Nos. 14-1361, -1366

IN THE

United States Court of Appeals

FOR THE FEDERAL CIRCUIT

In Re: BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litigation

UNIVERSITY OF UTAH RESEARCH FOUNDATION, THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA, HSC RESEARCH AND DEVELOPMENT LIMITED PARTNERSHIP, ENDORECHERCHE, INC., and MYRIAD GENETICS, INC.,

Plaintiffs-Appellants,

—v.—

AMBRY GENETICS CORPORATION,

Defendant-Appellee.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE CENTRAL DISTRICT OF UTAH IN CONSOLIDATED CASE NO.
2:13-CV-00640-RJS
JUDGE ROBERT J. SHELBY

BRIEF OF THE AMERICAN CIVIL LIBERTIES UNION, ASSOCIATION FOR MOLECULAR PATHOLOGY, BREAST CANCER ACTION, PUBLIC PATENT FOUNDATION, AND AARP AS *AMICI CURIAE* IN SUPPORT OF APPELLEE

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June 9, 2014

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

University of Utah Research Foundation, et al., v. Ambry Genetics Corporation
No. 14-1361, -1366

CERTIFICATE OF INTEREST

Counsel for Amici Curiae, American Civil Liberties Union et al., certifies:

1. The full name of every party or amicus represented by me is:
American Civil Liberties Union Foundation, Association for Molecular Pathology, Breast Cancer Action, Public Patent Foundation

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:
N/A

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the amici curiae represented by me are:
None

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:
Sandra S. Park; Lenora M. Lapidus
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John Mejia
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Daniel B. Ravicher
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[Please note: Barbara Jones of AARP Foundation Litigation represented additional amicus AARP on the same amici brief]

June 9, 2014
Date

/s/ *Sandra S. Park*
Signature of counsel
Sandra S. Park

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

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No. 14-1361, -1366

CERTIFICATE OF INTEREST

Counsel for Amicus Curiae, AARP, certifies:

1. The full name of every party or amicus represented by me is:

   AARP

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:
   N/A

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the amici curiae represented by me are:
   None

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

   Barbara Jones, AARP Foundation Litigation

   [Please note: Sandra S. Park, Lenora M. Lapidus, American Civil Liberties Union Foundation; John Mejia, American Civil Liberties Union Foundation of Utah, Inc.; and Daniel B. Ravicher, Public Patent Foundation (PUBPAT) represented other amici on the same brief]

June 9, 2014
Date

/s/ *Barbara Jones*
Signature of counsel
Barbara Jones

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

CONSTITUTIONAL PROVISIONS

OTHER AUTHORITIES

STATEMENT OF INTEREST OF AMICI

The American Civil Liberties Union ("ACLU") is a nationwide, nonprofit, nonpartisan organization with over 500,000 members dedicated to protecting the fundamental rights guaranteed by the Constitution and the laws of the United States. Its Women's Rights Project, founded in 1972 by Ruth Bader Ginsburg, works to address civil liberties issues affecting women and girls. This case implicates important constitutional values relating to freedom of scientific inquiry, and will have a major impact on access to genetic testing that many women seek in order to make life-changing medical decisions.

The Association for Molecular Pathology ("AMP") is an international, not-for-profit professional association representing over 2,000 physicians, doctoral scientists and medical technologists who perform laboratory testing based on knowledge derived from molecular biology, genetics and genomics. AMP members regularly report that they were forced to stop providing testing services and are reluctant to develop new tests that could directly benefit patients due to enforcement of improper patents relating to genes, such as the claims at issue in this case.

Founded in 1990, Breast Cancer Action ("BCAction") is a national, grassroots advocacy and education organization working to end the breast cancer epidemic. As the watchdog of the breast cancer movement, BCAction believes

that Myriad's monopoly on examination of the BRCA genes through its patents creates unacceptable barriers to research and testing, endangering the health of its members and the public.

The Public Patent Foundation ("PUBPAT") is a not-for-profit legal services organization affiliated with the Benjamin N. Cardozo School of Law. PUBPAT achieves its mission of protecting freedom in the patent system by representing the public interest against undeserved patents and unsound patent policy and ensuring that publicly beneficial competition is not improperly enjoined.

AARP is a nonpartisan, nonprofit, membership organization dedicated to addressing the needs and interests of people age fifty and older. AARP has a long history of advocating for access to affordable health care and for controlling costs without compromising quality. Patents such as those in this case significantly elevate the cost of genetic testing and interfere with diagnosis and treatment based on second medical opinions.

All of the *amici* were counsel, plaintiffs, or amici in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013) [hereinafter, "*AMP*"]. Thus, *amici* are well-positioned to inform this Court about the issues presented and decided in *AMP* and the public interest at stake in invalidating patents that create monopolies on genetic information.

Pursuant to Rule 29(a), *amici* inform the Court that all parties have consented to the filing of this brief. *Amici* also confirm, pursuant to Rule 29(c)(5), that (a) no counsel to any party authored this brief, in whole or in part; (b) no party or party's counsel contributed money intended to fund preparing or submitting the brief; and (c) no person other than amici and their counsel contributed money intended to fund preparing or submitting this brief.

