RAKER,

Plaintiffs-Appellees,

v.

UNITED STATES PATENT AND TRADEMARK OFFICE,

Defendant,

MYRIAD GENETICS, INC.; LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMPARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation,

Defendants-Appellants.

Appeal from the United States District Court for the Southern District of New York, in case no. 09-CV-4515, Senior Judge Robert W. Sweet

BRIEF FOR THE UNITED STATES
AS AMICUS CURIAE IN SUPPORT OF NEITHER PARTY

STUART F. DELERY
Acting Assistant Attorney General

BETH S. BRINKMANN
Deputy Assistant Attorney General

SCOTT R. MCINTOSH
MELISSA N. PATTERSON
(202) 514-1201
Attorneys, Appellate Staff, Civil Division
Department of Justice, 950 Penn. Ave., N.W.
Washington, D.C. 20530-0001

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INTEREST OF THE UNITED STATES

The United States respectfully submits this amicus brief pursuant to Fed. R. App. P. 29(a) and this Court's order of April 30, 2012. The United States' interest in the issues discussed herein is noted in its original amicus brief in this case.

QUESTION PRESENTED

What is the applicability of the Supreme Court's decision in Mayo Collaborative Services v. Prometheus Laboratories, Inc., 132 S. Ct. 1289 (2012), to Myriad's isolated DNA claims and to method claim 20 of the '282 patent?

STATEMENT

1. The district court held invalid fifteen claims from seven patents concerning the BRCA1 and BRCA2 genes exclusively licensed to Myriad Genetics, Inc. (Myriad). See A89-253; 702 F. Supp. 2d 181 (S.D.N.Y. 2010). On Myriad's appeal to this Court, the United States filed an amicus brief in support of neither party. The United States evaluated the composition claims in light of the established exception to 35 U.S.C. § 101 for products of nature, and concluded that although man-made complementary DNA molecules (cDNA) — which comprise

nucleotide sequences that do not exist in nature — are patent-eligible subject matter under 35 U.S.C. § 101, isolated but otherwise unaltered genomic DNA molecules are unpatentable products of nature.

With respect to the challenged composition claims, a panel of this Court unanimously held that cDNA molecules are patent-eligible, but divided regarding the patent eligibility of isolated but otherwise unmodified DNA. See 653 F.3d 1329 (Fed. Cir. 2011).

2. After this Court denied cross-petitions for panel rehearing, appellees filed a petition for a writ of certiorari. While the petition was pending, the Supreme Court issued its decision in Mayo. There the Court addressed the validity of a process patent that "purport[ed] to apply" what the Court concluded were "natural laws describing the relationships between the concentration in the blood of certain thiopurine metabolites and the likelihood that the drug dosage will be ineffective or induce harmful side-effects." Mayo, 132 S. Ct. at 1294. The Court concluded that the patented claims were invalid because they effectively claimed the natural law that they described.

The Court began its analysis by reiterating the longstanding "implicit exception" to patent eligibility under § 101 for "[l]aws of

nature, natural phenomena, and abstract ideas." Id. at 1293 (internal quotation marks omitted) (citing, e.g., Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980)). "Thus," the Court explained, it had held that "a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter," and "[l]ikewise, Einstein could not patent his celebrated law that $E=mc^2$." Ibid. (internal quotation marks omitted). The Court reiterated that "'[s]uch discoveries are "manifestations of * * * nature, free to all men and reserved exclusively to none."'" Ibid. (quoting Chakrabarty, 447 U.S. at 309, and Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948)).

The Court discussed its prior precedents that warn against upholding patents that "too broadly preempt the use of a natural law" and require patentees to add sufficient elements "to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." Mayo, 132 S. Ct. at 1294. The Court concluded that the metabolite correlations described in the challenged patents are natural laws, and that the patent claims did not "add *enough* to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws." Id. at

1296-97. The Court emphasized that a process utilizing a natural law is not patent-eligible "unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself." Id. at 1297.

After issuing its decision in Mayo, the Supreme Court granted the petition in this case, vacated this Court's judgment, and remanded for further proceedings in light of Mayo. See 132 S. Ct. 1794.

ARGUMENT

Mayo Supports The View That Isolated Genomic DNA Is Not Patent-Eligible Under 35 U.S.C. § 101.

