Appeal No. 2010-1406

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, 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, and KATHLEEN RAKER,

Plaintiffs-Appellees,

v.

UNITED STATES PATENT AND TRADEMARK OFFICE,

Defendant,

(For Continuation of Caption See Inside Cover)

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 OF *AMICI CURIAE* THE NATIONAL WOMEN'S HEALTH NETWORK, THE ASIAN COMMUNITIES FOR REPRODUCTIVE JUSTICE, THE CENTER FOR GENETICS AND SOCIETY, GENERATIONS AHEAD, THE PRO-CHOICE ALLIANCE FOR RESPONSIBLE RESEARCH AND ALLIANCE FOR HUMANE BIOTECHNOLOGY IN SUPPORT OF PLAINTIFFS-APPELLEES

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December 8, 2010

and

MYRIAD GENETICS, INC.,

Defendant-Appellant,

and

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-Appellants.

FORM 9. Certificate of Interest

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

The Association for Molecular Pathology v. U.S. Patent and Trademark Office, et al.

No. 2010-1406

CERTIFICATE OF INTEREST

Counsel for the (petitioner) (appellant) (respondent) (appellee) (amicus) (name of party) Jennifer L. Rubin certifies the following (use "None" if applicable; use extra sheets if necessary):

1. The full name of every party or amicus represented by me is:
The National Women's Health Network, The Pro-Choice Alliance for Responsible Research, Asian Communities for Reproductive Justice, The Center for Genetics and Society, Generations Ahead, and Alliance for Humane Biotechnology

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 party or amicus 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:
Akerman Senterfitt LLP - Jennifer L. Rubin, Esq.

12/3/10
Date

Signature of counsel

Debra L. Greenfield
Printed name of counsel

Please Note: All questions must be answered
cc: _____

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Other Authorities

STATEMENT OF INTEREST OF *AMICI CURIAE*[1]

Amici Curiae are women's health and social justice advocates with expertise in public policy and women's health. Their work specifically addresses the impact of health disparities on women, particularly women of color and low income women. Collectively, *Amici* conduct research, advocate for just public policy, and educate community-based organizations about the implications of new technologies for women's health and rights. *Amici* have the expertise to illustrate to the Court how patent claims on the BRCA 1/2 genes prevent women at risk for breast and ovarian cancer from obtaining the information they need about their own bodies, restricting the ability for improving health outcomes .

Amicus Curiae **The National Women's Health Network** is a nonprofit organization that improves the health of all women by developing and promoting a critical analysis of health issues in order to affect policy and support consumer decision-making. The Network aspires to a health care system that is guided by social justice and the needs of diverse women. Their mission supports individual

[1] The Parties have consented to the filing of this brief. No part of this brief was authored or funded by counsel for any Party, person, or organization besides *Amici* and their counsel. *Amici* have no direct personal stake in the outcome of this case but support affirmance of the district court's decision in order to help the lives of women they serve.

decision-making by providing evidence-based information free from corporate influence. The Network has particular expertise in research and evaluation of emerging drugs, devices and treatments and their impact on women's health.

Amicus Curiae **The Pro-Choice Alliance for Responsible Research (PCARR)** is a coalition of reproductive rights and justice advocates, academics and attorneys working together to promote accountability, safety and social justice in bio-medical research from a women's rights perspective. Since 2004, PCARR has been providing research and legal analysis to policymakers and consumers, and engaging with administrative agencies to ensure that women's health outcomes are protected in the implementation of new biotechnologies.

Amicus Curiae **Asian Communities for Reproductive Justice (ACRJ)** is a nonprofit community-based organization that promotes and protects reproductive justice. ACRJ believes that reproductive justice will be achieved when all people have the economic, social and political power and resources to make health decisions about their gender, bodies and sexuality for themselves, their families, and their communities. ACRJ works in communities of color to ensure that women and adolescents have the information they need to improve their own health status.

Amicus Curiae **The Center for Genetics and Society (CGS)** is a nonprofit

information and public affairs organization working to encourage responsible uses and effective societal governance of genetic, reproductive and biomedical technologies. CGS works with a growing network of civil society leaders, health professionals, scientists, and others who share a commitment to advancing the public interest in the development of policy regarding human biotechnologies.

Amicus Curiae **Generations Ahead (GA)** is a nonprofit community-based organization that brings different communities together to expand the public debate and promote policies on genetic technologies that protect human rights and affirm our shared humanity. By looking at the benefits and risks of these technologies for diverse communities including African-Americans, Latinos, Asian-Pacific Islanders, Native Americans, and people with disabilities, GA promotes policies that ensure full respect and human rights for all people.

Amicus Curiae **Alliance for Humane Biotechnology** (AHB) is a nonprofit association working for biotechnology that places the health and welfare of people and the natural environment above financial interests. AHB conducts outreach and education on the social implications of biotechnological developments, especially those concerning human genetic manipulation.