SUMMARY OF ARGUMENT

Despite the unanimous Supreme Court rulings in *Mayo* and *AMP*, Appellants ("Myriad") seek to assert its patent claims on basic methods of comparing sequences and on simple BRCA1 primers to stop all others from analyzing any person's BRCA1 gene. This Court should affirm the denial of the preliminary injunction because these patent claims cover products and laws of nature and Myriad's enforcement of them undermines the public interest. To rule otherwise would allow Myriad to once again obtain exclusive access to patients' genetic information, in violation of Supreme Court precedent.

The claims asserted by Myriad are invalid under Section 101 because they claim laws of nature, abstract thought, and products of nature. As this Court recognized in *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, claims on screening for a BRCA mutation by comparing or analyzing a patient's sequence against a reference sequence cover a mental process. 689 F.3d 1303,

1334 (Fed. Cir. 2012), *aff'd in part, rev'd in part sub nom. Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013). Pursuant to *Mayo*, the addition of routine, data-gathering steps such as "hybridizing," "amplifying," and "sequencing" does not alter the ultimate conclusion that these claims seek to monopolize a law of nature – whether a patient has a BRCA1 mutation or not – and medical professionals' ability to examine it. The primer claims also are invalid under Section 101 because the primers have the same sequence as naturally-occurring BRCA1 DNA and do not have markedly different characteristics from any found in nature. If Myriad were permitted to use these claims to monopolize analysis of the BRCA1 gene, that result would be in conflict with the First Amendment and Patent Clause of the U.S. Constitution.

Because these claims are invalid under Section 101, a preliminary injunction would harm the public interest. An injunction would also have detrimental effects on patients' access to genetic testing, clinicians' provision of medical care, and researchers' ability to innovate using the basic scientific methods and primers at issue here. Patients and physicians are best served when they can choose from the range of testing options that are offered by Ambry Genetics ("Ambry") and others, including testing of the multiple genes connected to breast and ovarian cancer risk, lower cost testing, access to confirmatory testing, and testing as part of research studies.

Myriad can continue to offer BRCA testing services to patients in the manner it selects. What it cannot be permitted to do, however, is stop all others from analyzing people's genetic information, the blueprint for our cells, organs, and bodies which contains significant medical clues about our susceptibility to diseases and responsiveness to treatments.

ARGUMENT

I. SUPREME COURT PRECEDENT ON SECTION 101 OF THE PATENT ACT PROHIBITS PATENT HOLDERS, LIKE MYRIAD, FROM MONOPOLIZING EXAMINATION OF GENETIC INFORMATION.

The claims asserted by Myriad in its preliminary injunction motion violate long-established precedent that prohibits the patenting of laws of nature, natural phenomena, products of nature, and abstract ideas. *AMP*, 133 S. Ct. at 2116; *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1293 (2012); *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010); *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). "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." *Mayo*, 132 S. Ct. at 1293 (quoting *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)). The Supreme Court has explained repeatedly that "[s]uch discoveries are 'manifestations of . . . nature, free to all men and reserved exclusively to none.'" *Chakrabarty*, 447 U.S. at 309 (second alteration in original) (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130

(1948)). A law or product of nature does not become a patentable invention based on novelty, hard work, or the need to recoup investment. *See AMP*, 133 S. Ct. at 2118; *Mayo*, 132 S. Ct. at 1303-05. Because Ambry has raised a "substantial question" concerning the validity of Myriad's method and primer claims, the district court was correct in concluding that "the preliminary injunction should not issue." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1364 (Fed. Cir. 1997).

A. Myriad's Method Claims Are Invalid Pursuant To The Decisions In *Mayo* And *AMP*.

Myriad's method claims – claims 7 and 8 of Patent '441 (A348) – are invalid under Supreme Court precedent. *Mayo* described two key factors in determining whether a method is patent-eligible: whether it is based on an inventive concept, and whether the patent ties up the use of the underlying natural phenomena. *Mayo*, 132 S. Ct. at 1294. These claims fail both tests.

Mayo explained in depth how a court must analyze a method claim for the existence of an inventive concept. The Court asked, does the claim arise from an "'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself"? *Id.* (quoting *Parker v. Flook*, 437 U.S. 584, 594 (1978)). Does it "add enough" or "simply append[] conventional steps, specified at a high level of generality, to laws of nature [or] natural phenomena"? *Id.* at 1297, 1300. The Supreme Court found that

Prometheus' claims were not inventive, despite putative transformations that occurred during the administration of a drug and determination of metabolite levels, because nothing of significance was added to the law of nature – the patient's response to a drug. *Id.* at 1297. The steps of administering a drug and determining metabolite levels were routine, conventional science. *Id.* at 1297-98. The only addition in the patent claim was the identification by Prometheus of the metabolite levels that indicate drug efficacy. *Id.* The claims simply "inform a relevant audience about certain laws of nature." *Id.* at 1298.

