No. 12-398

IN THE

Supreme Court of the United States

ASSOCIATION FOR MOLECULAR PATHOLOGY, *et al.*,

Petitioners,

v.

MYRIAD GENETICS, INC., *et al.*,

Respondents.

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

BRIEF *AMICI CURIAE* OF THE NATIONAL WOMEN'S HEALTH NETWORK, REPRODUCTIVE HEALTH TECHNOLOGIES PROJECT, DISABILITY RIGHTS LEGAL CENTER, FORWARD TOGETHER, THE CENTER FOR GENETICS AND SOCIETY, THE PRO-CHOICE ALLIANCE FOR RESPONSIBLE RESEARCH, ALLIANCE FOR HUMANE BIOTECHNOLOGY, G. MICHAEL ROYBAL, MD, MPH, AND ANNE L. PETERS, MD IN SUPPORT OF PETITIONERS

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INTEREST OF *AMICI CURIAE*[1]

Amici Curiae advocate in the area of women's health and the delivery of healthcare in a manner which prioritizes social justice. They have unique expertise regarding policy issues concerning women's health and health disparities for women and their families who are socio-economically disadvantaged and underserved, or of particular ethnic and racial backgrounds. *Amici Curiae* understand the implications of genetic technologies for women's health and use this knowledge to educate community based organizations and individuals, and to advocate for public policies concerning genetic technologies that are just and equitable. *Amici Curiae* also include physicians/researchers who work within our burdened healthcare system. Experts in clinical care and treatment of underserved populations they recognize the importance of accessibility and quality of genetic technologies for preventative medicine, treatments, and potential cures.

The continued allowance of the patenting of the BRCA 1/2 genes is a deep concern of *Amici Curiae. Amici* understand that these patents are for molecules which are the embodiment of important scientific information and knowledge regarding the human genome. *Amici* recognize that the preemption of knowledge regarding

1. The parties have consented to the filing of this brief and letters of consent to the filing were lodged with the Clerk of the Court. No counsel for a party authored this brief in whole or part, and no such counsel or party made a monetary contribution intended to fund the preparation or submission of this brief. No person other than *amici curiae* and their members or their counsel made a monetary contribution to its preparation or submission.

these genes, which indicate a susceptibility to breast and ovarian cancer limits access to quality genetic testing and inhibits innovative work in research and treatments for these serious conditions, with resultant detrimental effects for the health of the women, communities and patients they serve, particularly those most in need of the benefits of current and future genetic technologies.

Amicus Curiae **The National Women's Health Network** 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 has particular expertise in women's health issues as a result of their research and evaluation of emerging drugs, devices and treatments and their impact on women's health. The Network aspires to a health care system that is guided by social justice and reflects the needs of diverse women, including the support of individual decision-making by providing evidence-based information free from corporate influence.

Amicus Curiae **Reproductive Health Technologies Project (RHTP)** a national non-profit organization advocating on behalf of women to enable access to the safest and most effective methods for the protection of their health, the RHTP is a powerful vehicle for public education and policy development surrounding health technologies. Bringing together experts, using solid science and clinical data to influence political outcomes, and seeking consensus among diverse communities, the RHTP ensures that new technologies are developed and introduced with appropriate safeguards, a well-informed consumer constituency and broad-based public support.

Amicus Curiae **Disability Rights Legal Center (DRLC)** champions the rights of people with disabilities through education, advocacy, and litigation. Together with the Loyola University School of Law at Los Angeles, they direct a joint program, the **Cancer Legal Resource Center (CLRC)**. Founded in 1997, the CLRC has provided free information and resources on cancer-related legal issues to cancer survivors, caregivers, health care professionals, employers, and others coping with cancer, serving over 310,000 people through conferences, seminars, workshops, education and outreach programs, and other cancer community activities. To this end, the CLRC runs a free and confidential national Telephone Assistance Line that assists individuals with cancer and genetic-related legal issues, including the costs of testing, insurance coverage, employment, and access to health care and government benefits.

Amicus Curiae **Forward Together** is a nonprofit community-based multi-racial organization that engages in grass-roots action and training community leaders, working in communities of color to ensure that women and adolescents have the information they need to improve their own health status, and believing in policy that enables *all* people to have the economic, social, and political power and resources necessary for decision-making regarding their bodies.

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 just and equitable policies regarding human biotechnologies.

Amicus Curiae **The Pro-Choice Alliance for Responsible Research (PCARR)** is a coalition of reproductive rights and justice advocates, bioethicists, academics, and community leaders working together to promote accountability, safety and social justice in biomedical research from a women's rights perspective. PCARR believes that justice, safety, and dignity for women must be paramount in public policy and private practice in emerging biotechnologies. 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 **Alliance for Humane Biotechnology (AHB)** is a non-profit association that conducts outreach and education on the social and environmental impacts of human biotechnologies. Scholars, students and activists, the AHB publishes and speaks about commercialization issues concerning both human beings and the natural environment, working for a culture of science that places the health and welfare of people above financial interests.

Amicus Curiae **G. Michael Roybal, MD, MPH** is the Medical Director of the Roybal Comprehensive Health Center (CHC), established to address the inequity of communities and individuals without access to affordable healthcare. Dr. Roybal has spent his career working with the Department of Health Services for Los Angeles County, focusing on healthcare redesign and reform in an

attempt to improve healthcare delivery for underserved populations.

Amicus Curiae **Anne L. Peters, MD**, is the Director of the Diabetes Clinic at the Roybal Comprehensive Health Center (CHC) and a Professor at the USC Keck School of Medicine. An internationally known expert in the field of treatment for diabetes, she has received numerous grants to improve health environments and reduce obesity rates in underserved populations. Her work at the CHC provides over 80,000 yearly patient visits, mostly for the uninsured. A similar program she developed is situated at five additional safety-net sites in Los Angeles County.

SUMMARY OF ARGUMENT

The question in the case at bar asks whether human genes, which include the BRCA 1/2 genes, are patentable. *Association for Molecular Pathology, et al, v. Myriad Genetics, Inc., et al.*, 133 S. Ct. 694, 184 L. Ed. 2d 496 (2012). *Amici* argue that vital policy considerations and precedents of the Court impel this Court to decide that these genes are for phenomena of nature, patent-ineligible exceptions to the statutory categories of patentable subject matter per 35 U.S.C. § 101.