INTRODUCTION

The promise of human genetics has been described for decades by scientists and researchers working in biotechnology, resulting in the contemporary iconic stature of human DNA, the basis for the fundamental understanding of human biological processes. Its use in diagnostic testing as well as its potentiality for developing treatments and cures for illness and disease necessarily rests in the informational content of the human genome and unique, individual human genetic variation. Where, as cases emerge in "The Information Age," *Bilski v. Kappos* 130 S. Ct. 3218, 3228 (2010) "...biology is information, and crucially, that information is both material and immaterial" Eugene Thacker, *The Global Genome: Biotechnology, Politics and Culture* (2005) at 20, and, when considering the question presented in the case at bar "it is the information flow that is of interest in biotechnology, and hence of interest in biotechnology patenting..." Dan Burk, *The Problem of Process in Biotechnology*, 43 Hous. L. Rev. 561, 582-587 (2006).

Amici Curiae are advocates and educators working to improve the lives and health of the public, particularly women. We inform and instruct policy-makers and legislatures on specific issues pertaining to women's health and health disparities impacting women of color and low income women and their families, and provide educational outreach to communities regarding the implications of new and emerging genetic technologies. The embodied information and

information flow of human DNA molecules and genes is critical to this work. The decision regarding the patented claims at issue will determine whether women and their families - particularly those of lower income or racial and ethnic minorities - will be allowed access to the emerging and important scientific, medical and technical knowledge of human genetics in this "information age," or whether the knowledge will continue to be monopolized and privatized, exemplified by the patents granted on human genes and correlations between mutations in those genes and a predisposition to developing cancer.

The unique experience and expertise of *Amici* is informative when considering the implications of patents on the BRCA 1/ 2 gene sequences and correlations between mutations and a susceptibility to breast and ovarian cancer. These improvidently granted patents have resulted in policies and practices harmful to the lives and health of the women they serve. A restored ability to use the informational content embodied by the BRCA 1/ 2 genes will empower women, providing them with the information they need to protect their health and lives. It will reduce harms by improving access to quality healthcare for all women, including lower income women and minorities, and will allow for progress in biomedical research in furtherance of the objectives of the Patent Act.

Myriad's patent claims improperly grant ownership to the knowledge of the human genome and control over its use. Specifically excluded from patent-eligible

subject matter, these claims are physical phenomenon, laws of nature, and abstract ideas, part of "the storehouse of knowledge of all men...free to all men and reserved exclusively to none." *Diamond v .Chakrabarty,* 447 U.S. 303, 309 (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.,* 333 U. S. 127, 130 (1948)). Fulfilling the promise of human genetics depends upon a continuous and unfettered dissemination of important scientific and technological information. Thus, *Amici* urge that the decision of the District Court be upheld.

ARGUMENT

I. THE PATENT CLAIMS ARE EXCEPTIONS TO PATENT ELIGIBLE SUBJECT MATTER: THEY ARE PHYSICAL AND NATURAL PHENOMENON, LAWS OF NATURE, AND ABSTRACT IDEAS

There are enumerated categories of patentable subject matter according to the governing statute, 35 U.S.C. § 101. However, specific exceptions have been delineated: "Laws of nature, physical phenomenon, and abstract ideas" *Chakrabarty*, 447 U.S. at 309. Thus, "a new mineral discovered in the earth, or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that E=mc2; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of …nature, free to all men and reserved exclusively to none." *Id* (quoting *Funk Brothers,* 333 U.S. at 130).

The patented BRCA 1/2 DNA molecules, genes sequences and correlations are similarly excluded from the enumerated categories. Like new minerals found in the earth, DNA molecules and gene sequences are physical and natural phenomenon of nature, their removal from the human body does not render them patentable. Like pre-existing scientific principles such as gravity, the correlation between a mutation in a gene sequence and a predisposition for developing cancer is also a law of nature, an abstract idea. Like the speed of objects dropping on

Earth, a mutation occurring at a specific location on the nucleotide sequence of the BRCA 1 gene correlating to an increased risk of developing breast and ovarian cancer is a pre-existing scientific principle. Whether first observed by Newton or Mark Skolnick, they are equally laws of nature. Claims to the molecules and genes sequences and to the correlations between a mutation and a predisposition to developing cancer are not patent eligible subject matter.

A. THE COMPOSITION CLAIMS IMPROPERLY COVER PHYSICAL PHENOMENA

Appellants argue that the correct standard for determining whether the claimed patents represent exceptions to patentable subject matter is whether the claims are for "a non-naturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use' *Hartranft v. Wiegmann*, 121 U. S. 609, 615 (1887)" *Chakrabarty* at *309-310, and thus suitable subject matter for patent protection, or claims to 'hitherto unknown natural phenomenon' which are not so qualified." *Id.* Myriad Br. 41-42. Even according to this standard upon which Appellants rely, isolated and cDNA (complementary) BRCA 1/ 2 DNA molecules, gene sequences and genes are not patent eligible, rather they are "natural phenomenon."

1. Isolated BRCA 1/ 2 molecules and genes do not have a name, character or use distinctive from native BRCA 1/ 2 genetic material.