As the United States explained in its original amicus brief, unlike cDNA, isolated but otherwise unmodified DNA molecules are not patent-eligible because they are "'products of nature,'" not "'human-made inventions.'" U.S. Amicus Br. at 14 (quoting J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124, 130 (2001) (quoting Chakrabarty, 447 U.S. at 313)). Patent protection is not available to those who simply discover existing aspects of nature, even if the discovery requires arduous work, represents keen scientific insight, and is of great value to society. Mayo underscores this fundamental limitation on patent protection. See Mayo, 132 S. Ct. at 1293

(discussing this "important implicit exception" to § 101). As discussed below, the Court's guidance on policing this limitation reinforces the conclusion that Myriad cannot patent DNA it discovered in and isolated from nature.

I. Mayo Implies That A Composition Claim Is Not Patent-Eligible If It Effectively Precludes The Public From Using A Product Of Nature.

The principal issue in this appeal is whether composition claims for isolated genomic DNA are directed to patent-eligible subject matter or, instead, whether such claims are impermissible attempts to patent products of nature.[1] The answer to that question turns on the relationship between the claimed compositions and naturally occurring DNA.

To be eligible for a patent, a claimed composition must be "human-made" and "markedly different" from a naturally occurring substance. Chakrabarty, 447 U.S. at 310, 313. The members of this panel agreed on that basic proposition. See 653 F.3d at 1350-51 (Lourie, J.); id. at 1359-60 (Moore, J., concurring in part); id. at 1379 (Bryson, J., concurring in part and dissenting in part). But the panel

[1] Plaintiffs also challenge Myriad's method claims. See Appellees' Br. at 52-60. The United States takes no position on this issue.

members parted company in applying that general principle to the composition claims at issue here. More specifically, the panel members disagreed about whether distinctions between isolated and genomic DNA are *significant enough* to render isolated DNA "markedly different" for § 101 purposes.

The Supreme Court's decision in Mayo provides guidance regarding that question. To be sure, that guidance is indirect. Mayo involves process, not composition, claims, and the Court's analysis focuses on the standards for determining whether a claimed process effectively claims a law of nature. Thus, Mayo does not directly address the criteria to be used in deciding the parameters of the product-of-nature exception, and every nuance of the Court's analysis may not mechanically extend to products of nature. Nevertheless, in at least one respect, Mayo provides an important point of reference for deciding whether a claimed composition and a naturally occurring substance are "markedly different" for purposes of § 101.

In analyzing the claimed methods in Mayo, the Supreme Court repeatedly emphasized the need to ensure that claims not "tie up" laws of nature by preventing the public from exploring and exploiting those

laws. See, e.g., 132 S. Ct. at 1294 (warning "against upholding patents that claim processes that too broadly preempt the use of a natural law"); id. at 1301 ("The Court has repeatedly emphasized . . . that patent law not inhibit further discovery by improperly tying up the future use of laws of nature."); ibid. (warning against the "danger that the grant of patents that tie up [natural laws'] use will inhibit future innovation premised upon them"). To avoid that outcome, the Court held that a "process reciting a law of nature" is not patent-eligible "unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself." Id. at 1297. With respect to the method claims in Mayo, the Court concluded that "the steps add nothing of significance to the natural laws themselves" and "amount[] to nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients." Id. at 1298, 1302. For that reason, upholding such claims "would risk disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries." Id. at 1294; see also id. at 1302

(discussing "basic underlying concern that these patents tie up too much future use of laws of nature").[2]

The concerns implicated by patent claims that "t[ie] up the use of the underlying natural laws," and thereby "inhibit[] their use in the making of further discoveries," may also be present when a patent contains a composition claim that relates to a product of nature. Products of nature, like laws of nature, are "manifestations of * * * nature" that are "free to all men and reserved exclusively to none." Chakrabarty, 447 U.S. at 309 (internal quotation marks omitted). A composition claim that effectively prevents the public from studying and making use of a product of nature is just as objectionable, and for the same underlying reason, as a method claim that effectively prevents the public from studying and exploiting a law of nature.

Mayo thus suggests one way (though by no means the exclusive way) for determining whether proffered differences between a claimed

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[2] The Court also pointed to the conventional nature of the steps added to the underlying nature law in the challenged claims. See, e.g., 132 S. Ct. at 1294. The Court did not suggest, however, that a patent is invalid simply because it incorporates a known process or other invention. Such a rule would be at odds with 35 U.S.C. § 100(b), which defines "process" to include "a new use of a known process, machine, manufacture, composition of matter, or material."

composition and a product of nature suffice to render the composition "markedly different" under Chakrabarty and related precedents. Mayo suggests that a court should ask whether a patent on the claimed composition has the practical effect of preempting the public's ability to use the product of nature itself. Issuance of a patent should leave others free to study and exploit the natural substance and to devise other alterations to it. If it does not, that is a strong indication that the differences between the claimed composition and the product of nature are insufficient to render the composition patent-eligible.