Amici advocates, educators, and clinicians, who work to improve the health of women and their families and to eliminate disparities in the delivery and quality of healthcare, understand that the continued allowance of the patenting of human genes, specifically the BRCA 1/2 genes at issue in this case has a deleterious effect on the health and well-being of women and their families, and a disproportionately harmful effect on those who are socio-

economically disadvantaged and underserved or are of particular racial and ethnic backgrounds, unable to benefit from current advancements in genetic technologies. The work of *Amici* is impeded as these patents preclude and limit access to the most current and accurate scientific and biomedical knowledge regarding the human genome and the BRCA 1/2 genes. *Amici* understand that progress and innovation in research and treatment for breast and ovarian cancer is inhibited by Myriad's patents on these human genes.

Fundamental to this understanding is the recognition that the isolated DNA/cDNA molecules of the BRCA 1/2 genes revealing a susceptibility to breast and ovarian cancer are structures that are the embodiment of important scientific information and knowledge regarding the human genome. The specific patent claims on these molecules are broad, general, and sweeping claims which preempt, restrict, and limit access to these basic tools necessary for scientific work. As a result, these exclusionary patents privatize and monopolize the use of this knowledge, which necessarily produces grave harms for the health of women and their families.

The exclusionary patents restrict basic biomedical research and inhibit research and development of alternative testing methods for breast and ovarian cancer. The accessibility of genetic tests as well as the quality of testing methods is limited by the existence of Myriad's patents. The progress of biomedical science is significantly slowed as the development of innovative new methods in the field of personalized medicine for diagnostics and treatments of breast and ovarian cancers is inhibited as a result of the continued patenting of

the BRCA 1/2 genes. The health of socio-economically disadvantaged and underserved women and their families and women from particular ethnic or racial backgrounds is disproportionately harmed as a result of these patents which limit both access to and the quality of testing for these groups. *Amici* argue that these impediments to the advancement of science which create grave harms for the health of women and the communities they serve should be an important consideration for this Court in deciding the present question.

Amici also argue that recent decisions of this Court considering 35 U.S.C. § 101 subject matter eligibility warn against patents on phenomena of nature whose preemption create impediments to the advancement and progress of science, *see, e.g.*, *Mayo v. Prometheus*, 132 S. Ct. 1289, 182 L. Ed. 2d 321 (2012), and that the claims at issue are similarly patent-ineligible phenomena, laws and products of nature, whose preemption from use impedes scientific and biomedical innovation. The claims to the isolated DNA/cDNA do not rest upon inventive concepts, rather the claims are for laws of nature which simply describe natural relationships and pre-existing scientific principles, and products of nature, molecules that despite the technical processes of isolation are not markedly different from the DNA, the BRCA 1/2 genes in their natural state.

Analogous to recent decisions of this Court, Myriad's patent claims tie up too much of the future use of fundamental information and knowledge of the human genome regarding the BRCA 1/2 genes. The resultant inhibition of innovation and progress in biomedical research and healthcare treatment for breast and ovarian cancer is not justified by Myriad's original identification of the claims at issue.

For these reasons this Court should find Myriad's claims ineligible for patent protection according to 35 U.S.C. § 101.

ARGUMENT

I. Patents on the BRCA 1/2 Genes Create Grave Harms for the Health of Women and Their Families.

Amici recognize that the continued allowance of these previously granted patents on the BRCA 1/2 genes have increasingly negative implications for the health of women and their families. In 2012, 226,870 new cases of invasive breast cancer and 57,650 cases of in-situ breast cancer, with a resultant 39,920 deaths, and 22,280 cases of ovarian cancer with a resultant 15, 500 deaths were estimated. American Cancer Society, Cancer Facts and Figures, 2011-2012, [hereinafter, "ACS"]. While the average woman in this country has around a 12%-13% risk of developing breast cancer in her lifetime, women with BRCA mutations face a cumulative risk of between 50%-80% for breast cancer and a 20%-50% cumulative risk of ovarian cancer. *Ass'n for Molecular Pathology v. United States PTO*, 689 F.3d 1303, 1314 (Fed. Cir. 2012)

Testing for BRCA mutations is critical for decisions regarding clinical care, including surgical and therapeutic options. *Id.* at 18-19. Patents which exclude the scientific and medical community from the use of important information and scientific knowledge, specifically the embodied information of the BRCA 1/2 genes, necessarily inhibit progress and innovation in breast and ovarian cancer biomedical research and treatment, with resultant harmful effects for the health of woman and their families.

The agreed upon facts of the case define the fundamental nature of a human gene, the ordering of the nucleotides of the isolated DNA/cDNA molecules of the BRCA 1/2 genes as the physical embodiment of genetic information and scientific principles. *Ass'n for Molecular Pathology v. United States PTO*, 702 F. Supp. 2d 181, 193 (S.D.N.Y. 2010). Myriad's specific patent claims illustrate the reach of these patents which cover all isolated forms of the naturally occurring genes, whether previously identified or not. The patents are exclusive grants given for all uses of the informational content embodied in the genes' chemical structures, thus access to basic scientific principles for scientists, researchers, clinicians and patients is denied, with resulting restrictions on biomedical research and the development of treatments for breast and ovarian cancer.

The scope of Myriad's claims on the isolated DNA/cDNA of the BRCA 1/2 genes inhibit and restrict basic biomedical research and research and development of alternative genetic testing methods for breast and ovarian cancer. The patents restrict access to genetic testing and negatively affect the quality of genetic tests. The patents also inhibit future innovation in the development of personalized medicine by creating uncertainty and high transactions costs for the implementation of new diagnostic techniques such as whole genome sequencing (WGS) and whole exome sequencing, as well as creating impediments for the development of new and targeted treatments, dependent upon knowledge regarding the BRCA 1/2 genes. Socio-economically disadvantaged and underserved women and their families and woman of particular ethnic and racial backgrounds are disproportionately harmed as a result of limited access to and the diminished quality of

BRCA 1/2 testing. Restrictions on the use of the isolated DNA/cDNA molecules of the BRCA 1/2 genes create grave harms for the health of women and their families.

A. Claims to Isolated DNA/cDNA of the BRCA 1/2 Genes are for the Physical Embodiment of Information whose Preemption Restricts Access to and the Use of Vital Scientific Principles and Biomedical Knowledge.

DNA is a chemical molecule composed of four standard repeating chemical units, adenine, thymine, cytosine and quinine (aka, A, T, C, G) known as nucleotides, or bases. *Ass'n. for Molecular Pathology v. United States PTO*, 702 F. Supp.2d 181, 193 (S.D.N.Y. 2010). The ordering of these bases is described as nucleotide sequences, DNA sequences or gene sequences. *Id.* at 194. Gene sequences constitute biological information, describing the structural and chemical properties of a particular DNA molecule that is the cellular "blueprint" for the productions of proteins, and are of a double nature: they are both "chemical substances of molecules as well as physical carriers of information, i.e., where the actual biological function of this information is coding for proteins." *Id.* at 194, 228, citing Strauss Decl. at P 20.