Diamond v. Chakrabarty considered whether "a live, human-made organism is patentable subject matter under 35 U.S.C. §101." 447 U.S. at 305. The organism was a new, genetically engineered strain of a bacterium with enhanced capacities for the ability to eat oil. Previously, the control of oil spills required "the use of a mixture of naturally occurring bacteria, each capable of degrading one component of the oil complex." *id*, n. 1-2, as naturally occurring individual bacteria contain only a single plasmid, a ring of floating DNA..." *Id.* Chakrabarty's new strain contained at least two energy generating plasmids, each new DNA having been inserted with a separate oil-eating pathway. The Court held that Chakrabarty had "produced a new bacterium with markedly different characteristics from any found in nature," and that "His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under §101. *Id* at 310.

The patents at issue are highly distinguishable. Unlike the oil-eating bacterium the patented isolated BRCA 1/ 2 DNA molecules, sequences and genes are not a "product of human ingenuity," despite the ingenuity of the techniques used in their identification, isolation and replication. Although minor structural differences exist between the isolated and native BRCA 1/2 genes (A288:19 6-15; A4322; A3468-3470; A7340), unlike the engineered bacterium, these differences do not result in a

distinctive "name, character, and use" from DNA as it exists within the human body: the patented genetic materials are nature's handiwork.

The isolated molecule is the same three-dimensional structure that exists in nature with only an elimination of non-essential parts to that structure, or where that exact structure has been recreated. What is being patented is the structure of the chemical bases that, in their ordering, "direct the synthesis of *other* molecules in the body-namely proteins…" (A 217). This embodied information constitutes both the isolated *molecule* as well as its linear structure when described as a sequence, the ordering of chemical bases As, Cs Ts and Gs. Accordingly native DNA inherently contains the claimed *isolated* compound. The patent claims are broad, encompassing both the known natural composition of the native DNA and the claimed isolated naturally occurring compound. (See e.g., Claim 1 of the '282 patent)(A569).

Appellants and their Amici instead assert that the isolation technique yields a new and separate chemical compound that does not exist in nature. See e.g., BIO Br. 5. Yet isolated DNA is not distinctive in name, character or use from native DNA. The DNA is simply "excised;" separated from the cellular environment from which it was "unbundled." BIO Br. 8. The resultant isolated DNA molecule is the same structure of nucleotides, the same sequence as it existed within the chromosome.

As such, an isolated DNA molecule is a physical embodiment of information regarding the ordering of the chemical bases as they occur in nature. Straus Decl. 20. Unlike the engineered bacterium in *Chakrabarty* no new DNA has been added to change the essential character of the DNA found in nature, no "new" or unique DNA molecule is being created and no new "pathways" are being introduced.

There is also nothing distinctive about the isolated molecule's name, character or use. "Isolated" only describes the molecule being removed from its cellular environment, its character and use remains fundamentally unchanged. The existent structural differences are a result of the *removal* of the DNA from the chromosome and cell; they do not create a molecule with a distinctive character from that found in native DNA. Myriad's claims to isolated DNA fail their own argued-for test for patent-eligibility as the isolated DNA molecules are not distinctive in name and character. Moreover, they fail the U.S. Supreme Court's test by not being "markedly different" from the native molecules and genes. *Chakrabarty* at 310.

Appellants argue that the application of isolated DNA in primers, probes, and diagnostics makes their use distinctive from that of native DNA. Myriad Br. 7-8. However the primers, probes and diagnostics rely on the *non-distinctive* natural biological characteristics of DNA sequences to code for a protein and to anneal to its complementary nucleotide sequence. If isolated DNA had a

distinctive character or *use* from native DNA, these applications would not be possible. Despite conventional techniques used to excise and separate genes from the chromosomes and cellular components, these processes do not impart the isolated DNA molecule with a distinctive name, character and use. The isolated molecule is simply, "a hitherto unknown natural phenomenon."

2. cDNA molecules do not have a name, character or use distinctive from native BRCA 1/ 2 molecules.

cDNA molecules (see, e.g., claim 2 of U.S. Patent No. 5, 747, 282) (A569) do not have a distinctive name, character or use from that of native DNA. cDNA molecules are derived from the naturally occurring mRNA (the template for the order of the sequence information of DNA)(A132) and are composed of exons, "nucleotide stretches that contribute directly to the production of proteins …" (A133-134) BIO Br. 8. Following the processes of translation and transcription which create the template mRNA, introns, the extraneous non-coding materials are *removed* by the process of "splicing." (A131). Whereas each native BRCA 1/ 2 DNA molecule is comprised of more than 70,000 nucleotides, the resultant cDNA molecules together have fewer than 16,000. (A3656-3657) BIO Br. 9. Accordingly, this creates structural differences from native DNA. BIO Br. 9.

