

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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

Plaintiffs,

v.

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

Defendants.

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COMPLAINT

INTRODUCTION

1. Every person's body contains human genes, passed down to each individual from his or her parents. These genes determine, in part, the structure and function of every human body. This case challenges the legality and constitutionality of granting patents over this most basic element of every person's individuality.

2. The gene patents that are challenged in this case are patents covering the *BRCA1* and *BRCA2* genes, which relate to an increased risk of breast and/or ovarian cancer. Ease of access to genomic discoveries is crucial if basic research is to be expeditiously translated into clinical laboratory tests that benefit patients in the emerging era of personalized and predictive medicine. The patents make ease of access more restricted. Because of the patents, defendant Myriad has the right to prevent clinicians from independently looking at or interpreting a person's *BRCA1* and *BRCA2* genes to determine if the person is at a higher risk of breast and/or ovarian cancer. Because of the patents and because Myriad chooses not to license the patents broadly, women who fear they may be at an increased risk of breast and/or ovarian cancer are barred from having anyone look at their *BRCA1* and *BRCA2* genes or interpret them except for the patent holder. Women are thereby prevented from obtaining information about their health risks from anyone other than the patent holder, whether as an initial matter or to obtain a second opinion. The patents also prevent doctors or laboratories from independently offering testing to their patients, externally validating the test, or working cooperatively to improve testing. Many women at risk cannot even be tested because they are uninsured and/or cannot afford the test offered by Myriad.

3. The patents cover the human genes themselves. In this respect, they cover the healthy gene and numerous variations of the gene, some of which Myriad identified, some of which it did not, and some of which have not yet been identified. Some of those variations correlate with an increased risk of breast and ovarian cancer. Some do not. The patents also cover any new methods of looking at the human genes that might be developed by others, the concept of comparing one *BRCA1* or *BRCA2* gene to another

BRCA1 or *BRCA2* gene for the purpose of discerning differences, and the correlations found in nature between mutations in the human gene and an increased risk of breast or ovarian cancer.

4. The patenting of human genes, the concept of looking at or comparing human genes, and correlations found in nature between certain genes and an increased risk of breast and/or ovarian cancer violates long established legal principles that prohibit the patenting of laws of nature, products of nature, and abstract ideas. These patents also violate the First Amendment and Article I, section 8, clause 8 of the United States Constitution.

JURISDICTION AND VENUE

5. This Court has jurisdiction pursuant to 28 U.S.C. §§ 1331, 1338(a), and 2201. Litigation is authorized by 42 U.S.C. §1983.

6. Venue is proper pursuant to 28 U.S.C. § 1391(b)(1) and (2), (c) and (e).

PARTIES

7. Plaintiff ASSOCIATION FOR MOLECULAR PATHOLOGY (AMP) is a not-for-profit scientific society dedicated to the advancement, practice, and science of clinical molecular laboratory medicine and translational research based on the applications of genomics and proteomics. AMP members participate in basic and translational research aimed at broadening the understanding of gene/protein structure and function, disease processes, and molecular diagnostics, and provide clinical medical services for patients, including diagnosis of breast cancer. AMP supports attaching intellectual property rights to true acts of invention such as new therapeutics, diagnostics or technology platforms, but believes a single gene or a sequence of the genome is a

product of nature and should not be patentable. AMP sues on behalf of its members, some of whom are ready, willing, and able to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated.

8. Plaintiff AMERICAN COLLEGE OF MEDICAL GENETICS (ACMG) is a private, non-profit voluntary organization of clinical and laboratory geneticists. The Fellows of the ACMG are doctoral level medical geneticists and other physicians involved in the practice of medical genetics. With more than 1300 members, the ACMG's mission is to improve health through the practice of Medical Genetics. In order to fulfill this mission, the ACMG strives to 1) define and promote excellence in medical genetics practice and the integration of translational research into practice; 2) promote and provide medical genetics education; 3) increase access to medical genetics services and integrate genetics into patient care; and 4) advocate for and represent providers of medical genetics services and their patients. ACMG sues on behalf of its members, some of whom are ready, willing, and able to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated.

9. Founded in 1922, the plaintiff AMERICAN SOCIETY FOR CLINICAL PATHOLOGY (ASCP) is the largest and oldest organization representing the medical specialty of pathology and laboratory medicine. The ASCP has 130,000 members working as pathologists and laboratory professionals. ASCP members design and interpret the tests that detect disease, predict outcome, and determine the appropriate therapy for the patient. The ASCP is recognized for its excellence in continuing professional education, certification of laboratory professionals, and advocacy--championing causes at the state and federal levels. ASCP is a not-for-profit entity

organized for scientific and educational purposes and dedicated to patient safety, public health, and the practice of pathology and laboratory medicine. ASCP sues on behalf of its members, some of whom are ready, willing, and able to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated.

10. Plaintiff COLLEGE OF AMERICAN PATHOLOGISTS (CAP) is a national medical society representing more than 17,000 pathologists who practice anatomic pathology and laboratory medicine in laboratories worldwide. The College's Commission on Laboratory Accreditation is responsible for accrediting more than 6,000 laboratories domestically and abroad and approximately 23,000 laboratories are enrolled in CAP's proficiency testing programs. It is the world's largest association composed exclusively of board-certified pathologists and pathologists in training worldwide and is widely considered the leader in laboratory quality assurance. The CAP is an advocate for high-quality and cost-effective medical care. CAP sues on behalf of its members, some of whom are ready, willing, and able to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated.

