UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

ASSOCIATION FOR MOLECULAR PATHOLOGY; AMERICAN COLLEGE OF MEDICAL GENETICS; AMERICAN SOCIETY FOR CLINICAL PATHOLOGY; COLLEGE OF AMERICAN PATHOLOGISTS; HAIG KAZAZIAN, MD; ARUPA GANGULY, PhD; WENDY CHUNG, MD, PhD; HARRY OSTRER, MD; DAVID LEDBETTER, PhD; STEPHEN WARREN, PhD; 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; KATHLEEN RAKER,	:	09-CV-4515 (RWS)
Plaintiffs,	:	ECF Case
vs.	:	
UNITED STATES PATENT AND TRADEMARK OFFICE; MYRIAD GENETICS; LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation,	:	
Defendants.	:	

BRIEF FOR AMICI CURIAE

March of Dimes Foundation, Canavan Foundation, Claire Altman Heine Foundation, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, National Tay-Sachs & Allied Diseases Association

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INTERESTS OF *AMICI CURIAE*

***Amicus Curiae* March of Dimes Foundation** is a non-profit organization dedicated to improving the health of babies by preventing birth defects, premature births, and infant mortality. For over 70 years, March of Dimes has carried out its mission through research, community services, education, and advocacy, originally to

there is currently no cure for the disease. Genetic testing is an important part of prevention and early detection.

However, low-cost carrier screening and prenatal testing programs for families at risk for Canavan disease were stopped by the holder of the patent on the Canavan gene based on patent claims very similar to those at issue in this case.

***Amicus Curiae* Claire Altman Heine Foundation (CAHF)** is a non-profit organization and a publicly supported charity. The Foundation is dedicated to establishing population-based pan-ethnic carrier screening for Spinal Muscular Atrophy (SMA), which is the number one genetic killer of children under two. The Foundation aims to raise awareness by educating the public and medical communities, and it works closely with medical associations, genetic counselors, leading SMA researchers, clinicians, laboratories, the NIH, Congress, industry and federal agencies such as the National Human Genome Research Institute (

NTSAD's mission is (1) to support research aimed at treating and curing these diseases, (2) to provide support for the individuals and families afflicted with these diseases, and (3) to educate the public about these diseases and genetic screening for carriers through community outreach efforts. NTSAD has funded research initiatives aimed at producing gene therapies for Tay-Sachs and other related genetic diseases. NTSAD is particularly concerned with the currently limited availability of prenatal testing for disorders such as Tay-Sachs and Canavan. NTSAD strives to ensure that carrier screening for Tay-Sachs, Canavan, and other related diseases is readily available. Patent rights, like those of Myriad in this case, directly affect clinical access to carrier screening for this family of diseases and the ability to conduct research for new treatments and cures.

Patient Group *Amici Curiae* Members Are Adversely Affected by Myriad's Patents

Amici Curiae patient groups and their members cannot achieve their goals and objectives for widespread and easy access to genetic screening and research and development of treatments and cures for their target diseases if Myriad's patent claims to gene sequences and bare correlations, and similar claims in other patents related to other diseases, are held to be valid.

Already, Myriad's gene sequence and correlation patents have caused problems for *Amici Curiae*. For example, Myriad's BRCA sequence patents and BRCA correlation patents interfere with the goals of MBCC in preventing and eliminating breast cancer, diagnosing women predisposed to breast cancer, or testing pregnant women interested in prenatal genetic testing, by restricting access to affordable genetic diagnostic testing. Furthermore, women are not able to use diagnostic tests from another provider for a second opinion before undertaking radical surgery, such as the removal of their breasts and ovaries. Myriad's patent claims also prevent

access to new technologies and better testing methods, limit research and innovation, and thus prevent the development of new screening procedures and preventions, treatments, and cures.

