

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,

09 Civ. 4515 (RWS)

ECF Case

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,

DECLARATION OF
SHOBITA
PARTHASARATHY,
Ph.D.

Defendants.
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I, Shobita Parthasarathy declare under penalty of perjury:

1. I am currently an Assistant Professor of Public Policy and Co-Director of the Science, Technology, and Public Policy Program at the University of Michigan's Gerald R. Ford School of Public Policy.

2. My research focuses on comparative and international politics of genetics and biotechnology; the patentability of human biotechnology such as genes and stem cells;

regulation of genetic medicine; the roles of patient advocacy groups; and the relationship between science and democracy.

3. I teach courses in genetics and biotechnology policy, science and technology policy analysis, and political strategy.

4. I received my undergraduate degree in Biology from the University of Chicago and M.A. and Ph.D. degrees in Science and Technology Studies from Cornell University. I have held postdoctoral fellowships at Northwestern University, University of California, Los Angeles, and the University of Cambridge. During the 2007-2008 academic year, I was awarded fellowships from the Woodrow Wilson International Center for Scholars in Washington, D.C., the American Council of Learned Societies, and the Max Planck Institute for Intellectual Property, Competition, and Tax Law in Munich, Germany. Further details of my background are contained in my current curriculum vitae, attached as an Exhibit.

5. In 2007, I published a book entitled *Building Genetic Medicine: Breast Cancer, Technology, and the Comparative Politics of Health Care* (Cambridge, MA: MIT Press), which traces the development and deployment of genetic testing for breast and ovarian cancer (BRCA testing) in the United States and Britain. The book describes the history around the patenting of BRCA1 and BRCA2 and the ways in which the patenting of the genes impacted the commercialization of the test and allowed for one company, Myriad Genetics, to become the sole provider of BRCA testing in the United States.

6. I began the research for *Building Genetic Medicine* in 1998. In addition to an extensive review of the published literature, I conducted interviews both in the United States and Europe of all of the major stakeholders in the development of BRCA testing.

These included the scientists who were involved in researching and finding the BRCA genes, officials at each of the institutions that developed BRCA testing, health care professionals at genetics clinics providing genetic testing, patent office officials, bioethicists and activists who commented on the patenting of the genes and development of the testing, and journalists and authors who had followed these developments.

Overall, I interviewed 111 individuals in the United States, Britain, Belgium, