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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09 Civ. 4515 (RWS)

ECF Case

PLAINTIFFS' RULE 56.1 STATEMENT OF MATERIAL FACTS

Pursuant to Local Rule 56.1, plaintiffs submit the following statement of material facts.

PLAINTIFFS

1. 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 believes that a single gene "is a product of nature and should not be patentable . . . 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.'" D. Sobel ¶¶ 2, 4-5.[1]

2. 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. It is ACMG's position that "Genes and their mutations are naturally occurring substances that should not be patented." D. Watson ¶¶ 2, 4-5.

3. 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,

[1] D. ____ identifies a declaration filed in support of the motion for summary judgment. Thus, D. Sobel is the declaration of Dr. Mark Sobel.

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 believes "the practice of gene patenting harms patients, impedes advances in medicine, and limits those in the practice of pathology and laboratory medicine from doing what they are educated to do – provide high quality health care and engage in research that will enhance the practice of medicine and patient care." D. Ball ¶¶ 2, 5.

4. 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. CAP is an advocate for high-quality and cost-effective medical care. CAP "believes that genes and their variants (to include mutations) are naturally occurring substances and should not be patented." D. Scott ¶¶ 2, 4-5.

5. 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 and Arupa Ganguly, another plaintiff, designed tests to screen the *BRCA1* and *BRCA2* genes in their lab and provided screening to approximately 500 women per year starting in 1996 until they were forced to stop offering testing by Myriad. D. Kazazian ¶¶ 1-5.

6. Plaintiff ARUPA GANGULY, PhD, is an Associate Professor in the Department of Genetics at the Hospital of the University of Pennsylvania. Dr. Ganguly's work previously included *BRCA1/2* screening for both research and clinical purposes. She was compelled to stop *BRCA* screening after Myriad accused her lab of violating the patents. D. Ganguly ¶¶ 1, 3-4.

7. 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. Because of the patents, Dr. Chung currently cannot tell research subjects in her studies the results of their *BRCA1/2* tests and cannot offer clinical *BRCA* testing services. D. Chung ¶¶ 1-9, 11-13, 16.

8. 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. 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. Because of the patents, Dr. Ostrer currently cannot tell research subjects in his studies the results of their *BRCA1/2* tests and cannot offer clinical *BRCA* testing services. D. Ostrer ¶¶ 1-4, 8, 10, 12.

9. 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 testing services for individuals with or at risk for genetic diseases. Because of the patents, Dr. Ledbetter cannot offer comprehensive *BRCA* genetic testing to patients. D. Ledbetter ¶¶ 1-8, 16.

10. 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. These laboratories would offer *BRCA* genetic testing but for the patents. D. Ledbetter ¶¶ 1, 16.

11. Plaintiff ELLEN MATLOFF, M.S., 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 would like to have the option to send patient samples to laboratories other than Myriad Genetics for *BRCA1/2* sequencing. D. Matloff ¶¶ 1-4, 11.

12. 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 explains the results for the women. Ms. Reich would like to have the option to send patient samples to laboratories other than Myriad Genetics for *BRCA1/2* sequencing. D. Reich ¶¶ 1-3, 8.

13. Plaintiff BREAST CANCER ACTION (BCA) is a national organization of approximately 30,000 members based in San Francisco, California. Breast Cancer Action is dedicated to carrying the voices of people affected by breast cancer in order to inspire and compel the changes necessary to end the breast cancer epidemic. Its members include breast cancer survivors, family members of people diagnosed with breast cancer and other people affected by or concerned about breast cancer. BCA advocates for policy changes directed at achieving prevention, finding better treatments, and reducing the incidence of breast cancer; provides information about breast cancer to anyone who needs it via newsletters, web sites, e-mail and a toll-free number; and organizes people to get involved in advocacy to advance its policy goals. BCA believes that the *BRCA* gene patents interfere with people's ability to participate fully in decisions relating to breast cancer treatment and to gain access to information about breast cancer and quality health care. D. Brenner ¶¶ 1-4.

14. Plaintiff BOSTON WOMEN'S HEALTH BOOK COLLECTIVE (BWHBC), doing business as Our Bodies Ourselves (OBOS), 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. OBOS believes that the BRCA gene patents are a barrier to a woman's ability to know about her body and make informed health decisions. D. Norsigian ¶¶ 1-4, 7.

15. 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. However, Myriad will not accept the MassHealth coverage. Ms. Ceriani is unable to pay the full cost out-of-pocket. D. Ceriani ¶¶ 1-5.

16. Plaintiff RUNI LIMARY is a 32-year-old Asian-American woman who was diagnosed with aggressive breast cancer in 2005. Ms. Limary obtained *BRCA* testing through Myriad and received the following result: "genetic variant of uncertain significance." D. Limary ¶¶ 1-5.

17. 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 *BRCA* sequencing. D. Girard ¶¶ 1-7.

18. 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. 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. D. Fortune ¶¶ 1-5.

19. 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 offered by Myriad 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. Ms. Thomason is unable to afford the extra cost. D. Thomason ¶¶ 1-8.

20. 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 offered by Myriad 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 not cover the full cost of that test. Ms. Raker is unable to afford the extra cost. D. Raker ¶¶ 1-9.

EXPERT DECLARANTS

21. Dr. John Sulston, Nobel Prize winner for Physiology or Medicine and Chair of the Institute for Science, Ethics, and Innovation at the University of Manchester (UK), is qualified to express expert opinions in the area of human genetics. D. Sulston ¶¶ 1-9.

22. Dr. Wayne Grody, Professor in the Department of Pathology and Laboratory Medicine, Pediatrics, and Human Genetics at the UCLA School of Medicine, is qualified to express expert opinions in the area of human genetics. D. Grody ¶¶ 1-3.

23. Dr. Debra Leonard, Professor of Pathology and Laboratory Medicine at Weill Cornell Medical College and New York-Presbyterian Hospital, is qualified to express expert opinions in the area of human genetics. D. Leonard ¶¶ 1-10.

24. Dr. Christopher Mason, Post-doctoral Associate in the Program on Neurogenetics at Yale University, is qualified to express expert opinions in the area of human genetics. D. Mason ¶¶ 1-3.

25. Dr. Susan Love, Clinical Professor of Surgery at the University of California at Los Angeles and President of the Dr. Susan Love Research Foundation, is qualified to express expert opinions in the area of breast cancer treatment and research. D. Love ¶¶ 1-7.

26. Dr. Elizabeth Swisher, Associate Professor of Obstetrics and Gynecology at the University of Washington School of Medicine, is qualified to express expert opinions in the area of human genetics. D. Swisher ¶¶ 1-9.

27. Dr. Shobita Parthasarathy, Assistant Professor of Public Policy at the University of Michigan School of Public Policy, is qualified to express expert opinions in the area of the history of human genetic testing and research. D. Parthasarathy ¶¶ 1-7.

28. Dr. Myles Jackson, the Dibner Family Professor of the History and Philosophy of Science and Technology at the Polytechnic Institute of New York University, reviewed 12 court cases involving patents that were challenged, including 9 Supreme Court cases to compare the scientific principles and products either granted or denied patents. Dr. Jackson is qualified to express expert opinions in the area of science and patents. D. Jackson ¶¶ 1-6.