As with the BRCA genes, the genes responsible for other diseases such as Tay-Sachs disease, Canavan disease and Spinal Muscular Atrophy, are also subject to similar patent claims to the gene sequences themselves and bare correlations. Such claims interfere with *Amici Curiae's* missions to identify, screen for, treat, and cure genetic-related diseases. Genetic tests are an important way to identify such diseases. If a gene patent or a bare correlation patent for a genetic-related disease is held valid, it would cause the harmful result of limiting innovation and preventing development of genetic tests and treatments for those diseases. Such patents will prevent the public from accessing better genetic testing and new treatment methods. *Amici Curiae* understand the need to encourage innovation and investment, but patents on gene sequences themselves and bare correlations to a disease hinder rather than promote vital progress. The exclusivity such patent rights provide is wholly out of proportion to the innovation they foster. *Amici Curiae* therefore urge the Court to deny Defendants' motions to dismiss and grant Plaintiffs' motion for summary judgment that the disputed claims are invalid.

SUMMARY OF ARGUMENT

The central issue in this case concerns the scope of patentable subject matter under the Patent Act of 1952. The Act provides: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. Although the scope of patentable subject matter is thus broad, it is settled precedent that "[e]xcluded from such patent protection are laws of nature, natural phenomena, and abstract ideas." *Diamond v. Diehr*, 450 U.S. 175, 185 (1981).

The patents-in-suit, U.S. Patent numbers 5,693,473, 5,709,999, 5,747,282, 5,710,001, 5,735,441, 5,837,492, and 6,033,857 (the "Myriad patents," or the '473, '999, '282, '001, '441, '492, and '857 patents respectively) claim the DNA sequences of two normal ("wild-type") genes, BRCA 1 and BRCA 2, mutations of those DNA sequences that contribute to susceptibility

2. A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the germline sequence of the BRCA2 gene or the sequence of its mRNA in

Thus, there are special dangers in allowing only one laboratory, in this case Myriad, exclusive rights to conduct research on a particular genetic phenomenon. If laboratories can both compete with and collaborate with one another through common access to natural phenomena and laws of nature, test quality will improve, second opinions will be available, the tests will become more affordable and allow for collaborative research, all of which will allow science to advance more rapidly and benefit patients.

In crossing over the line between patents on human invention and patents on nature itself, the Myriad patents upset the "careful balance" inherent in the patent laws that is "the very lifeblood of a competitive economy." *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146 (1989). A United States patent confers upon its owner the powerful right to exclude others from practicing whatever invention is claimed in the patent for a defined period of time. *See* 35 U.S.C. § 271 (defining infringement) and § 154 (twenty-year term). Such powerful rights should not be conferred upon claims to natural phenomena and laws of nature so as to preempt the future progress of scientific research and advances in medical technology.

Allowing Myriad's patent claims to stand will damage such future research and scientific progress. These patents and others just like them allow no room to design around, imitate, or improve upon the so-called "invention" of a law of nature or natural phenomena. DNA technology has opened up a vast array of tests based on naturally occurring biochemical mechanisms. But if claims like these are sustained, such tests will be blocked by patents on the products of nature and laws of nature on which they are based. Myriad's claims are monopolies to existing "facts" or information, not man-made products or processes. If a discovered gene sequence causes a disease, or is associated with an increased susceptibility to a disease, *that*

sequence is the critical sequence which must be used and detected in genetic testing, not any other sequence. Consequently, it is impossible to invent around gene patents.

Patent claims like Myriad's are especially harmful given the nature of modern genomic research, which focuses not on one gene or gene function at a time, but rather on complex interconnections among genes and gene functions. Such interconnections cannot be studied if portions of the larger genomic map are blocked out. By contrast, invalidating these patent claims and reaffirming the principles set forth in Supreme Court precedent will not disrupt or impede scientific research, but rather improve the progress of science thereby benefiting those affected by genetic diseases and conditions.