However, despite the lack of non-coding regions (introns) there is nothing *distinctive* in the character of cDNA from DNA in its native state. Its name, cDNA (or complementary DNA) describes this fundamental character, (i.e., a DNA

sequence complementary to an mRNA sequence; consisting of the same exon sequence as native DNA). The cDNA molecule is constructed of the identical nucleotide structures that code for proteins. These consist of the same ordering of the nucleotides and thus, the same informational content embodied in the exons: "...it's not the string, but the three dimensional configuration of the molecule...that encodes the information...the information is only useful when embodied in such structures...ultimately, no one is interested in strings of human-readable letters - they are instead interested in what can be done with the structures the letters represent." Dan Burk, *The Problem of Process in Biotechnology*, 43 Hous. L. Rev. 561, 582-587 (2006) (discussing patented DNA molecules as "channels for informational transfer processes"). Unlike Chakrabarty's bioengineered bacterium, nothing new has been *added* such as new DNA or new pathways for their introduction. The *use* of cDNA is not distinctive from that of native DNA: a code for the making of proteins. As with isolated DNA, applications of cDNA in diagnostics take advantage of the *non-distinctive* natural biological characteristics of DNA sequences to code for a protein and to anneal to its complementary nucleotide sequence.

3. Restrictions on the use of the natural and physical phenomena of the BRCA 1/ 2 genes limit significant research

The Secretary's Advisory Committee on Genetics, Health, and Society, *Revised Draft Report on Gene Patents and Licensing Practices and Their Impact on*

Patient Access to Genetic Tests, 2-5-2010 *(herein SACGHS Report*) noted that "…patent claims to genes may be diminishing research that builds on disclosed genetic discoveries..." *Id* at1087-1089. Additionally, "the licensing of some gene-based diagnostic tests does appear to be having an inhibiting effect on research…" Stephan A. Merril & Anne-Marie Mazza, eds., *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation and Public Health.* (2006). Data establishes that "patents may actually diminish the production of public genetic knowledge," and that "more knowledge would be generated if the patented genes were only published and not patented." *SACGHS Report* at 1050-64.

Based upon their exclusionary patents Myriad Genetics and its limited number of licensed laboratories are the only laboratories that perform the analysis of the tissue samples collected during a BRCA1 or BRCA2 genetic test. As such, the Myriad database contains more than 95% of the entire BRCA1/2 testing data in the United States. This resulting monopoly on BRCA 1 & 2 tissues and data allows Myriad to *control* who can perform research using that data and what types of research can be performed.

This necessarily suggests a damaging limitation on research on the variants in the BRCA 1 and 2 genes. Breast cancer is the second highest cause of death for women (over 240,000 new cases reported in 2008): an illness which threatens *all*

women as well as men. American Cancer Society, *Breast Cancer Facts and Figures 2007-08* (2008). Initially, it was thought that women with the BRCA1/ BRCA2 gene mutations indicating an elevated risk for breast or ovarian cancer were exclusively or primarily of Jewish European Ashkenazi descent, however recent research suggests that racial differences are not implicated, and that high-risk (having a family or personal history of breast or ovarian cancer) African-American, Latina, and Asian women carry a similar risk for the genetic mutation as other high risk women. BRCA 1/ 2 mutations were found in 12.5% of women tested across ethnic groups. Michael J. Hall et al., *BRCA1 and BRCA2 Mutations in Women of Different Ethnicities Undergoing Testing for Hereditary Breast-Ovarian Cancer*, 115 Cancer 2222, at 2222 (May 15, 2009).

The reach of Myriad's patents limits research concerning other mutations of the BRCA genes. Four variants of undetermined pathology of the BRCA genes were discovered in African-American women. Tuya Pal, et.al., *BRCA1 and BRCA2 Mutations in a Study of African American Breast Cancer Patients*, 13 Cancer Epidemiol. Biomarkers Prev. 1794 (Nov. 2004). Yet, investigations regarding those mutations are potentially restricted by Myriad's broad patents (see, e.g., U.S. Patent No. 5, 747, 282) (A569) and the control of its genetic databank. An international consortium of researchers tested 300 families with known familial cases of breast or ovarian cancer but with negative BRCA1/ 2 test results, finding

significant numbers of previously undetected mutations including 22 different genomic rearrangements of BRCA 1/ 2. Tom Walsh et.al. Spectrum of Mutations in BRCA1, BRCA2, CHEK2, and TP53 in Families at High Risk of Breast Cancer, J. Amer. Med. Assoc. Vol. 295 No. 12 (Mar. 22/29, 2006) 1379. Myriad's exclusive control of *all* the information contained in the BRCA genes is a severe limitation on the ability of researchers to understand and cure breast and ovarian cancer.

B. THE METHOD CLAIMS ARE UNPATENTABLE LAWS OF NATURE AND ABSTRACT IDEAS

Excluded from patent protection are laws of nature, natural phenomenon and abstract ideas. *Diamond v. Diehr,* 450 U. S 175 (1981). Examples include Newton's law of gravity, *Parker v. Flook,* 437, U. S. 584, 593 n. 15 (1978), the Arrhenius equation *id* at 595, and Einstein's law of the inter-conversion of energy and mass, *Diamond v. Chakrabarty,* 447 U. S. 303, 309 (1980). They reveal "a relationship that has always existed." *Flook*, 437 U. S. at 593. n. 15. Scientific principles are synonymous as are ideas and abstract concepts, the necessary basis for scientific and technological work. *Gottschalk v. Benson*, 409 U. S. 63, 67 (1972).