29. Dr. Mildred Cho, Associate Director of the Stanford Center for Biomedical Ethics, is qualified to express expert opinions on the need or lack thereof for gene patents to spur

research into genes and the effect of such patents on research and clinical practice. D. Cho ¶¶ 1-8.

30. Dr. Madhuri Hegde, Senior Laboratory Director at the Emory Genetics Laboratory, is qualified to express expert opinions in the area of human genetics. D. Hegde ¶¶ 1-5.

31. Dr. Roger Hubbard, President and Chief Executive Officer of Molecular Pathology Laboratory Network, Inc., is qualified to express expert opinions in the area of human genetics. D. Hubbard ¶¶ 1-6.

32. Dr. Jeffrey Kant, Director of the Division of Molecular Diagnostics at the University of Pittsburgh Medical Center, is qualified to express expert opinions in the area of human genetics. D. Kant ¶¶ 1-3.

33. Dr. Haig Kazazian is qualified to express expert opinions in the area of human genetics. D. Kazazian ¶¶ 1-3.

34. Dr. Arupa Ganguly is qualified to express expert opinions in the area of human genetics. D. Ganguly ¶¶ 1-3.

35. Dr. Wendy Chung is qualified to express expert opinions in the area of human genetics. D. Chung ¶¶ 1-7.

36. Dr. Harry Ostrer is qualified to express expert opinions in the area of human genetics. D. Ostrer ¶¶ 1-3.

37. Dr. David Ledbetter is qualified to express expert opinions in the area of human genetics. D. Ledbetter ¶¶ 1-6.

38. Ms. Ellen Matloff is qualified to express expert opinions in the area of human genetics. D. Matloff ¶¶ 1-4.

39. Ms. Elsa Reich is qualified to express expert opinions in the area of human genetics. D. Reich ¶¶ 1-2.

GENES

40. Genes and human genetic sequences are not inventions of humans. They are naturally occurring and are products of nature. D. Sulston ¶ 10; D. Ostrer ¶ 14; D. Chung ¶ 25; D. Mason ¶ 33; D. Ledbetter ¶ 27; D. Leonard ¶ 15.

41. Genes are the basic units of heredity in all living organisms. A gene is a segment of DNA, the molecule that makes life possible. DNA encodes the instructions for the development and functioning of each of our cells. D. Sulston ¶ 11.

42. Each human gene has its place on one of the twenty-four chromosomes (numbered 1-22, plus the X and Y sex chromosomes), which together constitute the whole genome. D. Sulston ¶ 15.

43. Scientists have long recognized the role of genes in heredity. But it wasn't until 1953 – the year that Watson and Crick identified the double-helix structure of DNA – that the scientific community came to understand how DNA plays its role. This central discovery for modern biology made it immediately apparent that the structure embodies a linear digital code. This code – nucleic acid sequence – gets copied more or less faithfully from one generation to the next. D. Sulston ¶ 13; D. Mason ¶¶ 8-10, 13.

44. The genetic code is similar to the English alphabet, except that it consists of four letters (A, T, C, and G) rather than 26 (A through Z). The letters of the genetic alphabet correspond to 4 chemical bases (adenine (A), thymine (T), cytosine (C) and guanine (G)). Each gene is typically thousands of bases long, and its sequence of As, Ts, Cs and Gs usually encodes a protein. The code is a set of three-letter words – for example TTT, CAG – each of which

corresponds to one of the twenty amino acids that are the building blocks of proteins. D. Sulston ¶¶ 14-15.

45. When the body creates proteins, it relies on the processes of transcription and translation. During transcription, the DNA unwinds itself inside the cell and a temporary copy is created called a messenger RNA (mRNA). This mRNA contains sections that are unnecessary for the creation of proteins. These regions, known as introns, are removed by the body as a natural process because they will not be necessary for creation of a protein. The regions that remain are called exons and are necessary for creation of a protein. Translation is the naturally-occurring process of converting the processed mRNA into a protein. The tri-nucleotide segments of mRNA (codons) are converted into amino acids, which create the poly-peptide (protein). In other words, the DNA represented by three letters creates a single amino acid. The amino acids, when linked together, create a protein and the protein does the work of the body. D. Mason ¶¶ 11-12.

46. The genome is contained within almost every cell of the body. It defines obvious traits such as skin tone, eye color, and sex, but also directs the manifestation of very complex traits such as Alzheimer's disease. There are approximately 25,000 genes that make up the human genome. D. Mason ¶¶ 4-5; *see* D. Sulston ¶¶ 10-11.

47. A genetic sequence is the sequence of letters of a specified section of the human genome. D. Sulston ¶ 16; D. Mason ¶ 13; D. Chung ¶ 10.

48. A genetic sequence is biological information. Like strings of alphabetic text, the genetic sequences are the same regardless of the medium. Whether the data reside in the DNA of an organism, a computer, or as letters on a printed page, the information is the same. The

physical form in which they occur is unimportant; what matters is the informational content. D. Sulston ¶ 16.

49. The information contained in the genetic sequence is a product of nature. The informational content of a human genetic sequence is fixed. While many inventive steps may have been necessary to allow scientists to extract and read a genetic sequence, the ordering of the 4 letters is determined by nature. D. Sulston ¶ 17.

50. Genes are so basic to science that any restriction that prevents scientists from looking at the genes themselves or examining the effects of the genes is fundamentally inconsistent with the advancement of human knowledge. D. Sulston ¶¶ 28, 37; D. Ostrer ¶ 14; D. Chung ¶ 25; D. Swisher ¶ 21; D. Ledbetter ¶ 27; D. Love ¶ 19.

51. Except for identical twins, no two humans are genetically the same. Variation in the human genome is very common, and each person is estimated to be 99.5% similar, or to have one to five differences every 1000 base pairs (bp). D. Mason ¶ 14; D. Sulston ¶ 12.

52. Small scale variation can occur, manifested as slight sequence differences between the same genes in different individuals. Thus, for example, a sequence of a gene represented by …GACTCG… might contain a variation that omits the first C (GATCG) or that adds an extra C at that point (GACCTCG) or that reverses the order of two of the letters (CCATCG). D. Mason ¶ 16.

53. Large scale variation can also occur in the genome, such as the addition or deletion of substantial chromosomal regions. Thus, a particular gene may omit several hundred letters at one point or may add several hundred letters where they do not normally exist. Structural variants also can occur, so that up to millions of nucleotides can be missing or

duplicated. These extra copies or missing copies of the genome that are larger than 1000 bp are called copy number variants. D. Mason ¶¶ 15, 18.

54. Some variants appear to have little or no effect on the body's processes. There are also variants whose significance is currently unknown ("variants of uncertain significance"). Other variants that interfere with a body's processes, including those that appear to correlate with an increased risk of particular diseases, are called mutations. Mutations can be in the form of the insertion or deletion of a single letter, or rearrangements, deletions or repeated segments of groups of letters. D. Mason ¶ 19; D. Sulston ¶ 18.