In Chakrabarty, for example, the patent the Supreme Court upheld on a genetically altered bacterium would not have interfered with the public's ability to investigate or further modify the original bacterium or to experiment on the DNA plasmids that the patentee inserted into it to create the "new bacterium." Chakrabarty, 447 U.S. at 310; see also id. at 305 n.1 (discussing insertion of "four different plasmids, capable of degrading four different oil components" into a bacterium). Similarly, cDNA molecules, which must be synthesized by scientists in the laboratory, are not created in the process of studying

native DNA and pose little risk of preempting study of naturally occurring DNA. See U.S. Amicus Br. at 15-16; A134.

In contrast, patents on isolated but otherwise unmodified DNA would significantly impair the public's ability to study and make use of genomic DNA. As Judge Bryson explained in dissent, "[t]he only material change to those genes" is that "necessarily incidental to the extraction of the genes from the environment in which they are found in nature." 653 F.3d at 1375. And, as is true in many fields, removing the product of nature from its natural surroundings is a prerequisite to any serious study or commercial exploitation of native DNA.[3] If the

[3] DNA sequencing technologies rely on isolating and breaking down DNA into segments shorter than — and thus potentially contained within — the BRCA genes. See, e.g., Rizzo & Buck, Key Principles and Clinical Applications of "Next-Generation" DNA Sequencing, Cancer Prevention Research, 1-5 (published online before print May 22, 2012, DOI:10.1158/1940-6207.CAPR-11-0432) (PubMed ID # 22617168) (discussing "first-generation" automated Sanger sequencing that "can read DNA fragments of 500 [base pairs] to 1 [kilobase] in length" and "next-generation sequencing" technologies that "offer shorter average read lengths (30–400 [base pairs])"); Kepler et al., Metastasizing patent claims on BRCA1, Genomics, 95, 312-314 (2010) (estimating that "most human genes contain at least one and usually several oligonucleotides covered by" claim 5 of Myriad's '282 patent, and noting that "if full-genome sequence analysis becomes feasible," claim 5 "would likely be deemed to be infringed by any form of genomic sequencing"). Moreover, even those emerging technologies that aim to sequence longer DNA strands still rely on its isolation, and

process of removing the product from its natural environment necessarily results in creation of the patented composition (and thus in infringement of the patent) — as is the case here[4] — the patent on the composition is in practical effect a patent on the product of nature itself. The "markedly different" standard is a flexible one, but Mayo suggests that it should interpreted and administered in a way that avoids this result.[5] Thus, Mayo provides guidance to courts attempting

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could require creation of gene-length segments, thus potentially infringing even Myriad's gene-length isolated DNA claims. See Hayden, Nanopore genome sequencer makes its debut, Nature News, February 17, 2012 (available at http://www.nature.com/news/nanopore-genome-sequencer-makes-its-debut-1.10051, last visited June 14, 2012) (discussing new nanopore technology that could sequence DNA strands 100,000 base pairs long).

[4] Myriad relies entirely on the fact of isolation to assert that its isolated DNA claims fall within § 101. See U.S. Amicus Br. at 20 (noting that absent the limitation of "isolation," Myriad's claims would encompass genes in the human body). Anyone who isolated either BRCA gene, or any fragment thereof at least fifteen nucleotides long, would infringe one or more of Myriad's contested claims.

[5] As explained in the United States' original amicus brief, the Supreme Court has also identified the creation of new utility — as distinct from potential applications of a substance's inherent properties — as an indication of patent eligibility. See U.S. Amicus Br. at 13-14 (pointing to Chakrabarty's invocation of the new bacterium's "potential for significant utility"); id. at 32-33 ("[T]he mere act of culling a natural product from its environment to uncover or exploit its preexisting natural qualities or functions — however useful those qualities or functions may be — is insufficient to create patentable subject

to determine when a change to a product of nature is "significant" or "marked" enough "in terms of patent law's objectives" to qualify for patent protection. Mayo, 132 S. Ct. at 1299.