The Court questioned whether a claimed method comprised of a series of steps whereby buyers and seller of commodities could hedge against the risks of

price changes was patentable. *Bilski v. Kappos* 130 S. Ct. 3218, 3228 (2010). Relying on *Benson, Flook,* and *Diehr*, it held that the claimed method was an ineligible abstract idea. *Id* at 3230. The claimed methods at issue are similarly analogous to *Flook* and are exceptions to patentable subject matter.

1. The method claims are essentially methods of calculations.

In examining a "method for updating alarm limits" in a catalytic converter the Court asked whether the "identification of a limited category of useful, though conventional, post-solution applications of such a formula," rendered the method eligible for patent protection. *Parker v. Flook,* 437 U. S. 584 (1978). The first step of the method measured the temperature; the second used an algorithm (defined as a 'procedure for solving a given type of mathematical problem') to calculate a new value for the alarm limit, and the final "post solution" step adjusted the alarm limit to the updated value. *Id* at 586 & n.1 (quoting *Gottschalk*, 409 U.S. at 65). The Respondent claimed that the presence of the post-solution activity made the process patentable. *Id.*

The Court considered the algorithm a mathematical formula, an un-patentable law of nature. *Id* at 592. As it pre-existed the claimed invention, it was treated as being within the prior art. *Id* at 594. One could not simply add the description of a practical application of an abstract idea to make it patentable. *Id.* Since there were no other inventive concepts in its application, the claim was

described as simply a new and perhaps improved method of calculating the values. *Id.* The Court held "if a claim is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is non-statutory." *Id* at 595.

Genes are composed of segments of DNA, typically thousands of nucleotides long, they contain the information used by the body to produce, or "code for" those proteins. (A121). The linear order of DNA nucleotides that make up a gene is referred to as the "nucleotide sequence, DNA sequence, or gene sequence" (A123). *BRCA* 1 and *BRCA* 2 are genes associated with a susceptibility or predisposition to breast and ovarian cancer. (A146). One cannot patent the physical molecular structures of these sequences without claiming the scientific relationship (in essence a mathematical formula for the production of proteins) existing within its native state. These correlations are products of evolution and as such are abstract ideas.

Diagnostic methods for determining whether these genes exist in a human body are exemplified by the method patents at issue. Claim 1 of the '999 patent consists of a process in which one "analyzes" a BRCA 1 sequence to see whether or not naturally occurring mutations exist. (A362). Claim 1 of the '001, '441 and '857 patents and claim 2 of the '857 consist of a process of "comparing" two gene sequences. (A649, A673, A870). These claims can be seen as "practical

applications" of pre-existent scientific principles and abstract concepts, the embodied information of the BRCA 1/ 2 genes treated as within the prior art. Used for a specific purpose, to identify a pre-disposition to breast and ovarian cancer, the claims are directed to 'new methods of calculating' by comparing or analyzing genes: neither of which are inventive concepts. Patents on these methods create "monopolies over procedures that others would discover by independent creative application of general principles." Bilski at 3228. Analogous to the processes in *Flook,* these methods should be considered non-statutory laws of nature.

2. Nothing is transformed by the patented methods.

The Court recently noted that "the machine or transformation test is a useful and important clue, an investigative tool for determining whether some claimed inventions are processes under §101. *Bilski*, 130 S. Ct. at 3227. The test asks whether a process is either tied to a particular machine, or, "it transforms a particular article into a different state or thing." *Id* at 3224.

Appellants rely on *Prometheus Laboratories v. Mayo Collaborative* Services, 581 F. 3d 1336 (Fed. Cir. 2009), *certiori granted, judgment vacated, and remanded,* 130 S. Ct 3543 (2010). Myriad Br.53-54, citing *Prometheus* at 1343-50. Inventors discovered that certain levels of metabolites correlated to the therapeutic value of a particular dosage of a drug in patients with gastro-intestinal disorders. The method administered a drug, determined metabolite levels and

identified a need to adjust the drug dosage on the basis of those measurements. *Prometheus* at 1340. The human tissues and blood samples became "a different state or thing," and the determining step was also transformative, thus the methods were patent-eligible. *Id* at 1345, 1347.

Appellants argue that Myriad's method claims involving "analyzing" and "comparing" are similarly transformative as it requires the extraction and sequencing of DNA from human tissue and blood samples. They contend that the district court's claim construction of "sequence" meaning "mere information" (*i.e.*, letters from the alphabet) rather than a physical molecule led to the court's erroneous conclusion that the comparisons/analyses were simply mental processes, not suitably patentable. Myriad Br. 55-60.

In *Prometheus*, chemical and physical changes in the level of metabolites in the blood were determined *after* the administration of specific drugs. *Prometheus* at 1340, 1346. No drugs are involved in the method claims at issue in this case, rather it is only the naturally occurring embodied nucleotide information, referenced as a sequence that is compared or analyzed. Despite isolation and sequencing, those techniques do not transform the sequences nor are they transformed by the comparisons and analyses. Had those sequences been *transformed* it is arguable that the utility and efficacy of the diagnostics would be in question.