55. Genetic sequencing is the process by which one "reads", or determines the ordering of the 4 letters (A, T, C, and G) within a specified part of the genome. In order to sequence, or read a gene, one has to remove it from the cell of an organism and place it in a form so that it can be replicated outside of the body. Most commonly, scientists use a technique called PCR to replicate small segments of the gene many times over. Amplifying these segments allows scientists to read out the genetic code. D. Sulston ¶¶ 20, 25; D. Chung ¶ 10.

56. Sequencing of a gene can be done by several processes that are well-known and understood by scientists. Anyone skilled in molecular biology has the knowledge and methods to sequence and examine any part of the human genome. D. Chung ¶ 10; D. Mason ¶¶ 24-30; D. Swisher ¶¶ 23-24; D. Kant ¶ 5; D. Sulston ¶¶ 20-21, 23; D. Ledbetter ¶¶ 21-22; D. Leonard ¶ 18.

57. Scientists and clinicians sequence and analyze genes literally every day. D. Chung ¶¶ 10-11; D. Hegde ¶¶ 6-7; D. Hubbard ¶¶ 3-6; D. Mason ¶¶ 22, 31; D. Sulston ¶¶ 21-22; D. Ledbetter ¶¶ 9-10, 22.

58. The process of sequencing is designed simply to illuminate the information that nature has dictated in that person's genome. In that respect, sequencing is essentially no

different than looking at something through a microscope. It takes something created by nature but too small to be seen and makes it visible. D. Mason ¶ 23; D. Sulston ¶ 18.

59. The process of sequencing a gene does not change the informational content of that gene. The resultant sequence is informationally and functionally identical to the sequence found inside the body. D. Sulston ¶ 27; D. Chung ¶ 10; D. Mason ¶¶ 32-33.

60. The alterations or mutations in the gene that scientists are able to see after sequencing the gene were made by nature, not by the process of sequencing or by scientists, and the effect of those alterations or mutations is dictated by nature, not by any scientist. D. Sulston ¶ 27; D. Chung ¶ 10.

61. Gene sequencing sometimes involves cDNA or complementary DNA. mRNA that is the result of the natural process of transcription (*see supra* ¶ 45) is reverse-transcribed into cDNA. Thus, the coding effect of a cDNA is the same as that of the original DNA from which it was originally derived. Thus, cDNA means a purely coding polynucleotide sequence that is produced from RNA that has had all of its non-coding regions (called introns) removed. D. Leonard ¶ 75.

62. Complementary DNA does not exist in the body but is simply a mirror of the RNA which does exist in the body. In the body, certain of the nucleotides, represented by the letters, always bind or attach to certain other nucleotides or letters. G always links to C, and A always links to T. If the RNA in the body is a G, then the cDNA in the lab is a C. Knowing that the cDNA is a C tells a scientist without exception that the RNA was a G. In other words, the cDNA is a sequence of nucleotides that "complements" the RNA. Because the RNA was a mirror of the DNA, the cDNA is again identical to the DNA. The only difference is the introns

have been removed. Thus, the functional sequence of the cDNA is identical to the functional sequence of the DNA. D. Mason ¶¶ 28-29, 32.

63. The sequence of a cDNA is dictated not by scientists but by nature. Even though the structure of cDNA does not exist in precisely the same form in the body, for literally all practical and information-based purposes its sequence is identical to that in the body. D. Mason ¶ 32.

64. "Isolated DNA" is a fragment of DNA that is separated from other cellular components. This separation could be accomplished through a number of well known techniques. D. Grody ¶ 13; D. Leonard ¶ 33.

65. "Isolating and purifying" a gene (removing it from the body and placing it in a form so that it can be sequenced and possibly used in other ways) is simply copying it into another format. D. Sulston ¶ 26.

66. Gene sequencing is used in diagnostic testing. Gene sequences are examined to determine if they contain any alterations or mutations that have been associated with a particular condition. D. Chung ¶ 10; D. Swisher ¶¶ 23-26; D. Mason ¶ 21; D. Sulston ¶ 24.

67. Scientists often refer to the "wild-type" or "normal" gene, which is the gene without variations. However, the notion that there exists a gene without variations is increasingly misleading. Newfound recognition of the high frequency of variation between individuals has implications for the definition (and patenting) of genes: such variation reinforces the emerging idea that no single DNA sequence can adequately capture either the human genome or a single gene, both of which occur naturally in a variety of forms. D. Mason ¶ 17.

68. Gene sequences can have alterations from the wild-type sequence that are caused by nature. D. Chung ¶ 10; D. Mason ¶ 20; D. Sulston ¶¶ 19, 27; D. Ledbetter ¶ 26.

69. Full sequencing is often the method used to identify when there is a substitution of one of the letters at a single point or where the insertion or deletion of a small number of bases has occurred. D. Swisher ¶ 23.

70. Full sequencing can miss large genomic rearrangements where whole sections of the gene have been deleted or moved to a different part of the sequence. Other tests have been developed that better detect large rearrangements. D. Swisher ¶¶ 23-24; D. Ledbetter ¶¶ 16-17.

71. When alterations or mutations are found in a gene sequence, they can be further investigated to see if they have any significance such as for increasing the propensity to a particular disease. D. Chung ¶ 10; D. Sulston ¶ 24.

72. The significance of alterations in a gene sequence is caused by nature. D. Chung, ¶ 10; D. Mason ¶ 20; D. Sulston ¶ 27; D. Ledbetter ¶ 26.

73. The significance of any person's genetic sequence, including its relationship to any disease, is dictated by nature. D. Mason ¶ 32.

74. From the beginning of the Human Genome Project, an international project initiated in 1990 with the aim of sequencing an entire human genome, most scientists and even some private companies recognized the importance of keeping the genome freely available to all. In 1994, the pharmaceutical company Merck funded a massive drive to generate genetic sequences and place them into public databases. D. Sulston ¶¶ 22, 29.

75. In 1996, a group of 50 of the most prominent geneticists in the world who were involved with the sequencing of the human genome adopted the Bermuda principles which included the mandate that all "human genomic sequence information should be freely available and in the public domain in order to encourage research and development and to maximize its benefit to society." D. Sulston ¶ 33.

***BRCA1/2* GENES**

76. Mutations on the *BRCA1* and *BRCA2* genes have been associated with a predisposition to develop breast and ovarian cancer. *BRCA1* is a particular portion of DNA found on chromosome 17. *BRCA2* is a particular portion of DNA found on chromosome 13. D. Leonard ¶ 39.

77. Breast cancer is the most frequently diagnosed cancer worldwide, and is heavily publicized as the leading cause of cancer death for women in Britain and the second leading cause of cancer death for women in the United States. D. Parthasarathy ¶ 8.

78. The relationship between mutations in the *BRCA1/2* genes and breast and ovarian cancer incidence is complex. Estimates for elevated risk of breast cancer for women who have *BRCA1* or *BRCA2* mutations have ranged from 3 to 86 percent. Male carriers of mutations are also at increased risk of breast and prostate cancers. D. Love ¶ 10; D. Parthasarathy ¶ 9.