For patenting purposes, "…since information is encoded as molecular structure, the information is only useful when embodied in such structures." *See*, Dan Burk, *The Problem of Process in Biotechnology*, 43 Hous. L. Rev. 561, 582-87 (2006). "The interest is not in the string of 'letters' of the sequence, but …the molecules that are the conduit for information transfer." *Id.* at 586-87.

The sole content of Myriad's isolated DNA/cDNA claims are these informational structures, the embodiment of the specified nucleotide sequences of the BRCA 1/2 genes. *See*, e.g. claims 2, 5, 6, 7 of U. S. Patent No.5,747,282; claims 1, 6, 7 of U. S. Patent No. 5,837,492. *Ass'n.*, 702 F. Supp.2d at 212. Claim 1 of the '282 patent is for "1) An isolated DNA coding for a BRCA-1 polypeptide[protein], said polypeptide having the amino acid sequence set forth in SEQ ID NO: 2." U.S. Patent No. 5,747,282 col. 154 11.56-58 (filed June 7, 1995). This is an extremely broad patent as multiple DNA sequences "correspond to the nucleotide sequence claimed in this claim." *Ass'n.*,702 F. Supp. 2d at 212.

Other claims are equally illustrative of the reach and scope of Myriad's patents. Claim 5 of the '282 patent covers any isolated DNAs "having at least 15 nucleotides" of the BRCA 1 gene, thus the claim covers the entire BRCA 1/2 genes. The patents cover both known and unknown mutations for increased susceptibility to breast and ovarian cancer, e.g., Claim 6 of the '492 patent is "directed to any DNA nucleotide encoding any mutant BRCA 2 protein that is associated with breast cancer," including all possible mutations and variations found within those genes.

The claimed ordering of the nucleotide sequences is informational content identical to the informational content found in the native DNA source, despite minor structural changes made to the isolated molecule itself. As a result, the utility of the isolated DNA molecules as biotechnological tools "relies on their ability to selectively bind to native or isolated BRCA 1/2 DNA molecules." *Id* at 197. Even though differences exist in its physical form,

derived from mRNA, a cDNA molecule (e.g., Claim 2 of the '282 patent) represents "an exact copy of one of the protein coding sequences encoded by the original genomic DNA," *id.* at 198, which is similarly being claimed for its embodied, replicated informational content.

These patents give Myriad the right to exclude anyone from using the DNA of the BRCA 1/2 genes, or copies of these genes outside the human body. The patents restrict all research and clinical testing of the BRCA 1/2 genes. Unlike patents on new drugs, no one can "invent around" Myriad's patents as one cannot invent a molecule of DNA which encodes the protein which embodies the genetic information of an individual's BRCA 1/2 genes. The preemptive effects of these patents inhibit progress and innovation in biomedical research and treatments for breast and ovarian cancer.

B. Myriad's Patents Inhibit and Restrict Biomedical Research and Research and Development of Alternative Testing Methods for the BRCA 1/2 Genes.

"Empirical evidence demonstrates...a real fear on behalf of clinical laboratory directors and researchers… that patent holders can and will prevent them from conducting their research." Richard Gold and Julia Carbone, *Myriad Genetics: In the Eye of the Policy Storm*, 12 Genetics in Medicine S39 (2010) [hereinafter "Gold"]. Clinical laboratories decide not to develop new or improved genetic tests in light of patents, where 53% of surveyed laboratory directors did not develop alternative tests. *See e.g.*, Mildred K. Cho, et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*,

5 J. Molecular Diagnostics 3, 5 (2003). Researchers have stated that Myriad prevented the development of improved BRCA 1/2 tests, the ability to assess the quality of Myriad's tests, and the development of treatments for breast and ovarian cancer. Gold, *supra* at S44.

Although Myriad claims it does not enforce its patents against researchers, Myriad has never publicly stated this policy in a written form, one which acts as a basis for the actions of others and which includes activities Myriad would consider as infringing. *See Secretary's Advisory Committee on Genetics, Health & Society: Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests*, 4-2010, at A26-27 [hereinafter "*Report*"]. Thus, "[a]mbiguity may itself stifle basic or clinical research as researchers either avoid the work altogether or are wary of public reporting results." *Id.* at A-27.

Prior to the issuance of Myriad's patents, researchers and scientists were studying BRCA genes, but ceased doing so when alerted to potential infringement liability. Laboratories reported nine instances of Myriad having enforced their BRCA patents, *id.* at 7, citing Cho, *supra* at 3-5, and two laboratories received cease and desist letters, including one at the University of Pennsylvania, the Genetics Diagnostics Laboratory (GDL). Gold, *supra* at S44. Scientists expressed concerns about contributing their research results on the BRCA genes to public databases as the basis for invoking patent infringement claims, and one researcher from the University of Alberta was specifically told not to contribute new mutations based upon this assumption. *Id.*

As a result of exclusive testing, Myriad accumulated significant amounts of data relating to previously unknown mutations, known as variations of unknown significance (VUS), but did not investigate these ambiguous results. *Statement Submitted by Dr. Marc C. Grodman to the House Judiciary Subcommittee on Courts, the Internet, and Intellectual Property* (Oct. 25, 2007). Myriad also denied access to this important information. In November 2004 they stopped contributing this data to the NIH open access Breast Cancer Information Core (BIC) mutation database, and ceased publishing information regarding the VUS in peer-reviewed literature, creating a major impediment to significant research. John Conley, Dan Vorhaus, Robert Cook- Deegan: Genomics Law Report, March 1, 2011: *How Will Myriad Respond to the Next Generation of BRCA Testing?*, available at http://www.genomicslawreport.com/index.php/2011/03/01/ how-will-myriad-respond-to-t.

C. Myriad's Patents Restrict Access to and Diminish the Quality of Genetic Tests for the BRCA 1/2 Genes.

Patent monopolies on human genes eliminate competition, likely resulting in higher prices, diminished patient access, and decreased quality in genetic testing. *See,* Roger D. Klein, MD, JD, *Gene Patents and Personalized Medicine, 2012, American Society of Clinical Oncology* at 82 [hereinafter "Klein"]. Generally, patients have greater access to genetic tests within competitive markets. Andrew S. Robertson, *The Role of DNA Patents in Genetic Test Innovation and Access*, 9 Nw. J. Tech. & Intell. Prop. 377 at 397-98.