Recent scientific developments illustrate that the methods of comparison do not necessarily implicate the processes of isolation and sequencing. "Massive parallel sequencing," makes whole-genome sequencing possible and suggests the possibility of the $1000.00 genome. John R. ten Boshch, Ph.D; Wayne W. Grody, M.D., Ph.D; Keeping Up with the Next Generation: *Massive Parallel Sequencing in Clinical Diagnosis*, Journal of Molecular Diagnostics, Vol. 10 No. 6, November, 2008. Whole genome *information* of the person/patient can be compared against a reference sample without the use of primers or probes to isolate or sequence the individual's DNA, including the BRCA genes. Despite the promise of these emerging technologies for use in patient care, Myriad argues that such an analysis would infringe its method claims. Unlike the claim in *Prometheus*, no "different state or thing" has occurred as a result of the patented method. The correlations, the comparisons, and the analyses are laws of nature, mental processes and abstract ideas.

3. The method claims at issue restrict the availability and quality of genetic testing and inhibit efforts at innovation and development in the field.

The *SACGHS Report* offered an "in-depth study assessing whether gene patenting and licensing practices affected patient and clinical access to genetic tests…" *SACGHS Report* at 148-49, 194-46. It stated that "…the patenting and licensing of genetic tests has limited the ability of clinical laboratories to offer

genetic testing. This limitation, in turn, can affect patient access, the quality of testing, and efforts to innovate." *Id* at 1476-79.

The *SACGHS Report* noted that patent-holders enforced their rights in order to narrow or eliminate the market for competing tests, and that Myriad shut down laboratories that had been offering the tests for BRCA 1/ 2 prior to the patents having been granted. *Id* at 1294-95; 1304-1305. Prior to the granting of the Myriad patents, Canadian researchers at Genetic Diagnostic Laboratories in British Columbia, Canada provided a similar genetic test offered by the British Columbia Cancer Agency (BCCA). Testing was halted in 2001 after Myriad obtained its patent on the genes and served a cease and desist order on the provincial Ministry of Health. Intending to assert its patent against the BCCA, Myriad indicated it would be charging 3,850 CND for the test, more than three times the cost of the Canadian test. The BCCA resumed the use of its own test, moving to Ontario in order to continue to serve women in need. Heather Kent, *BC Sidesteps Patent Claim, Transfers BRCA Gene Testing to Ontario*, 168 Can. Med. Assoc. J. 211 (Jan. 21, 2003).

Additionally, "Patents and licenses have a significant negative effect on the ability of clinical laboratories to continue to perform already-developed genetic tests," and that it was unknown whether patients who were denied access to these tests had testing performed by another laboratory . . ." *Id* at 518-522. Myriad's

exclusive patent rights were used to stop other laboratories from testing for the BRCA 1/ 2 genes. *Id* at 1518-29.

This denial of access is similarly implicated when exclusive tests are not covered by particular insurers, including Medicaid or Medicare. Patients who cannot afford to pay directly are likely to forgo the needed tests. Access would potentially be greater if an alternative test was offered by laboratories covered by insurers. *Id* at 1609-11. Most significant however, are the access problems affecting many of the plaintiffs as well as numerous women similarly diagnosed with breast or ovarian cancer: "Patients who desire a confirmatory test from a second laboratory are unable to obtain this second-opinion test in those cases where the patents right holder has cleared the market of other laboratories offering the test." *SACGHS Report* at 1683-86.

One of the important missions of *Amici Curiae* is to provide women with comprehensive information about their health options by analyzing and assessing biomedical research pertaining to diagnostic tests, drugs, and treatments. A centerpiece of that information is the AMA recommendation that women obtain a second opinion when faced with a diagnosis of a serious medical condition. American Medical Association, *Code of Medical Ethics Opinion 8.041* (Issued June 1992; updated June 1996). The exclusionary Myriad patents prevent women

who have been tested for BRCA1/2, in particular those women whose results are ambiguous, from securing this recommended and traditional practice.

Exclusionary patents negatively impact the quality of genetic testing. A breast cancer case study discusses the inability of Myriad's test to detect genomic rearrangements, insertions, and deletions. *SACGHS Report* at 1729. Myriad's test for BRCA 1/2 genes missed mutations relating to risk for breast cancer in about 12% of breast cancer patients from families with multiple cases of breast and ovarian cancer. Andy Pollack, "Flaw Seen in Genetic Test for Cancer Risk," New York Times, 3/22/2006, quoting Dr. Judy E. Garber, director of the cancer risk and prevention program at the Dana Farber Cancer Institute. "The ability to independently verify test results and the use of proficiency testing which entails multiple labs scrutinizing the same sample is the best means to ensure the quality of genetic tests." *SACGHS Report* at 1810-12. Myriad's exclusive patenting and limited licensing prohibits quality testing.