79. Ovarian cancer is the eighth most common cancer in women and causes more deaths in the Western world than any other gynecologic cancer. D. Swisher ¶ 10.

80. Between 10 and 15% of ovarian cancers are inherited genetically. For women who are diagnosed under the age of 50 years old, approximately 80% of inherited ovarian cancers are caused by *BRCA1* mutations and approximately 20% are caused by *BRCA2* mutations. Women with inherited *BRCA1* mutations have a 40-52% cumulative risk of ovarian cancer by the time they reach 70 years old. For women with inherited *BRCA2* mutations, the risk is approximately 15-25%. D. Swisher ¶ 11.

81. *BRCA1/2* mutations and the correlations between the mutations and the increased risk of disease are created by nature. D. Mason ¶ 20.

82. The existence of *BRCA1/2* mutations is an important factor in clinical care of breast and/or ovarian cancer. A patient will not only learn her risk for hereditary breast and ovarian cancer, but also can gain information that may be useful in determining prevention and treatment options. This information is useful for women who are facing difficult decisions regarding whether or not to undergo prophylactic surgery, hormonal therapy, chemotherapy, and other measures. D. Swisher ¶ 12; D. Love ¶¶ 8-19.

83. Testing results for the *BRCA1/2* genes can be an important factor in structuring an appropriate course of cancer treatment. Certain forms of chemotherapy can be more effective in treating *BRCA* mutation carriers. D. Swisher ¶ 13; D. Love ¶ 18.

84. Myriad Genetics offers multiple forms of *BRCA1/2* testing to the general public. Its standard test is a full sequencing test called Comprehensive BRACAnalysis. In 2006, it started offering a supplemental test to Comprehensive BRACAnalysis called the BRACAnalysis Rearrangement Test ("BART"). Unless a patient meets certain criteria, the patient must pay an extra fee for BART. Myriad also offers more limited forms of testing. D. Swisher ¶¶ 29-30; D. Reich ¶ 10; D. Parthasarathy ¶ 26.

85. Many researchers, clinicians, and molecular pathologists have the personnel, equipment, and expertise to sequence and analyze genes, including the *BRCA1* and *BRCA2* genes. D. Kazazian ¶ 11; D. Ganguly ¶¶ 3, 10, 14; D. Chung ¶¶ 11-12, 18; D. Ostrer ¶¶ 8-9; D. Ledbetter ¶¶ 16-18; D. Hegde ¶¶ 8-12; D. Mason ¶ 22; D. Kant ¶ 5.

PATENTS

86. The United States Patent and Trademark Office (USPTO) granted the patent claims at issue in this case. Patent 5,747,282 (Claims 1, 2, 5, 6, 7, and 20), Patent 5,837,492

(Claims 1, 6, and 7), Patent 5,693,473 (Claim 1), Patent 5,709,999 (Claim 1), Patent 5,710,001 (Claim 1), Patent 5,753,441 (Claim 1), Patent 6,033,857 (Claims 1 and 2).[2]

87. Patents prevent anyone from using what has been patented. 35 U.S.C. § 271.

88. Uses of the genes at stake in the patent claims in this case include research into or clinical testing of the *BRCA1* and *BRCA2* genes. D. Sobel ¶¶ 3-5; D. Watson ¶¶ 3-5; D. Ball ¶¶ 2-5; D. Scott ¶¶ 2-5.

89. The patent claims at issue in this case do not claim specific methods of sequencing genes. The patents.

90. If someone had the ability to sequence her own genes, she could utilize non-patented methodologies to sequence those genes, but could be infringing if she sequenced her own *BRCA1* and *BRCA2* genes. D. Norsigian ¶ 7.

91. A patent on a gene sequence and any mutations of that gene applies regardless of the person from whom the gene is taken or the sequencing process that is used. D. Sulston ¶ 27.

92. Certain of the patent claims at issue in this case cover the *BRCA1* and *BRCA2* genes without known alterations or mutations. D. Ravicher, Exs. 1, 6 (Patents '282 (Claims 1, 2, 5, 6) and '492 (Claim 1)).

93. The *BRCA1* and *BRCA2* genes are naturally-occurring and the sequence of nucleotides in them is created by and dictated by nature. They are products of nature. *See supra* ¶¶ 40-50.

94. The patents are on wild-type *BRCA1* and *BRCA2* human genes. None of the claim language covers genes that have been engineered by humans – their sequence and function are dictated by nature. D. Grody ¶¶ 10-33, 46-48; D. Leonard ¶¶ 30-53, 66-68.

[2] Hereinafter, references to "The patents" includes all of the patents at issue in this case. The patents are attached as Exhibits 1-7 of the Declarations of Daniel B. Ravicher.

95. The claims that are on genes are on "isolated DNA." Isolated DNA is just a fragment of DNA that has been separated from other things in order to be read. D. Grody ¶ 13; D. Leonard ¶ 33.

96. The process of sequencing a gene does not change the informational content of that gene. The isolated sequence is informationally and functionally identical to the sequence found inside the body. D. Sulston ¶ 27; D. Chung ¶ 10; D. Mason ¶¶ 32-33.

97. Certain of the patent claims cover the *BRCA1* and *BRCA2* genes in their altered or mutated form or gene alterations or mutations. D. Ravicher, Exs. 1, 2, 6 (Patents '473 (Claim 1), '282 (Claim 7), and '492 (Claims 6 and 7)).

98. Some of Myriad's patents cover mutations that were found by other scientists. Myriad filed for a patent on the *BRCA2* gene a day before a team of British researchers published the *BRCA2* sequence in the scientific journal, *Nature.* Scientists in the breast cancer genetic community tend to credit this team for being the first to sequence *BRCA2* rather than Myriad. D. Sulston ¶¶ 30-32; D. Parthasarathy ¶¶ 12-13.

99. The *BRCA1* and *BRCA2* gene sequences with mutations are naturally-occurring and products of nature. *See supra* ¶¶ 51-54, 60-72.

100. The "altered" or "mutated" DNA covered by the patent claims refers to naturally-occurring alterations or mutations in the *BRCA1* and *BRCA2* genes. D. Grody ¶¶ 37-39, 46-48; D. Leonard ¶¶ 57-59, 66-68.

101. Certain of the patent claims cover "analyzing" or looking at the genes. D. Ravicher, Ex. 3 (Patent '999 (Claim 1)).

102. "Analyzing" a *BRCA1* gene sequence for an alteration, as described in '999 cl. 1, simply refers to any method of looking at a *BRCA1* nucleotide sequence and inherently presumes

that the sequence is already provided. There are numerous methods for looking at or analyzing a sequence. D. Grody ¶¶ 43-45; D. Leonard ¶¶ 63-65.

103. Claim 1 of patent '999 patents looking at the *BRCA1* gene for alterations even if that person used a non-patented methodology to do so, including simply looking at a given sequence and thinking about whether it contains an alteration. Patent '999 (Claim 1).