Based upon its BRCA patents, Myriad is the sole provider of genetic testing for breast and ovarian cancer in the United States and has stopped other laboratories from conducting testing on the genes. *Report* at 40. Identifying and providing alternative testing methods by researchers other than Myriad is prohibited, restricting access to numerous testing methods. Robert Cook-Deegan, Subhashini Chandrasekharan & Misha Angrist, *The Dangers of Diagnostic Monopolies*, 458 Nature 405 (2009). For example, as Myriad has "little incentive to analyze samples other than blood samples," *House Judiciary Subcommittee on Courts, the Internet and Intellectual Property*, Washington D.C.: 2007, Statement of Wendy Chung, their decision not to use one alternative testing method (paraffin-embedded tissue) has "hampered availability of that type of testing in instances where it might be clinically useful." *Id.*

Alternative methods are ones which might be more cost-effective or efficient: "When compared to the most cost-effective mutation detection strategy analyzed…the average cost per mutation using the Myriad approach was five times as high," more than tests that had been developed and were used in Europe. *Report* at A-27. European methods do not necessarily insist upon initially testing the whole gene sequence as in the BRCA test, therefore Myriad has unilaterally established the "standard of care" in the United States; arguably precluding the use of potentially more efficient testing methods. *Id.* at A-28.

Myriad's patents deny the ability of patients to access a confirmatory test from a different laboratory, equivalent to a physician's independent second opinion. *Report* at 44. Patients for whom Myriad's initial test produced

inconclusive results may be forced to accept those results, relying only upon Myriad's data. This lack of information greatly impairs the decision-making of both a patient and their physician. "The ability to obtain a confirmatory test from a second laboratory is important because genetic test results can have implications for major medical decisions, such as whether to have a mastectomy or surgical removal of the ovaries." *Id.*

The quality of genetic testing for the BRCA 1/2 genes is diminished as a result of exclusive patenting practices. Any research resulting in a commercial or clinical service infringes Myriad's patents, notably "… the assessment of technology by third parties, e.g. to evaluate a test for sensitivity, specificity, or positive predictive value." Ozdemir, et al, *Shifting Emphasis from Pharmacogenomics to Theragnostics*, Nature Biotechnology, Vol. 24 No. 8 (2006).

Testing for the BRCA genes is limited to Myriad's laboratories, thus the test's accuracy in identifying mutations in the BRCA genes (analytical validity) and predicting a patient's risk for breast or ovarian cancer (clinical validity) cannot be determined by clinical geneticists outside of Myriad's purview without risking infringement liability. A study by non-clinical researchers found 10-20% of false negatives in patients at high risk. Walsh T., Casadei S, Coat KH et al., *Spectrum of Mutations in BRCA 1, BRCA 2, CHEK and TP53 in Families at High Risk of Breast Cancer*, 295 JAMA 1379 (2006) [hereinafter "Walsh"]. However since clinical geneticists cannot participate in similar studies, the effectiveness of Myriad's test cannot be validated.

Myriad's patent-based restrictions on the development of quality testing have produced serious harms. The 2006 study used an alternative molecular testing method and found that Myriad's test missed up to 12% of large genomic deletions or duplications, also known as "Large Genomic Rearrangements" (LGR). *Id.* Because this more accurate method requires the use of Myriad's patented gene sequence, the performance of the test would be considered an infringement.

Following the publication relating to their flawed BRAC Analysis test, Myriad developed an additional test, the BRAC Analysis Rearrangement Test (BART), which is separately offered for the detection of these missed mutations. K.M. Shannon et al., *Which Individuals Undergoing BRCA Analysis Need BART Testing?* 204 Cancer Genetics 416 (2011) [hereinafter "Shannon"]. Testing is based upon Myriad's criteria, a personal and family history that selects for individuals with a high pre-test probability (> 30%) of carrying a BRCA 1/2 mutation. *Id.* at 416. One genetic counselor noted that she had rarely mentioned the BART test to women undergoing testing, as information given to her from Myriad led her to believe that the additional BART mutations were "extremely rare among women…without an extremely strong family history of breast and ovarian cancer." Elizabeth Cohen, *When Breast Cancer Tests Gets it Wrong*, available at http://www.cnn.com/2011/10/27/health/brca-genetic-testing-ep/index.html. [hereinafter, "Cohen"]. Nonetheless subsequent studies showed that a substantial number of women have the BART mutations without a strong family history, *see*, *e.g.*, Shannon, *supra* at 418, suggesting the possibility of a woman developing breast and/or ovarian cancer as a result of missed preventative tests.

Myriad's patents also prevent labs from offering more rapid, cost-effective, and accurate testing methods such as genomic capture and massive parallel sequencing for multiple breast and ovarian cancer susceptibility genes:

> "Currently, the vast majority of genetic testing in the United States for inherited mutations in the BRCA 1 and BRCA 2 is done via a single company at a cost of ~$4000 for a non-comprehensive test that is complemented by an additional test to identify gene rearrangements. Far less clinical genetic testing for ovarian cancer risk is carried out for the other tumor suppressor genes. Targeted capture and massive parallel sequencing accurately identify mutations of all classes in all tumor suppressor genes in a single test. There is an increasing discrepancy between the falling cost of genomic sequencing and the current high cost of clinical gene by gene testing. As more cancer susceptibility genes are identified, it is not economically sustainable to assess risk by sequentially assessing individual genes, given that any one gene is mutant in only a small percentage of cases." Tom Walsh et al, *Mutations in 12 Genes for Inherited Ovarian, Fallopian Tube, and Peritoneal Carcinoma Identified by Massively Parallel Sequencing*, 108 Proc. Nat'l. Sci. U. S. 17857, 18036 (2011).

Thus, with Myriad's technology, if their initial tests are negative then testing for other breast or ovarian cancer genes is done selectively, based upon specific family or personal histories or physical examinations.

These extra tests cost thousands more dollars beyond the costs of both Myriad's standard ($3,300) and BART ($700.00) tests. However, with new methods, "it is possible to identify mutations in the 21 known breast and ovarian cancer genes in one sample for a cost…less than $1500.00… with further bar-coding and indexing strategies the costs could be reduced to less than $500.00 per sample." Walsh, Lee, Casadei, Thorton, Stray, Pennil, Nord, Mandell, Swisher, and Mary-Claire King; PNAS Early Edition, *Detection of Inherited Mutations for Breast and Ovarian Cancer Using Genomic Capture and Massive Parallel Sequencing*, www.pnas.org/cg/10.1073/pnas [hereinafter "King"].

These new testing methods are also more accurate than Myriad's tests. A new method of evaluating multiple genes in addition to BRCA 1/2 "identified a wide range of mutations in a variety of genes in 100% of [] test cases with zero spurious mutations called." *Id.* Six large deletions and duplications were identified which could have been missed by Myriad's standard test. *Id.* "By allowing comprehensive parallel testing of multiple cancer susceptibility genes, we will be able to confidently identify the fraction of women with breast and ovarian cancer who carry a germline alteration in a cancer susceptibility allele and the characteristics of the tumors of patients' inherited mutations in various genes." *Id.* Such tests, however, cannot be done on the BRCA 1/2 gene sequences without infringing Myriad's patents.

D. Myriad's Patents Inhibit Future Innovation in Personalized Medicine.

Myriad's patents inhibit future innovation in the area of personalized medicine, whose development rests

upon genotype-phenotype associations (e.g. BRCA 1/2 mutations and the susceptibility to breast and ovarian cancer). *See*, Klein, *supra* at 81. New methods of testing for these associations, able to detect millions of genetic variations and mutations in thousands of genes or even the entire genome will guide treatments, drug dosages and prevention for numerous diseases. However, "If we are to enter the next stage of personalized medicine, we cannot do so by parceling out information-genomes do not work that way, pleiotropy…doesn't stop at the lines drawn by the USPTO." Zachary Russ, *The Holes in Whole Genome Sequencing, Genetic Engineering & Biotechnology News*, available at: http:// www.genengnews.com/blog-biotech/the-holes-in-whole-genome-sequencing/676. Myriad's patents create uncertainty for the implementation of new diagnostic technologies and inhibit the development and delivery of new therapies.

The findings that approximately 20% of human genes are referenced in patent claims, the ownership of which is spread over a large number of assignees, have significant implications for the future use of new technologies including multi-plex testing, massive parallel sequencing, and whole genome sequencing (WGS).

"Patent thickets, blocking patents, royalty stacking, and high transactions costs" threaten the use of these next generation innovations in genetic testing. *Report* at 50-51. Fearing liability, laboratories using multiplex tests are not reporting results to patients or sending clinicians the results of tests involving patent protected genes. *Id.*

Myriad's patents on isolated DNA/cDNA create uncertainty where questions of liability are complicated

by varying interpretations of claim language. Myriad's attorney stated that "without an isolating procedure directed at gauging BRCA mutations, whole genome sequencing would not infringe Myriad's patents." Turna Ray, *At Appeals Hearing, Myriad Outlines Stance on BRCA IP Rights for Whole-Genome Sequencing*, April 4, 2010, available at: http://www.genomeweb.com/dxpgx/appeals-hearing-myraid-outlines-stance-brca-ip-rights. However he did not define "isolating." The interpretation of the term will be a factor in determining the question of patent infringement in the context of WGS. Scholar Robert Cook-Deegan questioned the limiting effect of the term isolated: "How do you do DNA sequencing without some purification step? Even nanopore or scanning-tunneling (electro-machining) means isolating some piece of DNA…That's an 'isolated' molecule you're measuring. It's a meaningless distinction." *Id.*

Thus, illustrative of high transaction costs, WGS industries may need to examine specific patent claims for "all or many of the thousands of human genome sequences subject to patent protection." Dan Vorhaus and John Conley, *Genomics Law Report, Whole Genome Sequencing and Gene Patents Coexist (For Now)*, August 11, 2009, available at: http://www.genomicslawreport.com/index.php/2009/08/11/whole-genome- sequencingand. The patents potentially inhibit the use of WGS in assessing for risk or existence of disease, and thus, patient care. National Society of Genetic Counselors, *Position Statement of Human Gene Patents*, available at: http://www.nsgc.org/Advocacy/PositionStatements/tabid/107/Default.aspx (2010).

Exome sequencing, targeted sequencing restricted to the protein-coding subset of human genes, is based upon an "enrichment of targeted DNA regions by hybridization with probes." Patricia F. Dimond, Ph.D., *Exome Sequencing Finds Sweet Spot Between Whole-Genome and Targeted Sequencing*, Genetic Engineering & Biotechnology News, available at: http://www.genengnews.com/key wordsandtools/print/3/25217/. The technique's costs relating to data collection, storage and analysis are significantly less than those in WGS techniques, and also lead to the discovery of highly pertinent variants. *Id.* However, "exome sequencing is more likely to face IP issues…because gene patents typically cover methods that would specifically target or enrich for the gene." Monica Heger, *Interpretation Remains Key Challenges in Clinical Sequencing; Patents May Impede Return of Results.* Genome Web, June 27, 2012. Available at: http://www.genomeweb.com/print/1096581.

The potential for infringement involving the use of these new methods could "slow some promising clinical technologies." Subhashini Chandrasekharan and Robert Cook Deegan, *Gene Patents and Personalized Medicine, what Lies Ahead?* Genome Medicine, 2009, 1:92. For example, holdout problems might result when drug manufacturers creating targeted therapies "do not own the underlying molecular pathological relationships." Klein, *supra* at 82.

Myriad's patents implicate these concerns. Numerous cancer patients, as many as 50% with inherited BRCA 1/2 mutations have a negative family history and do not qualify for testing according to Myriad's criteria. King *supra* at 4. However, the development of specific

treatments, inhibitors which effectively kill BRCA 1/2 mutated carcinomas having therapeutic as well as preventive applications, necessitates an increased need for identifying BRCA 1/2 mutations in women with breast and ovarian cancer through testing, which is restricted by Myriad's exclusive test on the patented sequences. *Id.*

The development of one treatment option, an inhibitor known as PARP for individuals with BRCA 1/2 associated cancers has been impeded as a result of Myriad's patents. Susan Domcheck, et al., *Challenges to the Development of New Agents for Molecularly Defined Patient Subsets: Lessons From BRCA 1/2 Associated Breast Cancer*, Journal of Clinical Oncology, Vol 29, No 32 (November 10) 2011, pp. 4224-4226. "A targeted therapeutic agent would presumably lead to widespread BRCA testing at diagnosis to identify those who would benefit…and thus would additionally expand the potential number of patients who are eligible for treatment." *Id.* at 4225. However,

> "…the United States Food and Drug Administration requires a companion diagnostic test that will define the population of interest before approval is granted for an agent directed toward that population. There is presently no US Food and Drug Administratively-approved diagnostic test for determining germline BRCA status, although mutation results have been used for more than a decade to make major decisions about preventive surgeries. The regulatory approval of such a diagnostic is hampered by ongoing uncertainty with respect to the status of the BRCA testing patent held by Myriad Genetics…." *Id.*

Thus, the subsequent development and delivery of an important treatment option has been impeded as a result of Myriad's patents.

E. The Health of Socio-Economically Disadvantaged and Underserved Women and their Families and Women of Particular Racial and Ethnic Backgrounds is Disproportionately Harmed as a Result of Myriad's Patents on the BRCA 1/2 Genes.

Socio-economically disadvantaged and underserved women and their families and women of particular ethnic and racial groups are disproportionately harmed by Myriad's exclusive and broad patents. One study reported ethnicity-specific mutation prevalence estimates ranging from 9.4% to 15.6%, with pooled estimates of 12.6% for women of European (Western and Central) ancestry and 14.1% for all women of non-European ancestry (Latin American, African, Asian, Native American, and Middle Eastern). Hall, et al., *BRCA 1 and BRCA 2 Mutations in Women of Different Ethnicities Undergoing Testing for Hereditary Breast Cancer*, Cancer, Volume 115, Issue 10, pages 2222-2233, 15 May 2009. However, despite similar mutation prevalence, "Testing volumes are disproportionately low among women from non-European ancestries and likely reflect the complex social, economic, and cultural factors that govern healthcare access and use." *Id.*

Disparities in the cancer burden among ethnic and racial minorities largely "reflect obstacles to receiving health care services" including early detection, and lowered socio-economic status is the overriding factor.

See, ACS at 43. There is less access to genetic testing for underserved ethnic and racial minorities than for those in the white population. Armstrong K., Micco E., Carney A., et al., *Racial Differences in the Use of BRCA 1/2 Testing Among Women with a Family History of Breast or Ovarian Cancer*, 293 JAMA 1729 (2005). E.g., African-American women are 78% less likely to use genetic BRCA testing than white women, and although less diagnosed, they are more likely to die from the disease. *Id.* Financial restraints including the lack of insurance, underinsurance, and incomplete Medicare/Medicaid reimbursements result in underserved populations having lesser access than whites to genetic testing services and is a significant barrier to comprehensive cancer care. Michael J. Hall, Olufunmilayo I. Olopade, *Confronting Genetic Testing Disparities*, 293 JAMA 1783 (2005).

The price of Myriad's test is necessarily prohibitive. "Myriad, as a monopolist, maximizes its profit through price discrimination in which it charges the highest price to those women who most value the test." *Report* at A-32. Thus, access to Myriad's test is severely limited for those without insurance, and even for the insured, the coverage for BRCA testing has been inconsistent and reimbursement is limited to those at high risk. *Report* at 37-38.

Myriad's policies regarding the supplemental BART test has had deleterious effects for the economically disadvantaged. The BART test, originally expected to be offered as part of its original test, is indicated for all patients with histories suggesting BRCA 1/2 mutations, however if a patient does not meet Myriad's defined criteria, the test is an additional $700.00. Shannon, *supra*

at 420. While some insurers reimburse the additional costs, many do not, and others consider BART to be an investigational test, excluded from coverage. *Id.*

Thus, the test is difficult to access for many women as a result of the added cost. One genetic counselor notes, "We know we're missing women out there with BART mutations because they can't afford to pay. If you miss just one BART mutation, that woman could be in danger, and so could her mother, her sisters, and her other relatives," Cohen, *supra*., including her daughters.

Myriad's patents also affect the quality of the tests for women of particular ethnic and racial backgrounds. Large genomic deletions or duplications, known as large genetic rearrangements (LGR) will be found in approximately 12% of patients with both breast cancer and a "severe" family history who test negative for the BRCA genes, and studies have advocated testing for LGR in specific ethnic populations. Shannon *supra* at 418. Data from Myriad suggests that these LGR BRCA mutations are over-represented and account for a larger percentage of mutations than previously thought in some populations, e.g., 20% of Latina women, suggesting a need for the additional BART test to be included in the standard BRCA analysis for all patients. *An Open Letter to Myriad Genetics*, Friday, July 22, 2011, available at http://yalecancergeneticcounseling.blogspot.com/2011_07_11archive.html.

The concern for quality testing for minority populations is implicated in the assessment of risk for breast and ovarian cancers, as the lack of access to Myriad's tests for underserved racial and ethnic populations diminishes

the quality of the test itself. Michael J. Hall, Olufunmilayo I. Olopade, *Disparities in Genetic Testing: Thinking Outside the BRCA Box*, 24 J. Clin Oncol 2197 (2006) [hereinafter "Hall"].

Models to assess risk used in BRCA testing need accurate estimates of the prevalence in specific populations to estimate probabilities in particularly high risk genotypes. *Id*. However the prevalence of Ashkenazi groups in testing shows a 10 fold increased prevalence in this group compared with estimates for the remaining U.S. population. *Id*. Without accurate estimates of mutation prevalence in minority subgroups, the reliability of these models is compromised. *Id*.

Myriad's patents on the embodied information of the BRCA 1/2 genes inhibit important scientific work in biomedical research and treatment for breast and ovarian cancer, with serious and harmful implications for the health of women, particularly socio-economically disadvantaged and underserved women or women of particular racial or ethnic backgrounds. As such Myriad's claims to the BRCA 1/2 genes should be considered ineligible for patent protection.

II. Isolated DNA/cDNA Molecules are Patent-Ineligible Phenomena of Nature. The Claims Do not Rest on Inventive Concepts and are Laws and Products of Nature, Whose Preemption Inhibits Scientific and Biomedical Progress and Innovation.

"Laws of Nature, natural phenomenon, and abstract ideas are not patentable subject matter under § 101 of the Patent Act." *Mayo*, 132 S. Ct. at 1293, citing *Diamond v.*

Diehr, 450 U. S. 175, 185, 101 S. Ct. 1048, 67 L. Ed. 2d 155 (1980). Additionally, "phenomenon of nature, though just discovered…are not patentable, as they are the basic tools of scientific and technical work." *Id*., citing *Gottschalk v. Benson*, 409 U. S. 63, 67, 93 S. Ct. 253, 34 L. Ed. 2d 273 (1972).

Deciding the patent eligibility of a claim to a diagnostic process, this Court recently clarified the law/product of nature doctrine by explaining what necessitates turning a patent-ineligible law of nature into a patentable application of that law. *Mayo v. Prometheus*, 132 S. Ct. 1289, 182 L. Ed. 2d 321 (2012). The nature of the medical diagnostic method at issue was described as a relationship, a law of nature, *id*., 132 S. Ct. at 1297, as nothing of significance had been added to the underlying natural phenomenon to make it a patentable application of that law, i.e., the claim did not rest on an inventive concept. *Id.,* at 1297-1300. Significantly, *Mayo* considered the preemptive effect of the patent relevant to their conclusion that the resultant inhibition of innovation rendered the process ineligible for patent protection. *Id*.at 1302.

Mayo's analysis is equally applicable to a composition claim. Myriad's patents on the BRCA 1/2 genes are for phenomena of nature analogous to the claimed relationship in *Mayo*. Lacking an inventive concept, nothing of significance has been added to the law/product of nature itself to render it patent-eligible. Myriad's claims to the isolated DNA/cDNA molecules of those genes simply describe natural phenomena, relationships which are laws of nature and pre-existing scientific principles. The molecules themselves are products of nature which are not markedly different whether inside or outside the

human body. The preemption of these phenomena of nature inhibits progress and innovation in scientific and biomedical research and treatments.

A. Myriad's Claims to Isolated DNA/cDNA do not Contain Inventive Concepts

Processes using a natural law must also contain an inventive concept so that the patent is "significantly more than a patent upon the natural law itself." *Mayo*, 132 S. Ct. at 1294. Mayo considered whether a process for measuring the relationship between concentrations of metabolites in the blood and a likelihood that a certain dosage of drug would prove effective or cause harm, was patent-eligible subject matter. *Id*., 132 S. Ct. at 1296. Despite administering a drug to trigger the manifestation of the relationship, the relationship existed apart from any human action and was an entirely natural process. *Id*. at 1296-97. The claims did not rest upon inventive concepts as nothing in the steps of the process added anything of significance to the law of nature itself. *Id*., at 1298. The process was essentially for the underlying relationship, a patent-ineligible law of nature. *Id*., at 1302.

The steps in *Mayo's* claimed process -- administering, determining, and a wherein step -- simply told doctors to gather data and draw inferences in light of the correlations. *Id*., at 1298. The steps were well understood, routine, conventional activity already engaged in by the scientific community. *Id*. The claims were not transformative and did not make a claimed law of nature a patentable application of that law. *Id*.

Claims to isolated DNA/cDNA molecules do not rest on inventive concepts. The claim terms indicating isolation or synthesis do not add anything of significance to render these laws and products of nature patent-eligible. "Isolated" simply denotes "a nucleic acid…which is substantially separated from other cellular components which naturally accompany a native human sequence." *Ass'n*, 702 F. Supp at 213, n.30. Having been derived from mRNA, a synthesized cDNA molecule represents an exact copy of one of the protein coding sequences encoded by the original genomic DNA. *Id*. citing Leonard Decl. P 75.

Well-established laboratory techniques are used in these processes for isolating the claimed molecules from their cellular environment. *Id*., at 198. DNA sequencing processes used to determine the ordering of the nucleotides within a DNA molecule are well known techniques understood and routinely performed by scientists skilled in molecular biology. *Id*., at 200. These conventional activities add nothing to the phenomenon of nature itself. Thus, these claims to phenomena of nature do not rest on inventive concepts.

B. Isolated DNA/cDNA Molecules of the BRCA 1/2 Genes are Laws of Nature.

The process in *Mayo* claimed a correlation, primarily a relationship between concentrations of metabolites in the blood and the likelihood that a certain dosage of drug would prove effective or cause harm: "The relation is a consequence of the ways in which thiopurine compounds are metabolized by the body-entirely natural processes." *Mayo*, 132 S.Ct. at 1297. Despite the human action of administering a drug to manifest the relation, "a patent

that simply describes that relation sets forth a natural law." *Id.,* at 1298.

Isolated DNA/cDNA molecules are patent-ineligible laws of nature, analogous to the claimed process of *Mayo*. Myriad's claimed molecules of the BRCA 1/2 genes are the embodiment of important information and pre-existing scientific principles; both their structure and function encodes the relationship between a DNA molecule and a protein. The structure of the nucleotides in the molecule enables the instructions for the building of proteins in the human body, or within identical and synthesized DNA. The patent claims disclose the sequential information embodied by the molecules, the ordering of the nucleotides.

This ordering of the chemical bases, the arrangement of nucleotides is, analogous to the law of nature in *Mayo*, a relationship, an entirely natural phenomenon. The ordering is a pre-determined relationship, a correlation that reveals a genetic susceptibility to breast and ovarian cancers in the BRCA 1/2 genes, a pre-existing scientific principle. The relationship remains unchanged apart from the human action of isolation or synthesis. The claims "simply describe the relations" between the order of the nucleotides and their resulting chemical, structural, and functional content and merely "point out a set of facts that exist in the world…." *Mayo v. Prometheus*, 2011 U.S. Trans. LEXIS 76 *39, *43 (2011).

The Court in *Mayo* also determined whether the steps involved in the questioned process were "sufficient to transform unpatentable natural correlations into patentable applications," *Mayo,* 132 S. Ct. at 1298, by looking at cases where processes "embodied the equivalent

of natural laws." *Id.* The process in *Diehr* embodied the Arrenhius equation to cure rubber; an algorithm in *Flook* was used to adjust alarm limits; and *Benson* used a mathematical principle to convert numbers on a computer, *id.*; all were recognized as underlying laws of nature, unsuitable subject matter for patent protection.

Myriad's claims to the isolated DNA/ cDNA molecules are analogous. The ordering or arrangement of chemical base pairs embodied as an isolated molecule is an equation, a formula for the production of proteins; the mathematical ordering or arrangement of chemical base pairs an algorithm which dictates biological processes. The fixed nature of the relationship of the nucleotides arranged in the BRCA 1/2 genes which reveal a susceptibility to breast or ovarian cancer is a mathematical principle. As such, Myriad's claims on isolated DNA/cDNA are laws of nature, exceptions to the categories of patentable subject matter described in 35 U.S.C. § 101.

C. Isolated DNA/cDNA Molecules of the BRCA 1/2 Genes are Products of Nature.

Products of nature are exceptions to the statutory categories of patentable subject matter under § 101. *Diamond v. Chakrabarty*, 447 U. S. 303, 100 S. Ct. 2204, 65 L. Ed. 2d 144 (1980). In two separate opinions resting upon identical rationales the Federal Circuit erred in its determination that claims to isolated DNA/cDNA molecules are patent eligible. See, *Ass'n for Molecular Pathology v. U.S. Patent and Trademark Office*, 653 F.3d 1329, 1351 (Fed.Cir. 2011); *Ass'n for Molecular Pathology v. Myriad Genetics, et al.*, 2012 U. S. App, LEXIS 17679 at 56-61.

In its latest decision, the Federal Circuit disregarded *Mayo* and relied solely on the test established in *Diamond v. Chakrabarty*, 447 U. S. 303, 100 S. Ct. 2204, 65 L. Ed. 2d 144 (1980) to determine that the claimed molecules were "markedly different" from what existed in nature, and thus patent-eligible. *Ass'n*, 2012 U. S. App, LEXIS 17679 at 56-61. What distinguished Chakrabarty's invention, a bioengineered oil degrading bacterium, from the invention in *Funk Brothers*, a mixture of cultures of root bacteria capable of inoculating the seeds of certain leguminous plants "…were "markedly different characteristics from any…found in nature." *Id*., citing *Chakrabarty*, 447 U.S. at 310.

The Federal Circuit reasoned that while DNA molecules exist in the body (native DNA) as part of a "large structural complex," (i.e., part of a chromosome), isolated DNA is "a free- standing portion of a larger natural DNA molecule" which had been cleaved (i.e., had covalent bonds in its backbone chemically severed, or synthesized to consist of just a fraction of a naturally occurring DNA molecule). *Id*., at 61-62. Solely as a result of this cleavage or synthesis, the isolated DNA/cDNA was declared a distinctive chemical identity, and thus "markedly different" from patent-ineligible products of nature. *Id*.

However, this minute change in physical structure does not make the isolated or synthesized molecules, "markedly different" from their native state or endow them with a distinctive identity Rather, the Federal Circuit dismissed established biological truths regarding the functionality of the molecules, finding their informational content irrelevant: "We recognize the biologists may think

of molecules in terms of their uses, but genes are in fact materials having a chemical nature and, as such, are best described in patents by their structures rather than their functions." *Id.*

This bifurcation of the gene as a hierarchy of structural and functional components denies the fundamental nature, or "identity" of the subject matter at issue. Unlike other chemicals, the isolated DNA/cDNA molecules describe and embody the nucleotide sequences which direct the proteins, cells and organs which make up the body. This biological function is the defining and identical characteristic of DNA/cDNA both before and after isolation or synthesis, and thus, these molecules are not markedly different from their native state. In fact, if these isolated or synthesized molecules had a truly distinctive chemical identity or were markedly different from what exists in nature their applications in research and diagnostics could not use the natural biological characteristics of DNA sequences to code for a protein and to anneal to its complementary nucleotide sequence. Products of nature, they "…serve the ends nature originally provided." *Funk Bros. Seed Co v. Kalo Inoculant Co.*, 333 U. S. 127, 131, 68 S. Ct. 440, L. Ed. 588 (1948).

D. Myriad's Patents Impede Progress and Innovation in Biomedical Science.

A patent is a right which allows the exclusion of others from making, or using the patented invention. 35 U.S.C. § 271(a) (2000). This Court has repeatedly emphasized the concern that "patent law not inhibit further discovery by improperly tying up the future use of laws of nature," as this might impede, rather than promote innovation. *Mayo*, 132 S. Ct. at 1301.

This Court's precedents, "…warn us against upholding patents that too broadly preempt the use of a natural law." *Id.*, citing *O'Reilly v. Morse*, 56 U.S. 62, 14 L. Ed. 601 (1854). Examples include general claims for underlying scientific principles, *id*, abstract and sweeping claims to a mathematical formula which covered both known and unknown uses of that formula, *id.*, citing *Benson*, 409 U.S. at 67, 93 S. Ct. 253, 34 L. Ed. 2d 273, a concept involving business transactions which precluded the use of its approach in all fields, *id.*, citing *Bilski v. Kappos*, 130 S. Ct. 3218, 177 L. Ed. 2d 792 (2010), and a formula that could be preempted from use in a broad range of possible uses. *Id.*, citing *Parker v. Flook*, 437 U. S. 584, 586, 98 S.Ct. 2522, 57 L. Ed. 2d 451 (1978).

Mayo recognized that patenting basic scientific tools posed a danger for future innovation, particularly if more future innovation was foreclosed than justified by the underlying discovery. *Id*., at 1301. Although the claimed law of nature in *Mayo* was narrow, these concerns were implicated, affecting the ability of doctors to determine treatment options and threatening the development of more refined treatment recommendations which would combine features of the correlation with later discoveries involving aspects of human physiology and biology. *Id*., at 1302. This preemption of future uses of laws of nature reinforced this Court's conclusion that the processes were not patent eligible. *Id*.

Myriad's patents on isolated DNA/cDNA "too broadly preempt natural laws." They are "general," preempting all uses of fundamental principles of molecular biology and genetics. The claims are "sweeping" covering both "known and unknown uses" of the embodied information

of the BRCA 1/2 genes, preempting this knowledge from all fields of biomedical research and healthcare, including a broad range of potential uses for diagnosing and treating breast and ovarian cancer.

The practical implications of this preemption inhibit progress and innovation. Because Myriad's patents give them a monopoly on genetic testing for breast and ovarian cancer in the United States, like the physicians in *Mayo* unable to change their treatment options, physicians in our country cannot give second opinions regarding a diagnosis for the disease. Like the physicians in *Mayo* unable to refine their treatment methods, physicians treating breast and ovarian cancer are unable to refine their treatment methods because basic biomedical research and research and the development of alternative genetic testing methods have been restricted by Myriad's monopolies on the BRCA 1/2 genes. These patents have limited scientific discoveries and will continue to inhibit innovation.

The monopolization of the BRCA 1/2 genes, laws and products of nature, tie up too much of their future use. The resultant inhibition of future discoveries in biomedical research and healthcare treatment is not justified by Myriad's original discovery. Myriad's claims isolated DNA/cDNA of the BRCA 1/2 genes are patent-ineligible laws and products of nature whose preemption impedes innovation and progress in science and medicine.

CONCLUSION

The patenting of the isolated DNA/cDNA molecules of the BRCA 1/2 human genes creates grave harms for the health of all women and their families. Additionally, these molecules are phenomena of nature, patent ineligible exceptions to the categories of patentable subject matter, per 35 U.S.C., § 101. For the foregoing reasons *Amici* respectfully ask that the Federal Circuit's decision regarding the patent eligibility of the human genes at issue be reversed.

Respectfully submitted,

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