The method claims at issue here do not cross the Section 101 threshold set out in *Mayo*, because the claims are clearly directed at whether or not a patient has a BRCA1 mutation, a law of nature. Steps like "hybridizing," "amplifying," and "sequencing" are simply routine, preparatory steps that were not invented by Myriad. *Mayo*, 132 S. Ct. at 1298 (discussing "[p]urely 'conventional or obvious' '[pre]-solution activity'") (alteration in original). The patents themselves disclose this fact. *See, e.g.*, Patent '441, 14:9-16, 17:20-25. (A277, A279.)[1] These conventional steps simply allow the technician to gather the data to ascertain the

[1] Numerous scientists laid the groundwork for Myriad's ultimate sequencing of the BRCA1 and BRCA2 genes, including Dr. Mary-Claire King and her team, who identified the locus of the BRCA1 gene and named it. (A6163-66; A5302.) Others made significant contributions as well. *See, e.g.*, Kenneth J. Abel et al., *A Radiation Hybrid Map of the BRCA1 Region of Chromosome 17q12-q21*, 17 Genomics 632 (1993).

natural phenomenon of whether a patient has a mutation or not and inform the relevant audience – the physician and patient – accordingly. And for the reasons described by Ambry and *infra* Part I.B, the use of simple primers and probes in the methods does not change that conclusion. Ambry Br. 41-43, 47. The probes and primers were not "invented" by Myriad but instead consist of nucleotide sequences found in the body whose function is determined by nature. In this respect, the methods here are even less inventive than the methods set out in Prometheus' claims because they assess pure biological facts that do not depend on the administration of a man-made drug for their existence. Adding routine steps such as "amplifying" using primers or "sequencing" amount to clever draftsmanship, and do not rescue the claims because they ultimately cover a law of nature. *Mayo*, 132 S. Ct. at 1294 (the Supreme Court's "cases warn us against interpreting patent statutes in ways that make patent eligibility 'depend simply on the draftsman's art'") (quoting *Flook*, 437 U.S. at 593).

Myriad attempts to distinguish *Mayo* by arguing that there, the correlation between the drug and metabolite levels was known, whereas here, the BRCA1 genetic sequence was unknown. Myriad Br. 35-36. As a preliminary matter, Myriad does not explain why the fact that a law of nature was previously unknown to scientists should render a method claim that preempts use of the law of nature patent-eligible. The Supreme Court's precedents suggest no such rule and instead

counsel the opposite: that patent claims cannot preempt use of laws of nature without running afoul of Section 101, regardless of whether the natural phenomenon could be considered "new." *AMP*, 133 S. Ct. at 2117; *Mayo*, 132 S. Ct. at 1303-04.

Moreover, the rule that Myriad urges this Court to adopt would weigh *against* patent eligibility of its claims, as scientists had developed a substantial body of knowledge about the BRCA genes before Myriad first sequenced them. As Dr. Tait explained in his declaration, scientists already knew how to amplify, sequence, or compare sections of the BRCA1 and BRCA2 genes before they were isolated in full. (A7528-29.) They also already knew that there would be mutations and polymorphisms in the BRCA1 and BRCA2 genes. (A7529-30.) Thus, the relevant knowledge embodied in Myriad's method claims – how to hybridize a BRCA1 gene probe to a BRCA1 allele and detecting the hybridization product, or how to amplify part of a BRCA1 gene and sequencing the amplicons – was known. The entire sequence of the BRCA1 gene was not yet known, but neither of the asserted claims requires such knowledge in order to carry out the methods they describe. (A7531-32.) Indeed, Myriad's position would have permitted the first scientists to amplify and sequence part of the BRCA1 gene to obtain claim 8 of Patent '441 and preclude Myriad from its subsequent work.

The patent ineligibility of these claims is further demonstrated by how they tie up uses of the BRCA1 gene. As *Mayo* reaffirmed, a key aspect of the Section 101 analysis turns on whether the patent preempts use of the laws and products of nature. Does the patent "risk disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries"? *Mayo*, 132 S. Ct. at 1294. "[M]onopolization of [basic scientific and technological] tools through the grant of a patent might tend to impede innovation more than it would tend to promote it." *Id.* at 1293. Thus, the Court's precedents "warn us against upholding patents that claim processes that too broadly preempt the use of a natural law." *Id.* at 1294*; see also Bilski*, 130 S. Ct. at 3231 ("Allowing petitioners to patent risk hedging would pre-empt use of this approach in all fields, and would effectively grant a monopoly over an abstract idea."); *Funk Bros.*, 333 U.S. at 130 ("He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes."); *O'Reilly v. Morse*, 56 U.S. 62, 113 (1853) (The patentee's claim on any machinery or process using electric current to mark characters at a distance "shuts the door against inventions of other persons...."). While every patent forecloses use of what has been patented, the Section 101 preemption inquiry focuses on whether the patent claim authorizes the patentee to foreclose use of the natural phenomena.

In *AMP*, the Supreme Court expressed concern that patents on isolated DNA unduly interfered with scientific activity such as genetic testing. "But isolation is necessary to conduct genetic testing, and Myriad was not the only entity to offer BRCA testing after it discovered the genes . . . [describing Myriad's assertion of patent exclusivity against others] . . . Myriad, thus, solidified its position as the only entity providing BRCA testing." *AMP*, 133 S. Ct. at 2114. In reaching its unanimous ruling, the Supreme Court clearly sought to ensure that patents on genes, or basic methods such as "isolating," would not stand in the way of scientific and medical activity, such as genetic testing. This concern applies with equal force to the methods asserted here, where Myriad is enforcing patent claims that recite conventional science to stop others from examining genetic information.

Myriad suggests that its claims are not preemptive because there may be other ways of studying the gene. Myriad Br. 39. Yet, *Mayo* directs that the analysis is a "*relative* one: how much future innovation is foreclosed relative to the contribution of the inventor." *Mayo*, 132 S. Ct. at 1303. *See also Bilski v. Kappos*, 130 S. Ct. at 3231 ("limiting an abstract idea to one field of use or adding token post solution components did not make the concept patentable," citing *Flook*). The method claims exclude study of a law of nature using routine steps regardless of whether the laboratory professional is focused on providing breast and ovarian cancer risk testing for patients; they are not limited to the breast and

ovarian cancer context. Any scientist who engages in the basic steps of amplifying part of the BRCA1 gene and sequencing the amplified segment as part of a research study would violate these claims. For that reason, the patents raise the same concerns about patenting a "building-block" that has previously troubled the Supreme Court. *Mayo*, 132 S. Ct. at 1303.

B. Myriad's Primer Claims Are Invalid Under Supreme Court Precedent.

Myriad's primer claims – cls. 16 and 17 of Patent '282 (A242) – are also invalid under Supreme Court case law.[2] The district court correctly recognized that the *AMP* decision was not limited to the patent eligibility of genomic DNA extracted from its natural environment, but also applies to other DNA molecules that have the same sequence as naturally-occurring DNA; moreover, in this case, the primers do not have markedly different characteristics from any found in nature.[3] (A75-87.) The primers here are defined by the fact that their sequences are the same as naturally-occurring sequences of the BRCA1 gene. As was the

[2] Myriad contends in its opening brief that *amici* were "conspicuously silent" on the patent eligibility of the primer claims in their district court brief. Myriad Br. 58 n.9. That is incorrect. *Amici* stated: "*Amici* agree that, for the reasons stated by Defendants in their opposition brief, the asserted primer claims are also invalid under the Patent Act." (A6448.)

[3] As the district court described, Myriad insisted throughout the *AMP* litigation that the claims on isolated DNA included primers and probes and should be evaluated accordingly. (A76-81.) As a result, the opinions of the *AMP* district court and court of appeals engaged in that analysis, and the Supreme Court's decision arose from that record.

case in *AMP*, Myriad did not patent a particular primer that it created with a nonnaturally occurring sequence. The *AMP* Court recognized that it might be possible to patent an isolated DNA that "included both the BRCA1 or BRCA2 gene and one additional nucleotide pair. Such a molecule would not be chemically identical to the molecule 'invented' by Myriad. But Myriad obviously would resist that outcome because its claim is concerned primarily with the information contained in the genetic *sequence*, not with the specific chemical composition of a particular molecule." *AMP*, 133 S. Ct. at 2118. Likewise, the claims here are concerned primarily with the information contained in the primers' sequence ("the sequence of said primers being derived from human chromosome 17q" (A242)), because that sequence exactly matches a naturally occurring sequence.

The Supreme Court's discussion of cDNA only confirms that "synthetic" DNA is patent-ineligible where it matches a naturally-occurring DNA sequence. *AMP* concluded that most cDNAs survive Section 101 because they do not have the same nucleotide sequence as genomic DNA; they do not include the sequence of intervening introns. *AMP*, 133 S. Ct. at 2119. In contrast, the Court held that cDNA would be a product of nature when it is based on a short DNA segment with no intervening introns, because it would be "indistinguishable" from natural DNA. *Id.* Thus, the *AMP* Court recognized that "synthesized" DNA such as cDNA could be patent-ineligible under Section 101, a ruling that echoed Judge Bryson's views.

Ass'n for Molecular Pathology, 689 F.3d at 1356 (Bryson, J., dissenting). For that reason, it would be clear error for this Court to read *AMP* as only excluding genomic DNA extracted from its natural environment from patent eligibility; otherwise, *AMP* would not have recognized the patent ineligibility of short cDNAs that are based on a single genomic exon. *AMP*, 133 S. Ct. at 2119.

In any case, the primer claims are invalid under prevailing case law because the primers do not have markedly different characteristics from naturally-occurring DNA. The Supreme Court's precedents have established that a patent-eligible composition must have "a distinctive name, character [and] use" and "markedly different characteristics from any found in nature." *AMP*, 133 S. Ct. at 2117 (citing *Chakrabarty*, 447 U.S. at 309-310); *see also American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 12 (1931) (chemical treatment of fruit did not give it a "distinctive name, character or use"). The primers here do not satisfy this standard, because they have the same sequences as naturally occurring BRCA1 sequences, and their function is based entirely on naturally-occurring qualities. Their ability to hybridize to complementary segments of DNA, like the ability of native DNA, relies on Watson-Crick pairing, and they function as naturally-occurring primers do during DNA replication. (A82-87; A6325; A7615-18.) They are thus analogous both to the isolated DNA of *AMP* and the strains of bacteria in *Funk Brothers*. Myriad did not invent their ability to hybridize to the BRCA1

sequences, just as it did not invent isolated DNA or any of the characteristics of DNA that are incidental to its isolation. *AMP*, 133 S. Ct. 2116, 2120; *see also Funk Bros.*, 333 U.S. at 130 (the patent holder did "not create [a] state of inhibition or of non-inhibition in the bacteria"); *In re Roslin Inst. (Edinburgh)*, No. 2013-1407, 2014 WL 1814014, at *4 (Fed. Cir. May 8, 2014) (disapproving of patent on cloned mammal because Roslin "'did not create or alter any of the genetic information' of the claimed clones, '[n]or did [Roslin] create or alter the genetic structure of [the] DNA' used to make its clones.") (alteration in original).

C. These Patent Claims Are Also Invalid Based On The First Amendment And Patent Clause Of The U.S. Constitution.

Even if these patents survive scrutiny under the Patent Act,[4] they also raise constitutional problems by monopolizing areas of knowledge and claiming thought, thereby interfering with scientific inquiry. The structure of intellectual property is created by Article I, section 8, clause 8, which covers copyright and patents: Congress has the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." U.S. Const. art. 1, § 8, cl. 8. Like

[4] Ambry raised other grounds of invalidity under the Patent Act, including anticipation under § 102 and obviousness under § 103, that the district court did not reach. (A69-70.) *Amici* agree with Ambry that these claims also are invalid under §§ 102 and 103. Thus, if this Court concludes that the district court erred in its Section 101 analysis, and that Myriad has satisfied the other criteria for a preliminary injunction, it should remand for further analysis under the Patent Act.

other legislative powers conferred by Article I, the power to award copyrights and patents is limited by the First Amendment. In copyright, where the potential conflict with the First Amendment is more obvious, the Supreme Court has suggested that the First Amendment requires doctrines, like the idea/expression distinction, that are incorporated into the statute. *Eldred v. Ashcroft*, 537 U.S. 186, 219 (2003); *Harper & Row Publishers, Inc. v. Nation Enters.*, 471 U.S. 539, 556 (1985); *see also Salinger v. Colting*, 641 F. Supp. 2d 250, 255 (S.D.N.Y. 2009), *vacated on other grounds*, 607 F.3d 68 (2d Cir. 2010); *Maxtone-Graham v. Burtchaell*, 631 F. Supp. 1432, 1435-36 (S.D.N.Y. 1986), aff'd, 803 F. 2d 1253 (2d Cir. 1986).

There can be little doubt that patents that give control over an entire body of knowledge would violate the Constitution, thus necessitating the Section 101 doctrine prohibiting patents on laws of nature, products of nature, and abstract ideas. Indeed, the Supreme Court's concern about tying up basic scientific and technological tools highlights the priority placed on preventing patents that attempt to claim a thought process, even where physical steps are involved. *Mayo*, 132 S. Ct. at 1302 (invalidating claims for method of determining drug efficacy because they "tell a treating doctor to measure metabolite levels and to consider the resulting measurements in light of the statistical relationships they describe. In doing so, they tie up the doctor's subsequent treatment decision whether that

treatment does, or does not, change in light of the inference he has drawn using the correlations."); *see also Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 135-36 (2006) (Breyer, J., dissenting from dismissal of writ of certiorari); Peter Yun-Hyoung Lee, *Inverting the Logic of Scientific Discovery: Applying Common Law Patentable Subject Matter Doctrine to Constrain Patents on Biotechnology Research Tools*, 19 Harv. J.L. & Tech. 79, 101-8 (2005); Gary L. Francione, *Experimentation and the Marketplace Theory of the First Amendment*, 136 U. Pa. L. Rev. 417, 428 (1987).

Rather than leading to a greater understanding or a better product, the patent claims asserted by Myriad exclude others from basic scientific and medical work examining naturally-occurring genes. (*See, e.g.*, A2704-07; A2793-94; A6324; A7531-32.) The method claims include what this Court found to be a mental step – comparing two genetic sequences. *Ass'n for Molecular Pathology*, 689 F.3d at 1334. This raises the same concern identified in *Mayo* about the claim's inclusion of mental steps; although the wherein clauses in Prometheus' claims were obviously intended to alert the physician to act in a therapeutic setting, the claims were not limited to the therapeutic setting or restricted to action taken as a result of the test levels. *Mayo*, 132 S. Ct. at 1297, 1302; *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04CV1200 JAH (RBB), 2008 WL 878910, at *6 (S.D. Cal. Mar. 28, 2008). Likewise, here, the claims asserted by Myriad target the

abstract thought of comparing two sequences after performing routine scientific activities but does not direct any subsequent actions. (*See* A2793; A2707.) And the claims on primers seek to monopolize naturally-occurring DNA sequences, interfering with the acquisition of knowledge about the BRCA1 gene. *See* A6323-26; *see also* Lee, *supra* at 81-86.

The ability to think and inquire without constraint is an essential attribute of human autonomy and an essential cornerstone of the First Amendment. *See* Laurence Tribe, *American Constitutional Law* § 12-1 (2d ed. 1988); Thomas Emerson, *The System of Freedom of Expression* 6 (1970). In Justice Harlan's words, "No other approach would comport with the premise of individual dignity." *Cohen v. California*, 403 U.S. 15, 24 (1971). Or, as Justice Brandeis famously stated in an opinion joined by Justice Holmes, the First Amendment protects the "freedom to think as you will and to speak as you think." *Whitney v. California*, 274 U.S. 357, 375 (1927) (Brandeis, J., concurring); *see also United States v. Reidel*, 402 U.S. 351, 355-56 (1971); *Stanley v. Georgia*, 394 U.S. 557, 564-66 (1969); *Griswold v. Connecticut*, 381 U.S. 479, 482 (1965); *Palko v. Connecticut*, 302 U.S. 319, 326-27 (1937).

Yet, Myriad seeks to use its patents to control the field of scientific and medical work relating to the BRCA1 and BRCA2 genes, and to exclusively amass genetic information critical to patients' health. (A2611-14; A5296; A5303-05;

A5308-09; A5311; A4496-97; A5498-99; A5502; A2794-95.) The claims thus give entire control over a body of knowledge and over pure information to Myriad. That, under the First Amendment, is impermissible. *See Ashcroft v. Free Speech Coal.*, 535 U.S. 234, 253 (2002) ("First Amendment freedoms are most in danger when the government seeks to control thought or to justify its laws for that impermissible end. The right to think is the beginning of freedom . . . ."); *see also* John A. Robertson, *The Scientist's Right to Research: A Constitutional Analysis*, 51 S. Cal. L. Rev. 1203, 1217-18 (1977) (concluding that "[i]f the first amendment serves to protect free trade in the dissemination of ideas and information, it must also protect the necessary preconditions of speech, such as the production of ideas and information through research") (footnote omitted).

The serious constitutional violation raised by these patent claims provides an additional reason for the Court to affirm the district court. The Court should apply the Patent Act to these claims in a manner consistent with constitutional bounds.

II. A PRELIMINARY INJUNCTION WOULD UNDERMINE, RATHER THAN SERVE, THE PUBLIC INTEREST.

The district court concluded that neither Myriad nor Ambry showed that the public interest weighed in their favor. (A103-06.) Myriad cannot meet its burden of demonstrating that the public interest supports issuance of the injunction. Its arguments ignore the public interest in increased scientific and medical work on the BRCA genes, while improperly relying on the general public interest in

upholding patent rights. Myriad Br. 60. For over 15 years, Myriad exercised invalid patent claims to shut down many laboratories and establish a monopoly on testing the BRCA1 and BRCA2 genes. The general public interest in upholding a patentee's rights does not apply here, where Myriad already has enjoyed a lengthy period of exclusivity based on invalid claims that it seeks to prolong by asserting other claims that also are invalid under prevailing case law.

The Court should be especially cautious to exercise its equity powers when the asserted patents are likely to be invalid under Section 101. As the Supreme Court repeatedly has recognized, authorizing monopolization of natural phenomena – the basic tools of scientific and technological work – 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; *see also Lab. Corp. of Am. Holdings*,, 548 U.S. at 126-27 (Breyer, J., dissenting). It is particularly vital that a court deny a preliminary injunction where the patents likely claim laws and products of nature, because scientists will otherwise be barred from innovating using what should properly be in the common domain, for the benefit of the public. The sequences of a person's BRCA1 and BRCA2 genes, "like the heat of the sun, electricity, or the qualities of metals, 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." *Funk Bros.*, 333 U.S. at 130. Here, the public interest is harmed by a preliminary

injunction that sanctions the resumption of Myriad's monopoly on using laws and products of nature – the BRCA1 and BRCA2 genes and their connection to disease risk.

Denying an injunction based on public interest in this case is also appropriate because of the serious, detrimental impact such an order would have on public health. *See Rite-Hite Corp. v. Kelley Co., Inc.*, 56 F.3d 1538, 1547-48 (Fed. Cir. 1995). This Court has found that a negative impact on public health is a sound basis for refusing to enter a preliminary injunction. *See Cordis Corp. v. Boston Scientific Corp.*, 99 Fed. App'x. 928, 935 (Fed. Cir. 2004); *Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1458 (Fed. Cir. 1988); *Datascope Corp. v. Kontron Inc.*, 786 F.2d 398, 401 (Fed. Cir. 1986). This Court has affirmed refusals to issue a preliminary injunction where the "strong public interest supports a broad choice" of medical options and concluded that the public interest is harmed when some physicians are denied their choice of medical products due to patent assertion. *Cordis Corp.*, 99 Fed. App'x. at 935-36; *see also Datascope Corp.*, 786 F.2d at 401. The district court found, and the record clearly supports, that Myriad's patent claims allow it to limit patients' access to BRCA genetic testing, chill research, control data, and impeded the development of new technologies. (A105.)

First, Myriad's monopoly on testing severely limits the options available to patients for clinical testing. Myriad has prevented full sequencing of these genes

by other laboratories, even when others could do so at lower cost, to confirm results, or to ensure testing quality. (A2612-13; A5297-98; A5305; A2791-92, A2794; A4486-89.) Many women, upon obtaining results from Myriad, wish to get a second opinion before they make life-changing medical decisions, such as obtaining or refraining from prophylactic surgery. (A2641.) Women cannot obtain confirmatory testing through other labs except for one small set of mutations. (A4492; A4522-24; A2612-13; A5303-04; A5306-07.) Myriad also prevents others from providing testing at a lower price, or for free. (A2586; A2612-14; A2640-41; A4486; A4525.) As a result, some patients are unable to access testing due to cost. (*See* A2613-14; A4513; A4525; *see also* A2641-42.) And Myriad has demonstrated a lack of transparency regarding the analytic sensitivity of its testing. (A4507; A4512-14; A5303-04.)

In *Mayo*, the Supreme Court expressed concern about patent claims that "threaten to inhibit the development of more refined treatment recommendations." *Mayo*, 132 S. Ct. at 1302. The same problem is presented here. Myriad is attempting to use its claims on routine ways of screening genes to dictate the standard of care for ascertaining hereditary breast and ovarian risk. This denies both physicians and patients the opportunity to seek out testing options that provide the comprehensive information they need to make major medical decisions. (A4313-14; A4516-27; A2641-43.) For example, Myriad performed

tests for thousands of patients over several years that did not identify all clinically significant classes of mutations known to the scientific community and refused requests by others to allow them to offer such testing. (A2612-13; A5297-301; A4509-11.) One study found that women with large rearrangement mutations that were not detected by Myriad's tests, and who were from high-risk families, received false negative results 12% of the time. (A4510-11; A5298; A5300.) Indeed, Myriad still does not perform rearrangement testing for every patient, charging an additional $700 for large rearrangement testing or BRACAnalysis Large Rearrangement Test ("BART") on top of the $3,340 it charges for the standard "Comprehensive BRACAnalysis," even though national guidelines recommend that patients receive rearrangement testing as part of the standard of care. (A4514-15; *see also* A2612-13; A7648; A2641-42.) Myriad also does not describe the full basis for its interpretation of genetic test results, depriving physicians and their patients of the ability to evaluate the results given. (A4498; A7649-50; A2795.) Moreover, Myriad's assertion of its patents threatens laboratories that want to include the BRCA1 and BRCA2 genes when clinically assaying the over dozen genes now known to be associated with hereditary risk for breast and ovarian cancer or when using next generation testing methods. (*See, e.g.*, A4516-17; A2791-92; A5299-301.)

Further, because the primer claims cover all basic BRCA1 primers used in PCR and the method claims generically append routine techniques used for screening the BRCA1 gene to the natural laws governing the relationships between mutations and the predisposition to breast and ovarian cancer, the claims give Myriad the authority to prevent study of the BRCA1 gene. Myriad's assertion of its patents stopped and deterred research on the genes. (A5498-99; A2791-92; A2527-28.) Other gene patents resulted in similarly dire consequences. Over half of all labs surveyed as part of a government-funded study reported "deciding not to develop a new clinical genetic test because of a gene patent or license." (A2526.) Another study found that 46% of surveyed geneticists felt that gene patents had "delayed or limited their research." *Id.* Some geneticists have felt a deep discomfort with conducting research on the BRCA1 and BRCA2 genes because Myriad has sharply limited what it considers to be research and prohibited them from disclosing genetic information to research subjects. (A5935-40.) *See also* Kimberly Blanton, *Corporate Takeover Exploiting the U.S. Patent System*, Boston Globe Mag., Feb. 24, 2002, at 10 (describing how a Yale researcher's work on breast cancer genes, "once a third of the research in his lab, has been snuffed out by restrictions imposed by a licensing agreement between Myriad and Yale"). And scholars looking closely at gene patents found they inhibit research and innovation. (A2526-30; A2708-09; A4687-700; *see also* A4516-22.) The filing of these

infringement actions, which also target basic screening of the BRCA1 and BRCA2 genes, will only further chill research.

Relatedly, an injunction would allow Myriad to continue to impede the acquisition of greater knowledge about the BRCA genes. Scientists routinely share information about the importance of particular genes and particular gene mutations. (A4494-96; A2586; A5501-02.) Because Myriad's patents authorized it to maintain a clinical testing monopoly, Myriad gained control over a huge amount of data on the nature and significance of variants in the BRCA1 and BRCA2 genes. For the last several years, Myriad has refused to share that data with the scientific community. (A4496-97; A5308; A5501-05.) Myriad's conduct flies in the face of the professional ethical standards set out by the American Medical Association, which calls on laboratories, researchers and providers to publicly share data on genetic variants. (A5310-11; A5481-89; A5503-05.) Ambry already has committed to sharing the data they obtain. (A4497; A3721-22.) Unless additional labs are able to engage in testing, the scientific community will continue to be stymied in learning more about the genes and the significance of many genetic alterations that are more likely to occur in patients of African, Hispanic, and Asian descent. (A5517-18; A2795.) If Myriad is allowed to control what testing is performed on the BRCA1 and BRCA2 genes, it will not only command the law of nature that is a person's genetic code, but also the laws of

nature relating to how these genes function in tandem with other genes and genetic factors and their relationships to diseases other than breast and ovarian cancer – key scientific insights required for the development of personalized medicine. (A4519-20; A2794-95.)

Lastly, these patents preclude scientists from engaging in foundational scientific activities that are the first steps toward the development of new drugs, instruments, and treatment methods. Although the genetic testing Myriad offers is a useful service, this value is dwarfed by the potential applications of the claims asserted here to the design of new therapeutics, biomedical devices and instruments, and sequencing technologies. (A5299-302; A5309; A4493-94; A2795; A2707-08.) Some of these new applications might relate to breast and ovarian cancer, but many will not.[5] Further, such applications are likely to involve areas of inquiry untouched by Myriad. Yet, they all are precluded by the method claims if they rely on the basic steps of amplifying part of the BRCA1 gene using simple primers and sequencing the amplified nucleic acids, and by the primer claims if they incorporate the basic activity of using BRCA1 primers in PCR. As

[5] The BRCA genes have been linked to other cancers, including prostate and pancreatic. *See, e.g.*, Srinath Sundararajan et al., *The Relevance of BRCA Genetics to Prostate Cancer Pathogenesis and Treatment*, 9 Clinical Advances Hematology & Oncology 748 (2011); Kathleen M. Murphy et al., *Evaluation of Candidate Genes MAP2K4, MADH4, ACVR1B and BRCA2 in Familial Pancreatic Cancer: Deleterious BRCA2 Mutations in 17%*, 62 Cancer Res. 3789 (2002).

in *Mayo*, these claims stand in the way of a scientist who wants to develop innovative applications that also rely on these basic steps or DNA segments.

The negative consequences for public health of Myriad's monopoly led the twenty plaintiffs in the *AMP* litigation, including organizations representing over 150,000 medical professionals, geneticists, patients, and patient advocates, to file suit. The United States filed briefs opposing patent claims approved by its own Patent Office, stating that "[t]he extent to which basic discoveries in genetics may be patented is a question of great importance to the national economy, to medical science, and to the public health." Br. for United States as Amicus Curiae in Support of Neither Party at 1, *Ass'n for Molecular Pathology*, 653 F.3d 1329 (Fed. Cir. 2011) (No. 2010-1406). Moreover, an additional 89 different organizations and individuals filed 58 amicus briefs in the district court, Federal Circuit, and Supreme Court opposing Myriad's patent claims, and the vast majority of these briefs discussed the detrimental effects on public health. *See, e.g.*, Br. of Amici Curiae American Medical Ass'n et al. in Support of Petitioners at 8, *AMP*, 133 S. Ct. 2107 (2013) (No. 12-398) ("Myriad's exclusive control has led to the misdiagnosis of patients and has precluded the deployment of improved genetic tests."); Br. for Canavan Foundation et al. as Amici Curiae in Support of Petitioners at 6, *AMP*, 133 S. Ct. 2107 (2013) (No. 12-398) ("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").

The decision on the preliminary injunction motions will not only affect Ambry, but also the biotechnology, scientific, and medical communities as a whole. The five other laboratories now involved in the multi-district litigation with Myriad include two of the largest laboratory testing service providers in the country – Quest Diagnostics and Laboratory Corporation of America Holdings. Many other commercial and academic laboratories began or were preparing to offer BRCA1 and BRCA2 testing following the *AMP* decision. Myriad's litigation to maintain its legally invalid monopoly on accessing BRCA1 and BRCA2 genetic information has discouraged others from engaging in testing, as pathologists, geneticists, and smaller laboratories weigh the enormous costs of defending a patent infringement suit. Issuance of a preliminary injunction will eliminate important options now available to patients, their physicians, and genetic counselors and cast a shadow of liability over the work of any scientists engaging in basic research on these genes.

CONCLUSION

For the foregoing reasons, the ruling of the district court should be affirmed.

Respectfully submitted,

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UNIVERSITY OF UTAH RESEARCH FOUNDATION et al.
v.
AMBRY GENETICS CORP.

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CERTIFICATE OF SERVICE

I hereby certify that I electronically filed the brief of the American Civil Liberties Union, Association for Molecular Pathology, Breast Cancer Action, Public Patent Foundation, and AARP as Amici Curiae In Support of Appellee with the Clerk of the Court for the United States Court of Appeals for the Federal Circuit using the appellate CM/ECF system on June 9, 2014.

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