Exclusionary patents limit innovations in genetic testing for breast and ovarian cancer, including the ability to use multiplex testing, the simultaneous testing of multiple genetic markers, which includes the possibility of whole genome sequencing. *Id* at 1835-39. The Association of Genetic Counselors indicates that exclusive patents and licenses "will hinder the cost effectiveness of genetic testing, particularly when the analysis of multiple genes or the entire

genome is necessary to assess the risk or existence of disease." National Society of Genetic Counselors, Position Statement on Human Gene Patenting, http://www.nsgc.org/Advocacy/PositionStatements/tabid/107/Default.aspx. (2010). Concerns are voiced that development and progress will be impeded by these barriers and costs, as will the accessibility of sequences to researchers, thus risking patient care. The organization "supports governmental policy that encourages open and unfettered access to human nucleotide sequences to promote the development of personalized medicine that will benefit the public." *Id.*

Amici are concerned that "challenges to innovators obtaining access to information may discourage the development of advanced tests and their application to medicine." *SACGHS Report* at 2309. They argue that the BRCA patents restrict access to, quality of and the future promises of genetic testing for breast and ovarian cancer.

II. THE PATENTED COMPOSITION AND METHODS CLAIMS RESTRICT THE CONSTITUTIONAL GUARANTEES OF FREEDOM OF SPEECH

"As genes play an increasingly powerful role in contemporary legal and political culture, individuals are called upon to refer to genetic information as a basis for assessing their rights and duties." Jonathan Kahn, "*What's the Use? Law and Authority in Patenting Human Genetic Material*," 14 Stan. L.& Pol'y Rev. 417, at 418. Although the District Court dismissed the First Amendment claim (A245), *Amici* argue that continuing to issue the improvidently granted restricts and limits the Constitutional First Amendment guarantees of freedom of speech and expression.

The First Amendment requires " that there be full opportunity for expression ... to convey a desired message..." *Young v. American Mini Theatres, Inc.*, 427 U.S. 50, 76 (1976) (Powell, J. concurring). This serves "society's interest in the information necessary for social and political decision-making." *Saxbe v.Washington Post Co.*, 417 U. S. 843, 862-63 (1974). The scope of this necessary information is expansive: "...Freedom of discussion... must embrace all issues about which information is needed or appropriate to enable members of society to cope with exigencies of their period." *Thornhill v. Alabama*, 310 U. S. 88, 101-

102. In an age where issues involving health and human genetics are serious public concerns, a free flow of this scientific knowledge and information is critical.

In *Buckley*, a limitation on campaign expenditures by individuals and groups for a clearly identified political candidate was challenged as an abridgment of First Amendment speech. The Court found that distinctions should not be applied as to the conduct/action that is a precursor to the speech and the speech itself in a formalistic manner. Instead, the relationship between the conduct (the contributions of money prior to political speech) and First Amendment values is the important consideration. *Buckley v. Valeo,* 424 U. S. 1 (1976). The actions, the necessary precursors to formulating speech related to human genetics and the BRCA genes should similarly be protected.

"Freedom of thought...is the matrix, the indispensable condition of nearly every other form of freedom." *Palko v. ConnecticutI,* 302 U.S. 319, 326-27 (1937). Myriad's patented method claims restrict this freedom of thought.

In *Metabolite*, inventors claimed a method where a correlating step consisted simply of a physician recognizing that elevated levels of homocysteine in the blood could be correlated to cobalamin or folate deficiencies. *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.,* 548 U.S. 124 (2006). Justice Breyer's dissent noted that the step embodied "only the correlation...that the researchers discovered." *Id* at 137-38. This court held that by thinking about this

correlation, the physicians directly infringed upon the patents. *Metabolite Labs, Inc. v. Lab. Corp. of Am. Holdings*, 370 F. 3d 1354, 1372 (2004). First Amendment guarantees were clearly restricted by this limitation of freedom of thought.

Myriad's method claims involve a similar restriction. No other geneticist or physician can think about a patient's pre-disposition to breast or ovarian cancer without infringing upon the BRCA 1/ 2 patents, which monopolize these correlations. The ability of individuals using potential computer technologies to analyze, or *think* about their own BRCA genes in order to determine if they have a pre-disposition to breast or ovarian cancer would similarly be restricted. *See, e.g.*, Steven L. Salzberg and Mihaela Pertea, "Do-it-Yourself Genetic Testing," Genome Biology 2010, 11:404. The free speech rights of doctors and patients, of all individuals to *think* about genetic information, particularly their own, must be guaranteed.

Activities are recognized as precursors for the formulation of expression, communication, and publication. *Richmond Newspapers v. Virginia*, 448 U.S. 555, 556 (1980); *Globe Newspaper Co. v. Superior Court,* 457 U. S. 596, 604 (1982). The enclosure of the information of patented human DNA represents a restriction on our ability to express or communicate speech relating to the human genetics and specifically the BRCA 1/ 2 genes. The collective nature of this information has been described as a natural resource belonging to the common heritage of

mankind, or as a commons, a part of the world which in essence, should not or cannot be enclosed, either by choice or necessity. See, e.g., Melissa L. Sturges, *Who Should Hold Property Rights to the Human Genome? An Application of the Common Heritage of Humankind,* 13 Am U. Int'l L. Rev. 219 (1997); David Koepsell, *Who Owns You? The Corporate Gold Rush to Patent Your Genes* Wiley-Blackwell (2009). Those working in the field of breast and ovarian cancer research and treatment must have access to this resource, and should not be restricted in their ability to study and use the BRCA 1/ 2 genes.