The members of this panel all relied on Chakrabarty's "markedly different" rubric but disagreed about how to apply that standard to DNA isolated from nature. See 653 F.3d at 1351-53 (Lourie, J.); id. at 1364-68 (Moore, J.); id. at 1374-75 (Bryson, J.). In light of Mayo, this Court should not rest patent-eligibility on the bare fact that isolating genes or gene segments involves the breaking of chemical bonds, or on the fact that scientists can use small gene segments to exploit the inherent chemical properties of DNA in ways that cannot be done with complete genes.[6] Instead, the Court should also ask whether the

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matter[.]"); id. at 34 (noting that isolated DNA "may have more potential applications than human genes in their natural context," but that "the same is equally true of mined coal, separated cotton fibers, pure metallic lithium, ductile uranium, and other products of nature whose industrial value to mankind likewise arises when they are extracted from their naturally occurring environments").

[6] The patent claims themselves do not refer to the chemical characteristics of isolated DNA invoked by the members of the panel majority. See 653 F.3d at 1351-53, 1361-65. Thus, assuming that the majority's chemical descriptions are accurate, it is clear that those characteristics are simply a consequence of separating DNA from its native environment.

differences identified in the original panel decision are sufficient to leave the public free to study and exploit the native BRCA1 and BRCA2 genes. The answer to that question is no, and this Court should conclude that the claims directed at isolated but otherwise unmodified DNA are invalid under § 101.[7]

II. Mayo Indicates That The Asserted Need For Financial Incentives In A Particular Field Does Not Alter § 101.

There is another respect in which Mayo illuminates the § 101 analysis here. In Mayo, the patent owner argued "that a principle of law denying patent coverage here will interfere significantly with the ability of medical researchers to make valuable discoveries." 132 S. Ct. at 1304. Although the Supreme Court's analysis of § 101 reflects a generalized balancing between providing financial incentives for innovation and preventing unduly broad and preemptive monopolies, the Court declined to give weight to the patentee's field-specific policy

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[7] This Court can hold that isolated DNA is not patent-eligible without determining whether, or under what circumstances, patents may be granted on "purified" versions of naturally occurring substances. See U.S. Amicus Br. at 30-31. "Purification" may involve substantial manipulations undertaken after the naturally occurring substance has been removed from its native environment, cf. 653 F.3d at 1377 n.4 (Bryson, J., dissenting in part), and could well leave the public free to study and exploit the product of nature itself.

argument. See id. at 1304-05. Noting that the two sides and their respective amici disagreed over the practical impact of according patent protection to the challenged methods, the Court stated that it did "not find this kind of difference of opinion surprising," since "[p]atent protection is, after all, a two-edged sword" that forecloses some forms of innovation while protecting others. Id. at 1305. The Court expressed reluctance about "departing from established general legal rules lest a new protective rule that seems to suit the needs of one field produce unforeseen results in another." Ibid. The Court thus refused to determine whether it was "desirable" to "increase[] protection for discoveries" concerning "diagnostic laws of nature" specifically. Ibid.

In this case, Myriad has argued that the extension of patent protection to isolated DNA is necessary in order to preserve financial incentives for making DNA discoveries. See, e.g., Myriad Opening Br. at 3-4. Mayo strongly suggests that the judicial inquiry should not focus on industry-specific incentive arguments of this sort, pro or con, and instead should focus on "established general legal rules." See U.S. Amicus Br. at 34-36 (arguing that appellants' assertions regarding financial incentives do not distinguish isolated genes from other, clearly

unpatentable products of nature). The potential incentive effects of allowing private parties to monetize discoveries about a particular naturally occurring product do not alter the boundaries the Supreme Court has set — and in Mayo reinforced — between unpatentable products of nature and patentable creations of man.

CONCLUSION

For the reasons stated above and in the United States' original amicus brief, the Court should reverse the district court's invalidation of the composition claims that are limited to cDNAs and similar man-made constructs, but affirm the district court's conclusion that the claims encompassing isolated human genomic DNA are invalid.

Respectfully submitted,

STUART F. DELERY
Acting Assistant Attorney General

BETH S. BRINKMANN
Deputy Assistant Attorney General

SCOTT R. MCINTOSH
MELISSA N. PATTERSON
(202) 514-1201
Attorneys, Appellate Staff, Civil Division
Department of Justice
950 Penn. Ave., N.W.
Washington, D.C. 20530-0001

CERTIFICATE OF COMPLIANCE WITH PAGE LIMITS AND FEDERAL RULE OF APPELLATE PROCEDURE 32(a)

I hereby certify that this amicus brief is 15 pages long and thus complies with the page limit specified in this Court's order of April 30, 2012. I further certify that this brief complies with the type-face requirements set forth in Federal Rule of Appellate Procedure 32(a) because the type face is Century Schoolbook, proportionally spaced, fourteen-point font.