104. Certain of the patent claims cover comparing two genes and then thinking that they are the same or different. D. Ravicher, Exs. 4, 5, 7 ((Patents '001 (Claim 1), '441 (Claim 1), and '857 (Claims 1 and 2)).

105. "Comparing" two genetic sequences, as described in '001 cl. 1, '441 cl. 1, and '857 cls. 1 and 2, means looking at two or more sequences to see if they are different in any way. "Comparing" two sequences inherently presumes that such sequences are already provided. D. Grody ¶¶ 40-42; D. Leonard ¶¶ 60-62.

106. Claim 1 of patents '001, '441, and '857 patent the mental process of comparing two given genetic sequences and thinking "these two genes are the same" or "these two genes are different." D. Ravicher, Exs. 4, 5, 7 (Patents '001 (Claim 1), '441 (Claim 1), and '857 (Claims 1 and 2)).

107. Claim 2 of '857 patents comparing a gene with the wild-type gene, wherein an alteration in the gene indicates a predisposition to breast cancer. D. Ravicher, Ex. 7 (Patent '857 (Claim 2)).

108. Claim 2 of patent '857 patents the mental process of comparing two genes and recognizing that an alteration in the gene "indicates a predisposition to" breast cancer. *Id.* Patent '857 (Claim 2).

109. Patents on correlations or associations between a gene sequence and a greater risk of disease allow the patent holder to control the use of that medical fact. D. Leonard ¶ 19.

110. Claim 20 of '282 patents an abstract method for comparing cell growth rates to screen for a possible cancer therapeutic. The claim covers comparing the growth rates of two cells contained an altered *BRCA1* gene, one of which has been exposed to the possible cancer therapeutic. Patent '282 (Claim 20).

111. The act of comparing covered by '282 claim 20 means simply looking at two or more things – such as cells – to determine if there is a difference between them – such as growth rates. *See* D. Grody ¶¶ 40-42; D. Leonard ¶¶ 60-62.

112. Claim 20 of patent '282 patents the mental process of comparing the cell growth rates and "this chemical had a therapeutic impact" on a cell with a *BRCA1* altered gene or "this chemical did not have a therapeutic impact." D. Ravicher, Ex. 1 (Patent '282 (Claim 20)).

113. The USPTO granted these patent claims pursuant to a formal written policy that permits the patenting of "isolated and purified" genes and pursuant to a practice that permits such patents and the patenting of correlations created by nature between natural elements of the body and a predisposition to disease. Utility Examination Guidelines, 66 Fed. Reg. 1,093 (Jan. 5, 2001).

114. It is scientifically inaccurate to compare DNA and genes to chemicals. One cannot "invent" a slightly different gene than that which occurs in nature – whether natural or mutated – in the way that one can invent a slightly different chemical. Because one can invent around chemicals, i.e. can synthetically produce new and better chemicals, but cannot invent around genes, they are not comparable. D. Jackson ¶¶ 12-16, 49.

115. The dye that was declared unpatentable in *Cochrane v. Badische*, 111 U.S. 293 (1884), is scientifically analogous to the patent claims at issue in this case. In both instances, the patent sought was over a product, not a process, and in both instances, the product is functionally identical to the product in nature. D. Jackson ¶¶ 7-16.

116. As with *Cochrane*, the paper pulp that was declared unpatentable in *The Wood-Paper Patent*, 90 U.S. 566 (1874), is scientifically analogous to the patent claims at issue in this case. Even though the pulp in that patent was superior in purity to previous wood pulp, it was identical in function. D. Jackson ¶¶ 17-25.

117. The adrenaline that was declared patentable in *Parke-Davis and Co. v. H.K. Mulford*, 189 F. 95 (S.D.N.Y. 1911), *aff'd* 196 F.496 (2nd Cir. 1912), is not scientifically analogous to the patent claims at issue in this case because the process for purifying the adrenaline relies solely on human intervention, while genes and their splicing can occur naturally without human intervention. D. Jackson ¶¶ 26-31.

118. The bacteria grouping that was declared unpatentable in *Funk Brothers v. Kalo*, 333 U.S. 127 (1948), is scientifically analogous to the patent claims at issue in this case because the bacteria grouping, though structurally different from any grouping found in nature, continued to perform in their natural way, just as the patented genes function in the same way as genes in nature. D. Jackson ¶¶ 32-34.

119. The patented B-12 in *Merck and Co. v. Olin Mathieson*, 253 F.2d 156 (4th Cir. 1958) is not scientifically analogous to the patent claims at issue in this case. The B-12 patent did not cover all uses of B-12 but the patent claims here cover all uses of the genes. In addition, the function of the patented B-12 was different from that found in nature, while the function of the patented genes in this case is identical to that found in nature. D. Jackson ¶¶ 35-37.

120. The tungsten that was declared unpatentable in *G.E. v. De Forest Radio*, 28 F.2d 641 (3rd Cir. 1928), is scientifically analogous to the patent claims at issue in this case. Purification of tungsten was insufficient to alter the fact that the function of the tungsten, like the functions of genes, was dictated by nature and it was therefore unpatentable. D. Jackson ¶¶ 38-40.

121. The new bacterium that was declared patentable in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), is not scientifically analogous to the patent claims at issue in this case. The bacterium was newly created and genetically engineered. D. Jackson ¶ 41.

122. The mathematical algorithms that were declared unpatentable in *Parker v. Flook*, 437 U.S. 584 (1978) and *Gottschalk v. Benson*, 409 U.S. 63 (1972) are scientifically analogous to the patent claims at issue in this case. The patent claims in those cases attempted to preclude all uses of the algorithms just as the gene "composition" claims in this case preclude all uses of the genes and the method claims prevent all methods of comparing genes. D. Jackson ¶¶ 42-45, 47-48.

123. The mathematical algorithm that was declared unpatentable in *Diamond v. Diehr*, 450 U.S. 175 (1981) is not scientifically analogous to the patent claims at issue in this case for the opposite reason. It did not preclude all uses of the algorithm. D. Jackson ¶¶ 46-48.

124. A specific method used to sequence genes is a process that could be patented if it met other patentability requirements. Patents on processes do not apply to the data – such as the genes – flowing through them. This is analogous to claiming a small thing viewed through the common microscope. D. Leonard ¶ 17; D. Sulston ¶ 23.

ENFORCEMENT OF PATENTS

125. Dr. Kazazian and the University of Pennsylvania received several cease and desist letters from defendant Myriad as a result of work that was being done in the Genetic Diagnostic Laboratory of the Department of Genetics. Dr. Kazazian was also told by defendant Myriad's Chief Science Officer during an in-person meeting that Myriad planned to stop the *BRCA* testing activity that Dr. Ganguly and he were performing. In November 1998, Myriad sued the University of Pennsylvania for infringing the *BRCA* patents. *Myriad Genetics v. University of Pennsylvania*, 2:98-cv-00829 (D. Utah) (filed November 19, 1998). As a result, 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. D. Kazazian ¶¶ 4-7; D. Ganguly ¶¶ 4-10; D. Parthasarathy ¶ 28.