Nor should any individual be restricted when attempting to learn about their own genomes. Myriad's patents are a severe limitation on a person's access to her own unique and personal genetic information, and thus restrict an individual's ability to formulate speech and expression related to her or his own medical history and medical requirements.

III. THE PATENT CLAIMS CREATE DISPROPORTIONATE HARMS TO WOMEN OF COLOR AND LOWER INCOME WOMEN, THEIR FAMILIES AND PATIENTS

Racial and ethnic minorities comprise nearly one-third of American women. Health disparities between Caucasian women and women of color, as well as disparities between racial and ethnic groups, are well documented, and racial and ethnic minorities continue to experience poorer health outcomes than Caucasians. These health disparities occur in the larger context of social and economic

disparities: people of color are disproportionately poor, less likely to have access to a regular source of care, more likely to experience bias and prejudice in the health care system, and less likely to get a full and complete education regarding their health. These disparities continue to exist even when controlled for factors such as income and insurance status. *See* Institute of Medicine of the National Academies, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*, National Academy of Sciences (2003). The disparities exist within the context of harms created by the claimed BRCA 1/ 2 compositions and methods.

Certain racial, ethnic, and socioeconomic groups in the United States carry a disproportionate burden of disease rates, health outcomes, and lower life expectancy. Institute of Medicine of the National Academies, *Examining the Health Disparities Research Plan of the National Institutes of Health: Unfinished Business,* National Academy of Sciences (Mar. 2006). For example, white women are most likely to be diagnosed with breast cancer, but African American women are most likely to die from the disease. American Cancer Society, *Breast Cancer Facts and Figures 2007-08* (2007).

Data show that health care costs are a greater barrier for women generally, and for women of color in particular. Women are more likely to delay or go without care due to cost (24%) than men (20%). Among women of color, one-third of Latinas (32%) and African American women (32%) report delaying or

forgoing needed care in the past year, as did 25% of white women. Alina Salganicoff et.al., *Women and Health Care: A National Profile, Key Findings from the Kaiser Women's Health Survey*, 28 Kaiser Family Foundation (July 2005). Among women enrolled in a Medicare managed care plan, even a small co-payment (more than $10) resulted in a significant decrease in mammography screenings. Amal N. Trivedi et al., *Effect of Cost Sharing on Screening Mammography in Medicare Health Plans*, 358 N. Engl. J. Med. 375 (Jan. 24, 2008). Myriad's patents on the BRCA 1/ 2 genes create a monopoly preventing the development of alternative tests for the genes, resulting in an inflated price for its test. An insurmountable barrier to needed testing for many at risk women is created for those who cannot afford this prohibitive cost.

Genetic testing for breast and cervical cancer is least occurs less frequently in underserved communities. African American women were 78% less likely to use genetic counseling and genetic testing for BRCA than white women. Katrina Armstrong, et al, *Racial differences in Use of BRCA ½ Testing Among Women With a Family History of Breast or Ovarian Cancer*, J. Amer. Med. Assoc. Vol. 293, No. 14 (Apr. 13, 2005) 1729. Lack of access to their genetic information deprives these women and individuals of their ability to improve their health and reduce their health risks. While a genetic predisposition cannot in and of itself be changed by behaviors, knowledge of such risk can allow people to take preventive

steps. For example, a woman who knows she has mutations of the BRCA1/2 genes associated with cancer could change her diet, stop smoking, and reduce her exposure to environmental hazards. She could schedule mammograms or other tests, increasing the chances of early detection of any developing cancer or she could have prophylactic surgery. The Myriad patents rob her of these opportunities to improve her chances of survival.

The pace of medical progress has been slowed by Myriad's limitations on its own testing processes. Without competition, Myriad has been slow to make data available to researchers, to develop new testing methodologies, and to study or investigate ambiguous results, referred to as "variants of unknown significance." *Statement Submitted by Dr. Marc C. Grodman to the House Judiciary Subcommittee on Courts, the Internet, and Intellectual Property* (Oct. 25, 2007). These ambiguous results are disproportionately given to women of color, who are then left without the definitive information needed for improving health outcomes. Beth Peshkin et.al, *BRCA1/2 Testing: Complex Themes in Result Interpretation,* J Clin Oncol 19:2555-2565 (2001).

Amici believe that the invalidation of the patents on the BRCA 1/ 2 genes would be particularly beneficial to women of color, ethnic and racial minorities and socio-economically disadvantaged women and their families, disproportionately harmed by patents on the BRCA 1/ 2 molecules and genes.

CONCLUSION

The judgment of the district court should be upheld.

Respectfully submitted,

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