/s/ Melissa N. Patterson
MELISSA N. PATTERSON

CERTIFICATE OF SERVICE

I hereby certify that on June 15, 2012, I caused copies of the foregoing amicus brief to be filed with the Court by hand delivery. In addition, I caused copies to be served upon the following counsel by first-class U.S. mail:

VIGNERY, BRUCE B.
AARP Foundation Litigation
601 E Street, NW, Washington, DC 20049

GREENFIELD, DEBRA L.
UCLA Center for Society
1323 Rolfe Hall, Box 957221, Los Angeles, CA 90095

MAEBIUS, STEPHEN B.
Foley & Lardner LLP
3000 K Street, N.W., Suite 500, Washington, DC 20007

RUDOLPH, BARBARA R.
Finnegan, Henderson, Farabow
901 New York Avenue, N.W., Suite 1100, Washington, DC 20001-4413

CHIN, ANDREW
University of North Carolina
School of Law, 160 Ridge Rd. CB #3380, Chapel Hill, NC 27599-7264

MCCLURE, KENT D.
Animal Health Institute
1325 G Street, NW, Suite 700, Washington, DC 20005

HANSEN, CHRISTOPHER A.
American Civil Liberties Union
125 Broad Street, 18th Floor, New York, NY 10004

WAXMAN, SETH P.
Wilmer Cutler Pickering Hale
1875 Pennsylvania Avenue, N.W., Washington, DC 20006

KEANE, J. TIMOTHY
Harness, Dickey & Pierce, PLC
7700 Bonhomme Avenue, Suite 400, St. Louis, MO 63105

BELT, ERIK P.
McCarter & English, LLP
265 Franklin Street, Boston, MA 02110

GAEDE, III, WILLIAM G.
McDermott, Will & Emery
275 Middlefield Rd., Suite 100, Menlo Park, CA 94025

HENDRICKS, JOHN L.
Hitchcock Evert, LLP
750 N. St. Paul Street, Suite 1110, Dallas, TX 75201

FRIERSON, LARRY JAMES
3265 Lake County Highway, , Calistoga, CA 94515

HOLMAN, CHRISTOPHER M.
University of Missouri - Kansas
School of Law, 5100 Rockhill Road, Kansas City, MO 64110

GORDON, JENNIFER
Baker Botts, LLP
30 Rockefeller Plaza, 44th floor, New York, NY 10112-0228

CASTANIAS, GREGORY A.
Jones Day
51 Louisiana Avenue, NW, Washington, DC 20001-2113

KEANE, J. TIMOTHY
Harness, Dickey & Pierce, PLC
7700 Bonhomme Avenue, Suite 400, St. Louis, MO 63105

KELLEY, JAMES J.
Eli Lilly & Company
940 S. East Street, Dock 88, Lilly Corp. Center - Drop Code 1104,
Indianapolis, IN 46225

GEORGE, ERIKA R.
Loyola University
Chicago School of Law, 25 East Pearson Street, Chicago, IL 60611

WALDBAUM, MAXIM H.
Schiff Hardin LLP
900 Third Avenue, New York, NY 10022

KIMBRELL, GEORGE A.
International Center for Technology
660 Pennsylvania Avenue, S.E., #302, Washington, DC 20003

FORMAN, DAVID S.
Finnegan, Henderson, Farabow
901 New York Avenue, N.W., Washington, DC 20001-4413

WRIGHT-BONILLA, JACQUELINE DAWN
Foley & Lardner LLP
3000 K Street, N.W., Suite 500, Washington, DC 20007

WAMSLEY, HERBERT C.
Intellectual Property Owners
1501 M Street., NW, Suite 1150, Washington, DC 20005

JARECKI-BLACK, JUDY DELEON
Merial Limited
3239 Satellite Blvd., Duluth, GA 30096

STIEFEL, AARON
Kaye Scholer LLP
425 Park Avenue, New York, NY 10022

CALIA, KURT G.
Covington & Burling LLP
333 Twin Dolphin Drive, Suite 700, Redwood Shores, CA 94065-1418

KOWALSKI, THOMAS J.
Vedder Price P.C.
1633 Broadway, 47th Floor, New York, NY 10019

ANDREWS, LORI
565 W. Adams, Suite 530, Chicago, IL 60661

PIZZULLI, FRANCIS
718 Wilshire Blvd., Santa Monica, CA 90401

COX, KRISTA L.
Universities Allied for Essential
2625 Alcatraz Ave., # 180, Berkeley, CA 94705

MCCRACKIN, ANN M.
University of New Hampshire
2 White Street, Concord, NH 03301

/s/ Melissa N. Patterson
MELISSA N. PATTERSON