126. Dr. Kazazian and Dr. Ganguly were screening for *BRCA* mutations using a different methodology than that used by Myriad, but were precluded from using that methodology by Myriad because the patents are on the genes themselves, not on the methodology for screening. D. Kazazian ¶ 9; D. Parthasarathy ¶ 23.

127. Myriad sent a letter to Barbara Weber, principal investigator on a project sponsored by the National Cancer Institute, regarding how Myriad's patent position might impact research sponsored by the Institute. As a result of that letter, the University of Pennsylvania laboratory that was doing *BRCA* analyses for Dr. Weber, stopped doing those analyses. D. Ganguly ¶ 12.

128. Myriad sent a letter to Georgetown University demanding that Georgetown stop sending genetic samples to the University of Pennsylvania laboratory. As a result of that letter,

the University of Pennsylvania laboratory that was doing *BRCA* analyses for Georgetown stopped doing those analyses. D. Ganguly ¶ 13.

129. Myriad and Oncormed, another company that undertook *BRCA*-related activity, were involved in a series of lawsuits against each other regarding patents that covered various aspects of the *BRCA1* gene sequence. D. Parthasarathy ¶ 27.

130. Sometime in or around December 2000, the director of the Yale DNA Diagnostics Lab received a cease and desist letter from Myriad concerning *BRCA1/2* genes. As a result of that letter, Yale ceased doing *BRCA1/2* testing. D. Matloff ¶ 7.

131. In 2005, Ms. Matloff contacted Myriad to obtain permission so that the Yale DNA Diagnostic Lab could do screening for mutations caused by large rearrangements, which Myriad was not then doing. Myriad denied permission. D. Matloff ¶ 8.

132. Myriad wrote to Dr. Ostrer prohibiting him from engaging in any *BRCA1* or *BRCA2* testing unless he entered a license, and even then the company would only allow him to do all but the most limited *BRCA1* and *BRCA2* testing. Dr. Ostrer refused that license because it was too narrow to allow him to do any meaningful *BRCA*-related activity. D. Ostrer ¶ 7.

133. A valid scientific survey of laboratory directors in the United States revealed that 25% had stopped performing a clinical test because of a gene patent or license. D. Cho ¶¶ 11-15.

134. A valid scientific survey of laboratory directors in the United States revealed that of those who stopped performing a clinical test because of a gene patent or license, the largest number stopped doing *BRCA1* and *BRCA1* testing (and the same number stopped ApoE testing). D. Cho ¶ 16.

135. Nine labs reported that they had stopped performing tests for *BRCA1* and *BRCA2* in response to a valid scientific survey of laboratory directors in the United States. D. Cho ¶ 16.

136. Labs have avoided or refrained from developing tests for *BRCA1* or *BRCA2* as a direct result of the gene patents held by Myriad. D. Ostrer ¶ 6; D. Ledbetter ¶¶ 14-16.

137. Other studies of other gene patents also reveal that labs frequently stop developing or offering clinical tests for disease as a result of gene patents. In a valid scientific survey of labs in the United States, 26% stopped doing testing for hemochromatosis as a result of gene patents. D. Cho ¶¶ 17-20.

138. Researchers, clinicians, and pathologists are aware that Myriad has sent cease and desist letters over the patent claims at issue in this case or are aware that it prohibits virtually all clinical testing of the *BRCA1/2* genes. D. Kazazian ¶¶ 5-11; D. Ganguly ¶¶ 4-14; D. Chung ¶ 15; D. Hegde ¶ 10; D. Matloff ¶¶ 5-7; D. Ostrer, ¶¶ 4-7; D. Swisher ¶ 28; D. Hubbard ¶¶ 7-8; D. Kant ¶ 4; D. Ledbetter ¶ 13; D. Reich ¶¶ 3, 5; D. Parthasarathy ¶¶ 28-31.

139. Researchers, clinicians, and pathologists are prohibited from sequencing and analyzing the *BRCA1* and *BRCA2* genes because of the patents at issue in this case. D. Ganguly ¶ 14; D. Chung ¶¶ 13, 17, 18; D. Ostrer ¶¶ 6-8; D. Hegde ¶ 10; D. Swisher ¶¶ 34-35; D. Hubbard ¶ 9; D. Kant ¶ 6; D. Ledbetter ¶¶ 16, 18; D. Reich ¶¶ 3, 5.

140. Myriad does not permit researchers to tell patients involved in research the results of their *BRCA1/2* testing. D. Ostrer ¶ 10; D. Chung ¶ 13.

141. The *BRCA1/2* patents prevent physicians from testing for breast and ovarian cancer genetic risk (*BRCA1/2* sequencing). D. Leonard ¶ 14; D. Swisher ¶ 34.

EFFECTS OF *BRCA1/2* GENE PATENTS

142. For a period of years, the testing done by Myriad did not reveal all known mutations in the *BRCA1* and *BRCA2* genes or utilize known methodologies that would have

revealed those additional mutations. D. Chung ¶ 19; D. Matloff ¶ 8; D. Swisher ¶ 26; D. Limary ¶ 7; D. Thomason ¶ 6; D. Raker ¶¶ 7-8; D. Ledbetter ¶ 16; D. Parthasarathy ¶ 29.

143. During this period, people who received Myriad's test may have gotten false negative results. A scientifically valid study from 2006 concluded that 12% of those from high risk families with breast cancer and with negative test results from Myriad carried cancer-predisposing genomic deletions or duplications in one of those genes. This result reinforced other similar studies done over the years. D. Swisher ¶¶ 25-26.

144. The Myriad test that Ms. Thomason, Ms. Raker, and Ms. Limary received did not look for all known large rearrangements in the *BRCA* genes. D. Thomason ¶ 6; D. Raker ¶¶ 7-8; D. Limary ¶ 7.

145. Myriad now offers a separate test called BART which looks for additional large rearrangements in the coding sequences of both *BRCA1* and *BRCA2*. This test is offered with the standard test for a limited number of women, but most women must pay an extra fee for it. D. Swisher ¶¶ 29-30; D. Reich ¶ 10; D. Matloff ¶ 14.

146. The BART test is not available to many women who should have access to it as a result of the strict criteria Myriad has adopted and the price Myriad charges for the test. Myriad's standard way of offering genetic testing is a partial testing strategy because it does not reflexively offer large rearrangement testing for all women who receive negative full sequencing test results. D. Swisher ¶¶ 30-31, 33; D. Reich ¶ 10; D. Matloff ¶ 14; D. Ledbetter ¶ 16.

147. The sensitivity and specificity of BART has never been fully and independently validated. D. Swisher ¶ 32.

148. Other methods for looking for *BRCA* large rearrangements, such as one called MLPA, are performed around the world. Myriad has never published comparisons of BART with MLPA. D. Swisher ¶ 33.

149. Other labs are in a position to offer more comprehensive testing than Myriad's standard test and would do so were it not for Myriad's patents. Some labs would use newer testing methods (such as microarray analysis) that are expected to result in improved testing quality and efficiency. Other labs would reflexively conduct large rearrangement testing after a negative test result is received through full sequencing. D. Ledbetter ¶¶ 17-18; D. Chung ¶ 18; D. Ostrer ¶ 9.

150. In the event the patents were invalidated, other labs would immediately consider and/or begin offering genetic testing to include all known methods of analysis of the genes. D. Ledbetter ¶ 18; D. Ostrer ¶ 9; D. Kant ¶ 6; D. Hegde ¶¶ 10-11; D. Chung ¶¶ 17-18; D. Hubbard ¶ 9; D. Ganguly ¶ 14.

151. When Ms. Limary was tested by Myriad, she was given the following test result: "genetic variant of uncertain significance." D. Limary ¶ 5.

152. Variants of uncertain significance in the *BRCA1* and *BRCA2* genes are reported disproportionately for members of minority groups. D. Chung ¶ 20; D. Ostrer ¶ 12; D. Matloff ¶ 9; D. Limary ¶ 8.

153. A lack of independent *BRCA1/2* testing and analysis undermines the ability of the scientific community to determine the meaning of variants of uncertain significance. Other labs would do extensive analyses for patients in the face of a result of "variant of uncertain significance." D. Chung ¶ 21; *see* D. Ostrer ¶ 12.

154. Myriad does not routinely perform genetic testing on tumor specimens preserved in paraffin from deceased family members, even though such testing can often provide valuable genetic information for living relatives and is often necessary for accurate test interpretation. Such testing could be performed in other research laboratories and would be, were it not for the patents issue in this case. D. Chung ¶ 24.

155. Because only Myriad performs full sequencing in the United States, women who receive a negative result cannot know for certain what the rate of false negatives might be. Women who receive a positive result cannot confirm the lab's findings or seek a second opinion on the interpretation of those results. D. Ledbetter ¶ 23; D. Ostrer ¶ 11.

156. After receiving a test from Myriad that indicated she was positive for a deleterious mutation on her *BRCA2* gene, Ms. Girard sought confirmatory testing of that test result but learned that Myriad is the only laboratory in the country that may provide full sequencing. The patents on the *BRCA* genes block her from getting a second full sequencing test done. Ms. Girard has been forced 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. D. Girard ¶¶ 4-9.

157. *BRCA* genetic testing is one of the very few tests performed as part of breast cancer care and prevention for which a doctor or patient cannot get a second confirmatory test done through another laboratory. D. Love ¶ 12.

158. Before taking major surgical steps, Ms. Ceriani would want a second opinion concerning her *BRCA1/2* status. D. Ceriani ¶¶ 9, 11.

159. Ms. Fortune would want a second opinion concerning her *BRCA1/2* status. D. Fortune ¶ 7.

160. Other pathologists, clinical laboratory scientists, medical professionals, and researchers could provide the testing now done by the patent holders at a cost less than that charged by the patent holders. D. Kazazian ¶ 8; D. Matloff ¶¶ 12, 14; D. Ostrer ¶ 8; D. Reich ¶¶ 6, 8, 13.

161. The *BRCA1/2* testing being done by Yale DNA Diagnostics Lab prior to receipt of Myriad's cease and desist letter cost less than Myriad charges. D. Matloff ¶ 7.

162. The *BRCA1/2* testing being done by the University of Pennsylvania Genetic Diagnostic Laboratory prior to receipt of Myriad's cease and desist letters cost less than Myriad charges. D. Kazazian ¶ 8.

163. The *BRCA1/2* testing offered by OncorMed was cheaper for patients than the testing offered by Myriad. D. Parthasarathy ¶ 24.

164. Ms. Ceriani's genetic counselor submitted a blood sample to Myriad on her behalf. However, Ms. Ceriani was notified that Myriad would not process the sample. Even though Ms. Ceriani's insurance company, MassHealth, 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. D. Ceriani ¶¶ 5-7.

165. Ms. Fortune is insured through Medi-Cal. Her oncologist and genetic counselor recommended that she obtain *BRCA1*/*BRCA2* genetic testing 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. D. Fortune ¶¶ 4-5.

166. Myriad's BART test is not covered by many insurers, and for most patients, they must pay separately for BART on top of the fee for the standard Comprehensive BRACAnalysis test. D. Reich ¶ 10.

167. Ms. Raker's 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. 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 course of medical care for herself. D. Raker ¶¶ 7-11.

168. Ms. Thomason has not been able to afford the additional *BRCA* testing recommended by her genetic counselor. D. Thomason ¶ 8.

169. Genetic counselors would recommend additional women for testing and additional tests if the cost came down. D. Matloff ¶¶ 13-14; D. Reich ¶ 6-13.

170. Data sharing is key to the future of genetic discoveries and bioinformatics. D. Sulston ¶ 36.

171. The Breast Cancer Information Core (BIC), an international resource, is an open access, on-line database that is a central repository for information about *BRCA* genes and *BRCA* genetic variants. It helps facilitate identification of deleterious mutations (mutations associated with a higher risk of cancer) and provides a mechanism to collect and distribute data about genetic variants. The value of the BIC comes from the amount and quality of data provided by the scientific community. D. Swisher ¶¶ 15, 17; D. Chung ¶ 22; D. Ostrer ¶ 13.

172. By gathering information about variants of uncertain significance in one place, the BIC plays an important role in helping to elucidate these variants. D. Swisher ¶ 18.

173. Myriad does not share its data with BIC. D. Swisher ¶ 19.

174. If other researchers had access to the data Myriad has collected as a result of its exclusive testing, additional information about the nature of the *BRCA1/2* variants and their

significance might be known. D. Sulston ¶ 36; D. Swisher ¶¶ 20-21; D. Matloff ¶ 9; D. Ostrer ¶¶ 12-13; D. Chung ¶¶ 21-22; D. Ledbetter ¶ 20.

175. Gene patents inhibit research. D. Sulston ¶ 37; D. Cho ¶ 24.

176. A scientifically valid survey of laboratory directors in the United States revealed that 53% decided not to develop a new clinical test because of a gene patent or license, 67% believed that gene patents decreased an ability to do research. A second study concluded that 46% of respondents believed that gene patents delayed or limited their research. D. Cho ¶ 10.

177. Gene patents are deleterious to unraveling the role of genes in medical conditions. D. Sulston ¶ 38.

178. New sequencing technologies are beginning to offer the option of faster and less expensive sequencing of single genes, multiple genes, and even the entire human genome. Patents on one or more genes may impede scientists' ability to develop a comprehensive test for complex diseases or provide a person with an analysis of his or her entire genome. D. Sulston ¶ 38; D. Ledbetter ¶ 24.

179. Gene patents directly interfere with the ability of physicians and researchers to investigate complex diseases. For example, *BRCA1* and *BRCA2* may be associated with cancers other than breast and ovarian cancer, or even other diseases, but so long as the patents on these genes remain, no one will be able to include these genes in tests for other disease predispositions. D. Ledbetter ¶¶ 24-25.

180. Imagine if Watson and Crick had patented the double-helix structure when they discovered it. D. Parthasarathy ¶ 28.

181. Gene patents inhibit clinical diagnostic laboratories from providing clinical tests and services. D. Cho ¶ 24.

182. Geneticists have refrained from developing and improving tests for diseases as a result of the impediment of gene patents. D. Ledbetter ¶¶ 14-15.

183. Gene patents are not necessary to create incentives for initial discoveries or the development of commercial applications, including diagnostics. D. Cho ¶ 25; D. Leonard ¶¶ 20-21.

184. Patents have not been necessary for rapid introduction of genetic testing. Clinical genetic testing has been offered for genetic testing prior to a patent being issued. D. Cho ¶ 21.

185. A study of gene patents issued in the U.S. for genetic diagnostics showed that 67% of these patents were issued for discoveries funded by the U.S. government. D. Cho ¶ 22.

186. Another study showed that 63% of patents on gene sequences resulted from federally supported research. D. Leonard ¶ 22.

187. Significant federal funds were provided to support research to find the *BRCA* genes. The National Institutes of Health (NIH) funded a six-person National Institute of Environmental Health Sciences research team. NIH also provided approximately $2 million in research grants to the University of Utah for this research. NIH contributed one-third of the funding for *BRCA1*'s discovery. D. Parthasarathy ¶ 18.

188. Patient care is promoted where more than one lab offers a particular genetic test utilizing different methodologies. D. Ostrer ¶ 11; D. Swisher ¶¶ 32-35; D. Leonard ¶ 24.

189. It is important for more than one lab to offer a particular genetic test in order to ensure that the testing being done is quality testing and the results are accurate. D. Chung ¶ 23; D. Swisher ¶¶ 32-35; D. Ledbetter ¶ 23; D. Reich ¶¶ 9, 11; D. Leonard ¶ 24; D. Parthasarathy ¶¶ 29, 31; D. Ostrer ¶ 11.

190. More than one lab should offer a particular genetic test because clinical laboratory testing takes place in a broader context of patient care and services. Allowing only one lab to offer testing means that one lab dictates the standards for patient care in testing for that disease. D. Parthasarathy ¶¶ 30, 31.

191. Research should allow for subjects to be told the results of their genetic testing as this can lead to valuable insights concerning their behavior. D. Ostrer ¶ 10.

192. Ethical standards require that physicians be able to provide genetic test results to research subjects, where such results are requested. D. Chung ¶ 14.

EFFECT OF PATENTS ON PLAINTIFFS

193. 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. D. Sobel ¶ 3; D. Hegde ¶¶ 6-12.

194. 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. D. Watson ¶ 3; D. Chung ¶¶ 4, 17-18; D. Ostrer ¶¶ 3, 8-9; D. Ledbetter ¶¶ 4, 18.

195. 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. D. Ball ¶ 2; D. Hubbard ¶ 2.

196. 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. D. Scott ¶ 3; D. Kant ¶¶ 4-6.

197. The laboratory of Dr. Haig Kazazian and Dr. Arupa Ganguly at the University of Pennsylvania has all of the resources and technological capability to offer *BRCA* testing. If the

patents are invalidated, they would immediately consider resuming *BRCA* testing. D. Kazazian ¶ 11; D. Ganguly ¶ 14.

198. Dr. Wendy Chung's laboratory at Columbia University has the personnel, expertise and facilities to do *BRCA* sequencing. If the patents are invalidated, she would offer clinical testing of the *BRCA* genes, including *BRCA* testing that is more comprehensive than that which Myriad offers. Dr. Chung would be in a position to tell the subjects in her research their genetic test results. Her lab would share the results of its work with the BIC database. D. Chung ¶¶ 17-18.

199. Dr. Harry Ostrer's laboratory at New York University has the personnel, expertise and facilities to do *BRCA* sequencing. If the patents are invalidated, he would offer clinical testing of the *BRCA* genes. He would inform participants in his research program about the results of their *BRCA1/2* genetic screening. His lab would share the results of its work with the BIC database. D. Ostrer ¶¶ 8-13.

200. The laboratories directed by Stephen Warren and David Ledbetter at Emory University School of Medicine have all of the personnel and expertise to offer *BRCA* genetic testing. If the patents are invalidated, they would offer clinical testing of the *BRCA1/2* genes, including testing that is more comprehensive and relies on different methodology than that offered by Myriad. They would contribute their research and clinical data to the public. They could have a *BRCA* testing program in operation within weeks. D. Ledbetter ¶¶ 9-12, 16-28; D. Hegde ¶¶ 10-12.

201. If the patents are invalidated, Ellen Matloff would immediately take steps to send samples to labs other than Myriad and advise patients regarding increased genetic testing options. D. Matloff ¶¶ 10-15.

202. If the patents are invalidated, Elsa Reich would immediately take steps to send samples to labs other than Myriad and advise patients regarding increased genetic testing options, including the availability of confirmatory testing. D. Reich ¶¶ 7-15.

203. Breast Cancer Action (BCA) sues on its own behalf and on behalf of its members, some of whom are ready, willing, and able to order testing and analysis at laboratories other than Myriad Genetics if the patents are invalidated. If the patents are invalidated, BCA would immediately use its existing resources to publicize other laboratories for *BRCA* genetic testing and research opportunities. The interests advanced by this case are central to the mission of BCA. D. Brenner ¶¶ 4-9.

204. If the patents are invalidated, Boston Women's Health Book Collective (BWHBC) would immediately use its existing resources to publicize other laboratories for *BRCA* genetic testing and research opportunities. The interests advanced by this case are completely in line with the mission of BWHBC. D. Norsigian ¶¶ 5-8.

205. Ms. Ceriani has not been able to obtain the *BRCA* genetic testing recommended by her doctor and genetic counselor. If the patents are invalidated, Ms. Ceriani is ready, willing, and able to utilize any additional resources for testing and research, including being tested by a plaintiff physician or geneticist. D. Ceriani ¶¶ 5-11.

206. Ms. Limary wants to access additional resources for *BRCA* 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 immediately any additional resources for testing and research, including being tested by a plaintiff physician or geneticist. D. Limary ¶¶ 5-9.

207. Ms. Girard has not been able to obtain confirmatory, full sequencing testing through another laboratory of her *BRCA* positive result. If the patents are invalidated, Ms. Girard is ready, willing, and able to utilize any additional resources for testing and research, including obtaining confirmatory testing from a plaintiff physician or geneticist. D. Girard ¶¶ 4-10.

208. Ms. Fortune has not been able to obtain the *BRCA* genetic testing recommended by her doctor and genetic counselor. If the patents are invalidated, Ms. Fortune is ready, willing, and able to utilize any additional resources for testing and research, including being tested by a plaintiff physician or geneticist. D. Fortune ¶¶ 4-9.

209. Ms. Thomason has not been able to obtain additional large rearrangement testing of her *BRCA1/2* genes. 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, including being tested by a plaintiff physician or geneticist. D. Thomason ¶¶ 4-10.

210. Ms. Raker has not been able to obtain additional large rearrangement testing of her *BRCA1/2* genes. 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, including being tested by a plaintiff physician or geneticist. D. Raker ¶¶ 5-12.

Respectfully submitted,

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