11. Plaintiff HAIG KAZAZIAN, MD, is the Seymour Gray Professor of Molecular Medicine in Genetics in the Department of Genetics at the University of Pennsylvania School of Medicine. He is a human genetics researcher and the previous chair of the Department. Dr. Kazazian received a cease and desist letter from defendant Myriad as a result of work that was being done in the Genetic Diagnostic Laboratory of the Department of Genetics. The laboratory directed by Dr. Kazazian was and is prohibited from doing routine screening for *BRCA1* and *BRCA2* genes for research or

part of clinical practice without Myriad's permission as a direct result of the patents challenged by this action.

12. Plaintiff ARUPA GANGULY, PhD, is an Associate Professor in the Department of Genetics at the Hospital of the University of Pennsylvania. Dr. Ganguly was engaged in research on and clinical practice relating to breast cancer. Dr. Kazazian received a cease-and-desist letter from defendant Myriad. Dr. Ganguly, the co-director of the laboratory was ready, willing, and able to resume research and clinical practice if the patents had been invalidated. If they are invalidated now, she would seriously consider resuming clinical practice that is now prohibited.

13. Plaintiff WENDY CHUNG, MD, PhD, is an Associate Professor of Pediatrics at Columbia University. Dr. Chung is a human geneticist whose current research includes research on the *BRCA1* and *BRCA2* genes. Dr. Chung is required to send samples to defendant Myriad for any analysis of the *BRCA1* or *BRCA2* genes if she wants to tell the subjects the results and use the results clinically. Dr. Chung could evaluate the samples herself, or find other laboratories to evaluate the samples, if the patents are invalidated. She is ready, willing, and able to do so if the patents are invalidated.

14. Plaintiff HARRY OSTRER, MD, is a Professor of Pediatrics, Pathology and Medicine and Director of the Human Genetics Program in the Department of Pediatrics at New York University School of Medicine. Dr. Ostrer's work has focused on understanding the genetic basis of development and disease, including disorders of sexual differentiation and genetic susceptibility to breast and prostate cancer and malignant melanoma. Dr. Ostrer is actively engaged in identifying genes that convey risk of breast

cancer and that may mitigate the effects of mutations in the *BRCA1* and *BRCA2* genes. These observations could infringe on the Myriad patents and, thus, could be prevented from entering clinical practice and benefitting people. Dr. Ostrer is also the Director of the Molecular Genetics Laboratory of NYU Medical Center, one of the largest academic genetic testing laboratories in the United States. His laboratory has the ability to evaluate *BRCA1* and *BRCA2* genes in samples, including in custom-designed tests that may be more cost-effective than Myriad's current offering. Dr. Ostrer could evaluate the samples himself, or find other laboratories to evaluate the samples, if the patents are invalidated. He is ready, willing, and able to do so if the patents are invalidated.

15. Plaintiff DAVID LEDBETTER, PhD, is a Professor of Human Genetics and Director of the Division of Medical Genetics at the Emory University School of Medicine. Dr. Ledbetter is a genetic researcher. Research in his laboratory focuses on the molecular characterization of human developmental disorders. Dr. Ledbetter directs the Emory Genetics Laboratory which provides superior testing services for individuals with or at risk for genetic diseases. Dr. Ledbetter's laboratory has the ability to evaluate *BRCA1* and *BRCA2* genes in samples. Dr. Ledbetter could evaluate the samples himself, or find other laboratories to evaluate the samples, if the patents are invalidated. He is ready, willing, and able to do so if the patents are invalidated.

16. Plaintiff STEPHEN T. WARREN, PhD, is the William Patterson Timmie Professor of Human Genetics, Chairman of the Department of Human Genetics, and Professor of Biochemistry and Professor of Pediatrics at Emory University. He is a past President of the American Society of Human Genetics. He personally supervises genetic research at Emory. He is also responsible for the laboratories at the Emory Genetics

Laboratory. The laboratory has the ability to evaluate *BRCA1* and *BRCA2* genes in samples. Scientists at Emory could evaluate the samples themselves, or find other laboratories to evaluate the samples, if the patents are invalidated. Dr. Warren is ready, willing, and able to do so if the patents are invalidated.

17. Plaintiff ELLEN MATLOFF, MS, is Director of the Yale Cancer Genetic Counseling Program. Ms. Matloff advises women on the desirability of obtaining an analysis of their genes to determine if the women have the genetic mutations that correlate with an increased risk of breast and/or ovarian cancer. If she determines that such an analysis is warranted and the individual woman concurs, Ms. Matloff arranges for the analysis and then advises the woman of the significance of the results. Ms. Matloff currently is forced to utilize defendant Myriad for analysis of the *BRCA1* and *BRCA2* genes. If the patents were invalidated, she would utilize other laboratories and other methods of analysis, some of which she believes could be offered at a substantially reduced cost. She is ready, willing, and able to utilize those additional resources if the patents are invalidated.

18. Plaintiff ELSA W. REICH, M.S. is a Professor in the Department of Pediatrics at New York University. She is a genetic counselor. She helps women decide whether to be tested for mutations in the *BRCA1* and *BRCA2* genes. If they need testing, she sends samples to defendant Myriad and interprets the results for the women. Having only one laboratory prevents independent confirmation of test results and interpretation of the meaning of variants of uncertain significance. She is ready, willing, and able to utilize alternative testing facilities for such tests if the patents are invalidated.

19. Plaintiff BREAST CANCER ACTION is a national organization of over 20,000 members based in San Francisco, California. Founded in 1990, Breast Cancer Action was started by women in a San Francisco breast cancer support group who were frustrated by the lack of knowledge about their disease. Their goal was to create an organization that would help transform breast cancer from a private medical crisis to a public health emergency. Breast Cancer Action continues this work, and is now a national education and activist organization that challenges assumptions and inspires change to end the breast cancer epidemic. The organization works with researchers to encourage innovative approaches to unresolved issues in breast cancer, including issues raised by research on the *BRCA1* and *BRCA2* genes that is not currently being done. Members of Breast Cancer Action have had their *BRCA1/BRCA2* genes analyzed or sought analysis to determine if they have genetic mutations that correlate with an increased risk of breast and/or ovarian cancer. In addition, Breast Cancer Action staff and volunteers provide information to members of the public about genetic analysis. If the patents are invalidated, Breast Cancer Action and its members are ready, willing, and able to utilize any additional resources for such analysis, and would directly benefit from any increased research on the *BRCA1* and *BRCA2* genes that would be made possible. Breast Cancer Action would also be able to provide information about testing options offered by labs other than Myriad without fear of inducing infringement. Breast Cancer Action sues on behalf of itself and its members.

20. Plaintiff BOSTON WOMEN'S HEALTH BOOK COLLECTIVE (BWHBC), doing business as Our Bodies Ourselves, is a nonprofit, public interest women's health education, advocacy, and consulting organization. OBOS provides clear,

accurate information about health, sexuality and reproduction from a feminist and consumer perspective. OBOS vigorously advocates for women's health by challenging the institutions and systems that block women from full control over their bodies and devalue women's lives. OBOS's long-standing commitment to serve only in the public interest and its bridge-building capacity are its hallmarks. In addition, OBOS staff provide information to members of the public about genetic analysis. If the patents are invalidated, OBOS is ready, willing, and able to provide information about testing options offered by labs other than Myriad without fear of inducing infringement, and would directly benefit from any increased research on the *BRCA1* and *BRCA2* genes that would be made possible.

21. Plaintiff LISBETH CERIANI is a 43-year-old single mother who was diagnosed with cancer in both breasts in May 2008. Ms. Ceriani is insured through MassHealth, a Medicaid insurance program for low-income people. Her oncologist and genetic counselor recommended that she obtain *BRCA1* and *BRCA2* genetic testing, because she may need to consider further surgery in order to reduce her risk of ovarian cancer. They submitted a blood sample to Myriad on her behalf. However, she was notified that Myriad would not process the sample. Even though her insurance has informed her that it would cover the BRCA genetic test, Myriad will not accept the MassHealth coverage. Ms. Ceriani is unable to pay the full cost out-of-pocket and, to date, has not been tested. Without the genetic test results, she cannot determine the best medical course for herself. If the patents are invalidated, Ms. Ceriani is ready, willing, and able to utilize any additional resources for testing and research.

22. Plaintiff RUNI LIMARY is a 32-year-old Asian-American woman who was diagnosed with aggressive breast cancer in 2005. Upon her diagnosis, she sought *BRCA* genetic testing, but her insurance company did not cover the test. Ms. Limary was not able to get tested through Myriad until two years later, when she obtained insurance that provided coverage for the test. Ms. Limary was given the following test result: “genetic variant of uncertain significance.” The test she received did not look for all known large rearrangements in the *BRCA* genes. Ms. Limary wants to access additional resources for testing and research that could reveal the significance of the variant in her genes, including whether the variant is correlated with an increased risk of breast or ovarian cancer. If the patents are invalidated, Ms. Limary is ready, willing, and able to utilize any additional resources for testing and research.

23. Plaintiff GENAE GIRARD is a 39-year-old woman who was diagnosed with breast cancer in 2006. Shortly after her diagnosis, she obtained *BRCA1/BRCA2* genetic testing from Myriad and tested positive for a deleterious mutation on the *BRCA2* gene. She sought a second opinion of that test result but learned that Myriad is the only laboratory in the country that can provide full sequencing. The patents on the *BRCA* genes block her from getting confirmation of the test she received. Ms. Girard has been forced to make, and continues to make, significant medical decisions for herself based on a test result that has not been verified by another laboratory. A second opinion on Ms. Girard’s test results is also crucial for her immediate family's options and screening. If the patents are invalidated, Ms. Girard is ready, willing, and able to utilize any additional resources for testing and research.

24. Plaintiff PATRICE FORTUNE is a 48-year-old woman who was diagnosed with breast cancer in February 2009. Ms. Fortune is insured through Medi-Cal, a Medicaid insurance program for low-income people. Her oncologist and genetic counselor recommended that she obtain *BRCA1/BRCA2* genetic testing, including the supplemental testing that is offered by Myriad separate from its standard test, but told her that Myriad would not accept her insurance. Ms. Fortune is unable to pay the full cost out-of-pocket and, to date, has not been tested. Without the genetic test results, she cannot determine the best medical course for herself. If the patents are invalidated, Ms. Fortune is ready, willing, and able to utilize any additional resources for testing and research.

25. Plaintiff VICKY THOMASON is a 52-year-old woman who was diagnosed with ovarian cancer in 2006. She obtained *BRCA1/BRCA2* genetic testing from Myriad in 2007 and was found to be negative for mutations covered by that test. Her genetic counselor advised her about additional *BRCA* genetic testing that looks for other large genetic rearrangements that are not included in Myriad's standard full sequencing test, but informed her that her insurance would not cover the full cost of that test. Upon information and belief, Ms. Thomason would need to pay up front for this additional test. Ms. Thomason is unable to afford the extra cost and, to date, has not received this testing. Without these results, she cannot determine the best medical course for herself. If the patents are invalidated, Ms. Thomason is ready, willing, and able to utilize any additional resources for testing and research that would become accessible to her.

26. Plaintiff KATHLEEN RAKER is a 41-year-old woman whose mother and maternal grandmother died from breast cancer. She obtained *BRCA1/BRCA2* genetic testing from Myriad in 2007 and was found to be negative for mutations covered by that test. Her genetic counselor advised her about additional *BRCA* genetic testing that looks for other large genetic rearrangements that are not included in Myriad's standard full sequencing test, but informed her that it was unclear whether her insurance would cover the cost of that test. Upon information and belief, Ms. Raker would need to pay up front for this additional test. Ms. Raker is unable to afford the extra cost and, to date, has not received this testing. Without these results, she cannot determine the best medical course for herself. If the patents are invalidated, Ms. Raker is ready, willing, and able to utilize any additional resources for testing and research that would become accessible to her.

27. Defendant UNITED STATES PATENT AND TRADEMARK OFFICE (Patent office) is an agency of the Commerce Department of the United States. Its principal office is in Alexandria, Virginia. The Patent office is sued solely on the constitutional claims.

28. Defendant MYRIAD GENETICS (Myriad) is a for-profit corporation located in Salt Lake City, Utah and doing business throughout the United States. Myriad is incorporated in Delaware. Myriad is a co-owner of patent 5,747,282, and formerly was a co-owner of several of the other patents challenged in this lawsuit. Upon information and belief, Myriad now has an exclusive license for all of the patents challenged in this action and is the sole clinical provider of full sequencing of the *BRCA1* and *BRCA2* genes in the United States.

29. Defendants 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 are Directors of the University of Utah Research Foundation. The foundation is a not-for-profit corporation that is operated, supervised and/or controlled by the University of Utah and located in Salt Lake City, Utah. The University of Utah Research Foundation is an owner or part-owner of all of the patents at issue in this case. Because Myriad holds the exclusive license to these patents, defendant patent-holders, including Myriad and the University of Utah Research Foundation, are hereafter referred to collectively as Myriad.

30. The United States of America, represented by the Secretary of Health and Human Services, is an additional owner of the patents 5,710,001, 5,753,441, 6,162,897 and 5,747,282. Endo Recherche, Inc., of Quebec, Canada, HSC Research and Development Limited Partnership of Toronto, Canada, and the Trustees of the University of Pennsylvania are additional owners of the patents 5,837,492 and 6,033,857. These other owners have not been joined as parties because their participation is unnecessary to the resolution of this action, and Myriad, as the exclusive licensee of all of the patents, is fully capable of representing the interests of all of the patent owners.

FACTS

31. Defendant U.S. Patent Office has granted, and Myriad holds, either through ownership or exclusive license, numerous patents relating to the human genes known as *BRCA1* and *BRCA2*.

32. Plaintiffs challenge the legality and the constitutionality of four categories of claims in these patents:

a. Patent Claims Over Natural Human Genes: Claims 1, 2, 5, and 6 of patent 5,747,282 ('282) and claim 1 of patent 5,837,492 ('492).

b. Patent Claims Over Natural Human Genes With Natural Mutations: Claim 1 of patent 5,693,473 ('473), claim 7 of patent '282, and claims 6 and 7 of patent '492.

c. Patent Claims Over Any Method, Including Non-Patented Methods, Of Looking For Mutations in Natural Human Genes: Claim 1 of patent 5,709,999 ('999).

d. Patent Claims Over The Thought That Two Genes Are Different or Have Different Effects, Including But Not Limited To The Thought That The Differences Correlate With An Increased Risk Of Breast And/Or Ovarian Cancer: Claim 1 of patent 5,710,001 ('001), claim 1 of patent 5,753,441 ('441), claims 1 and 2 of patent 6,033,857 ('857) and claim 20 of patent '282.

33. Every person's body is composed of cells. In the nucleus of each cell is the person's DNA. Genes are encoded by DNA. Genes instruct the body to create the proteins and gene products that that person's body uses to function. Human DNA and human genes consist of hundreds or thousands of nucleotides (i.e. bases) referred to as A, T, G, and C. A gene is represented in scientific research and the patents in this case, by the genomic sequence, the series of nucleotides (represented by the letters) corresponding to the bases.

34. DNA is a chemical structure made by the body. However, the genetic sequence is informational both for clinicians and researchers and for the body itself.

35. Not everyone's DNA or genes are identical. Genes vary in nature from one person to another and those variations are often called mutations or variants. Those variants can include such changes as a T appearing where an A normally appears or a G being deleted from the DNA sequence. Variants can be inherited and can also be acquired during a lifetime. They can also include much larger variations such as sections of DNA that are missing or displaced. Some of these variants have effects on the body's ability to create proteins necessary for sound health.

36. To find out if a person has a T where an A normally appears, a genetic researcher or clinician looks at the sequence of an individual's gene. The researcher or clinician can sequence that gene -- i.e. read the A, T, C, G letters of the gene. Once the sequence is known, the researcher or clinician can look at it to see if the letters show a healthy sequence, a sequence with mutations known to be associated with cancer, or a sequence with one or more variants of uncertain significance. Alternatively, the researcher or clinician can check just a small section of the sequence where a known mutation or variant is known to occur. The methods by which researchers or clinicians identify the sequence of either the whole gene or any part thereof are not patented in the claims at issue here and are well known in the field.

37. The genes covered by the patents in this case are called *BRCA1* and *BRCA2* because of their association with breast cancer. Every man and woman has *BRCA1* and *BRCA2* genes, but the genomic sequence of each person's *BRCA* genes can differ. Certain mutations in the genes are correlated with an increased risk of breast

and/or ovarian cancer. Scientists also have found that mutations in these genes may be associated with other cancers, such as prostate and pancreatic cancers.

38. Breast cancer is one of the leading causes of death among women. Approximately 5-10% of the women who develop breast cancer are likely to have a mutation, inherited from one of their parents, in their *BRCA1* or *BRCA2* genes, that predisposes them to an increased risk of breast and/or ovarian cancer.

39. Women with one of these significant gene mutations in the *BRCA1* or *BRCA2* gene have an approximately 40-85% lifetime risk of developing breast cancer. Inherited mutations on the *BRCA1* and *BRCA2* genes also increase the risk of ovarian cancer.

40. A *BRCA1/BRCA2* genetic test result that is positive for one of these mutations can have a substantial impact on a woman's medical decisions and health. It can also have an impact on that woman's relatives. Many women will obtain earlier and more vigilant screening for breast and/or ovarian cancers, and some women may choose to have prophylactic surgery to remove their breasts and/or ovaries in order to reduce the risk of future cancers.

41. In the 1990's, a number of genetic researchers around the world began looking for a human gene that correlated with an increased risk of breast and/or ovarian cancer. Many of those researchers, including the researchers who ultimately formed defendant Myriad, were funded, at least in part, by the federal government.

42. Researchers, using techniques widely available in the profession, determined in 1990 that one gene that correlated with an increased risk of breast and/or ovarian cancer was located in the body on chromosome 17.

43. Another researcher team, eventually associated with defendant Myriad, also using techniques widely available in the profession, sequenced the precise *BRCA1* gene. They subsequently formed Myriad. They sought, and ultimately obtained, several patents on this human *BRCA1* gene.

44. Scientists knew that *BRCA1* was not the only gene that predisposed women to an increased risk of inherited breast and/or ovarian cancer. Researchers from all over the world began looking for other similar genes, again using techniques widely available in the profession.

45. Defendant Myriad, using techniques widely available in the profession, filed patents over the *BRCA2* gene. Myriad ultimately obtained a series of patents over the human *BRCA2* gene.

46. Defendant Myriad did not invent, create or in any way construct or engineer the human *BRCA1* and *BRCA 2* genes. These genes are existing products of nature, naturally occurring within the human body. Myriad located them in nature and merely described their informational content as it exists and functions in nature.

47. Defendant Myriad did not invent, create or in any way construct the differences found when genes are compared or the correlations between certain mutations and an increased risk of breast and/or ovarian cancer. Nature did that. Myriad identified nature's laws.

48. As a result of the breadth of its patents, Myriad has the right to control all genetic testing related to breast and/or ovarian cancer linked to *BRCA1* or *BRCA2*. Researchers and clinicians cannot develop or implement new tests for breast/ovarian cancer linked to *BRCA1* or *BRCA2* if development or implementation involves looking

at *BRCA1* or *BRCA2*. Women cannot give their blood or DNA to a researcher or clinician and obtain a second opinion. The effect is to infringe on quality medical practice and to compromise quality assurance and improvement of testing.

49. Defendant Myriad has enforced its patent rights over *BRCA1* and *BRCA2* genes at least nine (9) times. For example, according to press reports, laboratories at Yale performed analyses of those genes, but they no longer do so as a direct result of a cease-and-desist letter received from defendant Myriad.

50. Defendant Myriad obtained its patents from defendant Patent Office pursuant to a formal written policy by the Patent Office which provides that naturally occurring genes can be patented if they are “isolated from their natural state and purified.”

51. An “isolated and purified” human gene performs the exact same function as a non-isolated and purified human gene in a person’s body. The information dictated by the gene is identical whether it is inside or outside of the body. According to the Patent Office policy, an “isolated and purified” gene includes one that is simply removed from the body and removed from other content of the cell. Removing a product of nature from its natural location does not make it any less a product of nature.

52. This policy permits the patenting of products of nature, laws of nature, natural phenomena, abstract ideas, and basic human knowledge and thought. It therefore violates the United States Constitution Article 1, section 8, clause 8 and the First Amendment, as well as 35 U.S.C. § 101 of the patent statute.

53. Defendant Myriad obtained its patents pursuant to the practice of the defendant United States Patent and Trademark Office that permits patenting of comparisons or correlations created by nature, but identified by a patent holder.

54. This practice permits the patenting of laws of nature and abstract ideas and basic human knowledge or thought. It therefore violates Article 1, section 8, clause 8 and the First Amendment of the United States Constitution, as well as 35 U.S.C. § 101.

PATENT CLAIMS OVER NATURAL HUMAN GENES

55. Several of the claims in Myriad's patents cover the human *BRCA1* and *BRCA2* genes in their natural, non-mutated form. These include claims 1, 2, 5, and 6 of patent '282 and claim 1 of patent '492.

56. Claim 1 of patent '282 covering *BRCA1* is for any strand of "isolated" DNA that creates a particular protein identified in the patent. This claim covers the DNA that includes the *BRCA1* gene in its "wild-type" or non-mutated form. It also includes any DNA that creates any portion of the identified protein. It thus includes DNA sequences that are identical in structure and function to the DNA as it exists in every person's body. It also includes any DNA that creates a fragment of the protein.

57. Claim 2 of patent '282 is very similar, but somewhat narrower. It covers a specific DNA sequence listed in the patent as the DNA sequence for the *BRCA1* gene.

58. Claim 5 of patent '282 also covers *BRCA1*, but it covers any DNA that has "at least 15 nucleotides" of the DNA referenced in claim 1. A nucleotide is one base. Claim 5 thus explicitly covers small fragments of the *BRCA1* gene.

59. Claim 6 of patent '282 covers any isolated DNA that has "at least 15 nucleotides" of the DNA referenced in claim 2.

60. Claim 1 of patent '492 is for any strand of "isolated" DNA that creates a particular protein identified in the patent. This claim covers the DNA that includes the *BRCA2* gene in its "wild-type" or non-mutated form. It also includes any DNA that creates the identified protein. It thus includes DNA sequences that are identical in structure and function to the DNA as it exists in every person's body.

PATENT CLAIMS OVER NATURAL HUMAN GENES WITH NATURAL MUTATIONS

61. Several of the claims in Myriad's patents claim the human *BRCA1* or *BRCA2* gene that contains variants or mutations caused by nature. These include claim 1 of '473, claim 7 of '282, and claims 6 and 7 of '492.

62. Myriad looked at human genes from many individuals. Some of those individuals had variants in *BRCA1* or *BRCA2*. Myriad recorded the DNA sequences of those individuals with those variants and obtained patents on the DNA with those naturally mutated sequences.

63. Claim 1 of '473 claims "isolated DNA comprising an altered *BRCA1* DNA having at least one" of the specified variants. Myriad asserts that some of the patented DNA containing specified variants correlate with an increased risk of breast and ovarian cancer. Myriad asserts that other patented DNA containing specified variants does not so correlate or that Myriad does not yet know their effect, if any.

64. Claim 7 of '282 claims "an isolated DNA" that has specified variants. In the text of the patent, Myriad describes all of the variants as cancer predisposing mutations.

65. Claim 6 of '492 claims any "isolated DNA" that creates any mutated form of the protein created by *BRCA2* if the mutations correlate with a "susceptibility to

cancer.” In other words, the claim covers any yet-to-be discovered mutations – discovered by anyone -- that correlate with an increased risk of any type of cancer.

66. Claim 7 of ‘492 also claims isolated DNA if the DNA contains sequences that include any mutations that correlate with an increased risk of cancer.

67. Claim 1 of ‘473, claim 7 of ‘282, and Claims 6 and 7 of ‘492 include DNA sequences that are identical in structure and function to the DNA inside the body of some people.

PATENT CLAIMS OVER ANY METHOD, INCLUDING NON-PATENTED METHODS, OF LOOKING FOR MUTATIONS IN NATURAL HUMAN GENES

68. Myriad’s patents also claim any and all methods, including non-patented methods, of looking at natural human genes. This includes Claim 1 of patent ‘999.

69. Claim 1 of patent ‘999 covers any method of analyzing a human being’s *BRCA1* gene for the purpose of finding whether the human being has any of the specified germline [inherited] variants.

70. The methods used to look at the gene are not patented and are well known in the field. All that is patented is the act of looking at the *BRCA1* gene to see if the gene has the specified variants.

PATENT CLAIMS OVER THOUGHT OR ABSTRACT IDEAS

71. Several of the claims in Myriad’s patents include comparing two genes, correlations between mutations in the human *BRCA1* and *BRCA2* genes that are currently known to be associated with an increased risk of breast and/or ovarian cancer, and correlations between cancer and mutations not now known, but identified in the future. These include claim 1 of ‘001, claim 1 of ‘441, claims 1 and 2 of patent ‘857, and claim 20 of ‘282.

72. Specifically, claim 1 of '001 involves taking a tumor sample from a person and looking at the *BRCA1* gene in that sample and comparing it to the *BRCA1* gene from the same person taken from a part of the body in which there is no tumor and seeing if there are any differences. The methods by which this is done are not patented. What is patented is performing this comparison of the tumor and germline sequences to identify somatic mutations in the *BRCA1* gene and thinking "there are differences and they must be somatic (environmentally caused)." What is patented is the abstract idea that nature has made the two forms of the *BRCA1* genes different.

73. Claim 1 of '441 similarly involves the comparison of two *BRCA1* genes. This claim covers comparing the *BRCA1* gene in a tissue sample taken from a person with the *BRCA1* gene in its "wild-type" or non-mutated state. The methods by which this is done are not patented. What is patented is performing this comparison of the *BRCA1* gene from the tissue sample and the *BRCA1* wild-type gene and thinking "there are differences." What is patented is the abstract idea that nature has made the two *BRCA1* genes different.

74. Patent '857 involves the comparison of two *BRCA2* genes. Claim 1 involves comparing a *BRCA2* gene taken from a person with a wild-type *BRCA2* gene. The methods by which this is done are not patented. What is patented is performing this comparison for *BRCA2* and thinking "there are differences" and that the differences reflect a mutation. What is patented is the abstract idea that nature has made the two *BRCA2* genes different.

75. Claim 2 of patent '857 involves the same comparison of two *BRCA2* genes. The only difference is that the thought that is patented is "there are differences"

and they “indicate a predisposition to [breast] cancer.” What is patented is the abstract idea that nature has made the two genes different in a manner that increases that person’s risk of breast cancer.

76. Claim 20 of ‘282 involves “a method for screening potential cancer therapeutics.” However, the method consists entirely of putting the potential therapeutic into contact with a cell that includes a *BRCA1* mutation and looking to see if the cell grows more slowly with the therapeutic than without. That method simply describes a scientific method that has been in place for many years, specifically for a cell with a *BRCA1* mutation. The only even arguably unique part of the method is the thought that the person has at the end of the process i.e. “this therapeutic worked” when used in the context of a *BRCA1* mutation or “this therapeutic did not work” in that context.

77. All of these claims (except claim 1 of ‘857 and claim 20 of ‘282) include comparisons not only of DNA, but of other derivatives of DNA such as RNA, and cDNA made from mRNA.

78. None of these claims is limited to identifying differences in genes that Myriad has itself identified as correlating with an increased risk of cancer. All identifying of differences, including those that are found in the future by anyone to correlate with an increased risk of cancer, are patented.

79. Myriad did not create any of the differences found in the genes. Nature did. Myriad did not cause any of the effects of those differences. Nature did. All of the effects of these differences occur in a person’s body as well as outside the body.

80. None of these claims is limited to “isolated” DNA.

IMPACT OF THE PATENTS

81. Defendant Myriad utilizes its patents by offering a test to determine if an individual has any mutations in the human *BRCA1* or *BRCA2* genes. The test consists of sequencing a person's gene, comparing it to either another gene in that person's body or one from another person, and reaching a conclusion about whether nature has caused a variant that increases that person's risk of breast and/or ovarian cancer.

82. There are thousands of doctors and scientists, including molecular pathologists, geneticists, and researchers, around the country, and the plaintiffs, who have the technical ability to look at human genes and who do so on a daily basis. The only thing that prevents those doctors and scientists from looking at the human *BRCA1* and *BRCA2* genes is Myriad's patents.

83. One of the conditions for receiving a patent is to disclose publicly all information about the patented thing. The purpose of that requirement is to enable others to "invent around" and build upon and improve the patented thing, thereby fostering scientific progress. Unlike most things that are granted patents, it is not possible to invent around the patented human *BRCA1* and *BRCA2* genes or correlations. These genes, their effects, and the correlations between the genes and disease were created by nature and exist in nature. They are pure information, and in order to build upon them, one needs to utilize the patented sequences, which is not permissible under the patents.

84. Because of its patents, Myriad maintains a monopoly over any genetic testing to determine the presence or absence of mutations on the human *BRCA1* or *BRCA2* genes. Thus, although others including plaintiffs have the technical ability to determine if a person has a mutation, and are willing to do so using non-patented

methods, they can be prohibited from doing so because of the patents on the *BRCA1* and *BRCA2* genes and can't tell any patient the results because of Myriad's enforcement of its patents.

85. Because Myriad maintains a monopoly on clinical testing to determine the presence or absence of mutations on the human *BRCA1* and *BRCA2* genes, the only types of tests that are offered to patients and the only mutations examined are those dictated by Myriad.

86. Myriad maintains the largest database of *BRCA1* and *BRCA2* data. It does not share the information in that database with the Breast Cancer Mutation Database set up by NIH to ensure the widest possible distribution of information about genes and breast cancer.

87. Myriad's monopoly has resulted in a disparity in the amount of information known about genetic mutations in *BRCA1* and *BRCA2* in ethnic groups other than Caucasians.

88. Gene patents can serve as a disincentive to innovation in molecular testing because they deny access to a vital baseline of genomic information that cannot be invented around. Moreover, threat of enforcement from a patent holder and ensuing litigation costs lead to a chilling effect as clinical laboratories are reluctant to develop new tests, even when new tests could directly benefit patients.

89. For at least some portions of the life of the patents, Myriad did not perform certain tests that were known to reveal additional mutations that increased the risk of breast and/or ovarian cancer. Myriad prohibited anyone else from offering those tests to patients even though it knew that they would provide women with essential

information about their risk of developing life-threatening cancer. Eventually, Myriad began to offer this additional testing, but chose to package it separately from its standard test.

90. Because of its patents on the *BRCA* genes, Myriad has the power to bar patients from obtaining testing other than through its laboratory. There are women, such as plaintiff Girard and any other women who have obtained full sequencing from Myriad, who cannot obtain a second opinion on their *BRCA* testing and are compelled to make major medical decisions based on a test that they cannot confirm. Plaintiff Limary, who received the result of variant of uncertain significance from Myriad, wants to obtain further testing and for information about her variant to be freely disclosed and studied.

91. Laboratories, such as that operated by Dr. Ledbetter, are increasingly adopting new generations of genetic sequencing technology that will permit faster, more comprehensive and potentially less expensive testing. That testing will be impeded by patents on genes that they cannot test.

92. Myriad charges more than \$3,000 for its exclusive Comprehensive BRACAnalysis test. Many researchers might be able to do the testing for a reduced cost.

93. There are women, including plaintiffs Ceriani and Fortune, who cannot afford the testing offered by Myriad and whose insurance Myriad will not accept. As a result, these women have not been tested.

94. Myriad offers another test, called BRACAnalysis Rearrangement Test or BART, that looks for large genetic rearrangements that are not caught by its standard Comprehensive BRACAnalysis test. Myriad will conduct BART testing for some

women who meet its criteria at no additional cost. However, other women must pay an additional price for BART testing – approximately \$650.

95. There are women, including plaintiffs Thomason and Raker, who have a significant personal or family history of cancer or who have been advised that they are appropriate candidates for BART testing by their doctors or genetic counselors, but whose BART testing was not included in the price of Myriad's standard Comprehensive BRCAAnalysis test. They have not been able to access the BART testing for large rearrangements. The *BRCA* gene patents gave Myriad the power to package this testing separately.

96. Researchers who want to look at the human *BRCA1* and *BRCA2* genes for research purposes are prohibited from doing so by the patents without the permission of the patent-holder.

97. Myriad has permitted some researchers to do pure research on the human *BRCA1* and *BRCA2* genes. Upon information and belief, Myriad has no official policy permitting the research and has not publicized its occasional permissiveness. At any time, Myriad can use its patents to prohibit researchers from doing research.

98. Researchers are chilled from engaging in research on the human *BRCA1* and *BRCA2* genes by the patents. Researchers are also chilled from engaging in research on other genes. It is increasingly clear that genes interact with other genes in ways that are not yet fully understood. Researchers are chilled from engaging in research on other genes that may interact with the *BRCA1* and *BRCA2* genes by the patents.

99. Researchers, such as plaintiffs Dr. Chung and Dr. Ostrer, study women for genetic research. Dr. Chung and some other geneticists believe that if they obtain the

results of a particular woman's *BRCA1/BRCA2* test, they are morally obligated to provide that woman with the option to find out the results. Genetic test results used in clinical management should be performed by a CLIA certified clinical diagnostic laboratory, and Myriad is the only such laboratory performing testing for *BRCA1/BRCA2* because Myriad will not permit other clinical laboratories to perform *BRCA1/BRCA2* testing except to a very limited extent.

100. The problems caused by patenting of DNA sequences are not limited to human genes inherited from one's parents. Every human body contains pathogens such as viruses and bacteria that also have DNA and genes. Modern medicine increasingly relies on analysis of the DNA of such entities to develop treatments for disease. If genes are patented, including human genes as well as their pathogens and commensals, there can be a serious and negative effect on diagnosis and treatment of disease.

101. The effect of the patents has been to stifle clinical practice and research on the genetic predispositions to breast and/or ovarian cancer. The public, and, in particular, women, have suffered unnecessarily as a result.

CAUSES OF ACTION

102. Because human genes are products of nature, laws of nature and/or natural phenomena, and abstract ideas or basic human knowledge or thought, the challenged claims are invalid under Article 1, section 8, clause 8 of the United States Constitution and 35 U.S.C. § 101.


103. All of the challenged claims represent patents on abstract ideas or basic human knowledge and/or thought and as such are unconstitutional under the First and Fourteenth Amendments to the United States Constitution.

PRAYER FOR RELIEF

For all of these reasons, plaintiffs respectfully ask the Court to:

1. Declare invalid and/or unenforceable
 - a. Claim 1, 2, and 5, 6, 7 and 20 of patent 5,747,282
 - b. Claims 1, 6, and 7 of patent 5,837,492
 - c. Claim 1 of patent 5,693,473
 - d. Claim 1 of patent 5,709,999
 - e. Claim 1 of patent 5,710,001
 - f. Claim 1 of patent 5,753,441
 - g. Claims 1 and 2 of patent 6,033,857;
2. Enjoin defendants from taking any actions to enforce these claims of these patents;
3. Grant plaintiffs attorneys' fees and costs; and
4. For such other and further relief as the Court deems just and necessary.

Respectfully submitted,


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*Motion for admission to the
Southern District of New York
bar to be filed