ARGUMENT

I. THE MYRIAD PATENTS IMPROPERLY REMOVE NATURAL PHENOMENA

characteristics not found in any natural bacteria, and thus were not products of nature. In *American Wood-Paper v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874), the Court invalidated a patent on a more pure version of cellulose than had been available at the time, stated that the cellulose was an extract, and an extract, "when obtained cannot be called a new manufacture." 90 U.S. at 594 (1874). "The substance of the products, therefore, was the same, and so were their uses." *Id.* In *Cochrine v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884), the Court

that the patent claim in issue to "a simple natural correlation" between high levels of homocysteine in the blood and deficiencies of two essential vitamins was "an unpatentable 'natural phenomenon.'" 548 U.S. at 137-138.

Thus, in

In sum, Supreme Court precedent clearly forbids patents on natural phenomena and laws of nature. For the reasons set out below, all the Myriad claims to gene sequences and bare correlations are unpatentable subject matter under this precedent.

B. The Myriad Patent Claims Improperly Assert Exclusive Rights To Natural Phenomena and Laws of Nature—Namely, Gene Sequences, Mutation Sequences, and the Correlations Between Certain Mutations and Susceptibility to Breast Cancer and Ovarian Cancer

The human genetic code is contained in twenty-three pairs of chromosomes, which are present in almost every cell of the human body. These chromosomes are passed on from generation to generation. The chromosomes comprise tightly wound bundles of the long, thin molecule called "DNA" ("deoxyribonucleic acid"). Along its length, DNA contains a sequence of four compounds called bases. This sequence of bases is a code that is the t .8dTD0 T-0.0007 Tw[

BRCA2, and the relationship between their sequences and the probability that a person will develop a cancer – that Myriad has claimed as its exclusive property.

Like the discoverers of a previously unknown plant in the wild, the inventors assert that they were the first to have uncovered these natural phenomena and laws of nature:

> It is a discovery of the present invention that the BRCA1 locus which predisposes individuals to breast cancer and ovarian cancer, is a gene encoding a BRCA1 protein, [. . .]. It is a discovery of the present invention that mutations in the BRCA1 locus [. . .] are indicative of a predisposition to breast cancer and ovarian cancer. Finally, it is a discovery of the present invention that somatic mutations in the BRCA1 locus are also associated with breast cancer, ovarian cancer and other cancers, which represents an indicator of these cancers or of the prognosis of these cancers.

'282 patent at col. 7, ll. 18-30. The BRCA genes were identified using well-known techniques of molecular biology. '282 patent at col. 7, l. 39 – col. 8, l. 14. Their relationship to cancer was mapped by testing cancer-prone families. '282 patent at col. 35, l. 39 – col. 36, l. 46.

The harm is particularly pronounced because BRCA genes are complex genes that are subject to a plethora of sequence variations of differing clinical significance. Genetic testing requires a database of clinical significance for known variants, because some variations affect susceptibility to cancer while others do not, that is, some variations or "mutations" of BRCA gene sequences give rise to a high probability of breast cancer, while other mutations result in a lower probability or have no effect. By suppressing virtually all external research related to

of this basic process to screening for potential cancer therapeutics (claim 20 of '282 patents), a method for detecting a mutation (claims 1 of '999, '001, '441 and '857 patents), and a method for diagnosing a predisposition to breast cancer (claim 1 of the '857 patent). Myriad's claims preempt these natural phenomena by precluding all others from testing and observing these phenomena. The basic method claimed by Myriad — comparing the patient's sequence to the non-mutated sequence, and thereby drawing a conclusion as to susceptibility to breast cancer — is nothing more than a law of nature.

Myriad's method claims are not limited to any particular kind of comparison or test. *Any* comparison of the BRCA sequences infringes. In fact, even just thinking about the results of the test – comparing the patient's sequence and the "wild-type" sequence – infringes the patent. Thus, for example, infringement might occur if a doctor sends a sample to a lab to be tested for BRCA1 and BRCA2 genes, and then receives the patient's sequence which he or she compares with the wild-type sequence. In this scenario, the doctor is an infringer even if the doctor had no idea how the sequencing was done. One may not even test one's own blood to observe the relationship without running afoul of these patents. The patents thus allow the patent holders to own a law of nature—the relationship between mutations in the BRCA1 and BRCA2 genes and an increased risk of breast or ovarian cancer.

In contrast to the patent claim upheld in *Diehr*, there are *no* other steps in the claimed process here. These patents cover every substantial practical application of the law of nature that BRCA gene mutations are correlated to breast cancer. Myriad's claims are similar to a method of estimating the risk of heart attack on the basis of measurements of blood pressure. Such a claim, like Myriad's methods claims here, preempts all uses of a particular law of nature.

In the language of *Diehr* and *Gottschalk*, the natural relationships between cancer and the BRCA genes have been "pre-empted" by the patent claims. Allowing Myriad to appropriate such a natural phenomenon and law of nature as their exclusive property would require departure from the Supreme Court's long-settled precedents.

II. THE MYRIAD PATENTS UPSET THE PATENT BALANCE CAREFULLY STRUCK BY CONGRESS AND THE COURTS, HARM RESEARCH AND INNOVATION IN THE LIFE SCIENCES, AND HARM PATIENTS AND OTHERS

The Constitution requires that patents "promote the *Progress* of Science and useful Arts." Art. I, § 8, cl. 8 (emphasis added). Fulfilling this constitutional purpose requires a balance between rewarding existing research and ensuring that other research may go forward freely in the future. Allowing a patentee to remove a natural phenomenon and laws of nature from the public sphere thwarts this constitutional purpose by impeding rather than promoting the progress of biochemical research, clinical diagnostics and medical treatments. Without access to testing and observing products of nature and laws of nature, medical researchers cannot build upon the discoveries of others.

Allowing patent claims such as those at issue here blocks medical information based on natural, biochemical relationships from appropriate further scientific use. This impediment is especially acute with respect to the field of genome analysis, which requires the study of multiple genes and multiple correlations. Disallowing claims such as these patents, by contrast, will cause little harm to scientific progress because a wide range of other appropriate claims would remain available to researchers and patentees like Myriad, such as patents on specific treatments that make use of genetic information about the predisposition to cancer. Thus, the balance struck in *Diehr* and similar cases on the scope of patentable subject matter should be preserved.

A. Existing Limitations On The Scope Of Patentable Subject Matter Reflect A Careful Balance Between Rewarding Existing Research And Ensuring Opportunity For Future Innovation

Patents are fundamentally a balance between allowing free competition and government-granted exclusive rights. "The Patent Clause itself reflects a balance between the need to encourage innovation and the avoidance of monopolies which stifle competition without any concomitant advance in the 'Progress of Science and useful Arts.'" *Eldred v. Ashcroft*, 537 U.S. 186, 215 (2003) (citing *Bonito Boats*, 489 U.S. at 146). *See Mazer v. Stein*, 347 U.S. 201, 219 (1954) (noting that the patent system is based upon the "conviction that encouragement of individual effort by personal gain is the best way to advance public welfare through the talents of authors and inventors").

Patent law seeks to strike a balance between these competing interests. Some features of patent law ensure adequate returns for the costs of research and development. For example, Congress has decided upon a twenty-year term for patents. *See* 35 U.S.C. § 154. Other features of patent law seek to preserve opportunities for future innovation. There are the requirements that patentable inventions are new, inventive, definite, and adequately described, among other things. 35 U.S.C. §§ 102, 103, and 112. As another example, there is a statutory safe harbor for certain activities relating to the development of generic forms of patented drugs that would otherwise constitute patent infringement. *See, e.g.*, 35 U.S.C. § 271(e); *Merck KGAA v. Integra Lifesciences, Ltd.*, 545 US 193 (2005) (exemption applied to certain preclinical research).

The definition of what constitutes patentable subject matter likewise reflects a balance that has been struck by Congress in section 101 of the Patent Act and by case law in interpreting that section. The key to this balance — which distinguishes human-made inventions from products of nature and laws of nature — is the recognition that there are interests in promoting innovation on *both* sides of any patent. As the Supreme Court stated in a different context in

When a doctor biopsies or removes a tumor, a small piece of tissue is sent for testing. But it is not practical to send multiple samples to separate laboratories to test for each cancer-associated sequence or correlation; it is more efficient to send it to one lab, which can test for everything at once. Ordinarily there should be several labs that could conduct the tests, located in different parts of the country. However, in this case there is only one lab where the doctor can have the BRCA genes tested – Myriad. Myriad's patents coupled with Myriad's refusal to license others in effect forces health care providers to order patented *and* unpatented tests from Myriad. But if a patentee possesses market power, as Myriad does, when it ties the purchase of a patented product to an agreement to buy unpatented goods, the Supreme Court has held that such tying is illegal. *See, e.g., Ill. Tool Works Inc. v. Indep. Ink, Inc.,* 547 U.S. 28 (2006), *and Morton Salt Co. v. G. S. Suppiger Co.*, 314 U.S. 488 (1942). Myriad's practice is akin to such a tie. Furthermore, if each of the cancer-associated sequences or correlations is eventually patented, there will simply not be enough tissue to send to all the different patent holders for complete testing.

Also, with no commercial incentives to research the clinical significance of rare sequence variants, Myriad reports "genetic variant of unknown significance" to some patients. Myriad does not follow up on these rare variants, and its refusal to license its patents prevents other laboratories, teaching hospitals and academic institutions from researching the clinical significance of rare sequence variants, even where others are willing and able to conduct research and to pay royalties. Consequently, Myriad suppresses research and development which otherwise could improve the standard of care for cancer patients.

As explained above, Myriad's claims in issue in this case cover natural phenomena – the gene sequences – and laws of nature – the bare correlations between the wild-type and mutant sequences that Myriad "discovered" indicate a predisposition to breast cancer. Myriad's claims preclude a person from testing their own genetic code, even though sequencing genes is so routine and straightforward that it is taught in high school. Yet testing for a relationship between a single gene mutation and a physical condition has demonstrated medical value and may even be life saving. The impediments to genetic research are compounded by the fact that modern genomic research has moved past one mutation/one function diseases to exploration of complex interrelationships among genes and genetic functions.[12] Without Myriad's basic blocking patents, science would advance more rapidly through competition and collaboration, resulting in increased benefits to patients.

C. Invalidating Myriad's Patent Claims Would Ne(ree)JTllimine a Ie mntiv anT

These pressures have led patent attorneys to seek and often obtain patents that stretch the boundaries of patentability into the natural realm. However, such increased scope is not necessary to advances in science, and, as already described, in fact impedes science. This case presents a vital opportunity for this Court to curb this pressure on the outer boundaries of patentability, and to return the balance to the baseline set by the Supreme Court in *Diehr* and related decisions.[14] In so doing, there is little danger that genetic or other biomedical research will be harmed by reduced incentives for making discoveries of nature.

Nothing in the argument advanced by *Amici Curiae* here would impede patents in the genetic area if those patents involve more than the mere discovery of a product of nature or a law

correlation with cancer, however, can readily be distinguished from inventive methods used to find the DNA sequences, or inventive therapies and tests that use those DNA sequences. The latter would be legitimately patentable under the principles set forth in *Diehr*, and ownership of rights to such tests and therapies is adequate to ensure research into products and laws of nature.

CONCLUSION

Amici Curiae appreciate the opportunity to add to the Court's understanding of the critical issues concerning patentable subject matter raised in this case. For the reasons set out herein, *Amici Curiae* respectfully submit that that Defendants' motions to dismiss be denied so that these vital patent issues can receive the full consideration that they deserve and that Plaintiffs' motion for summary judgment that the disputed claims are invalid be granted.

Dated: August 26, 2009

Respectfully submitted,

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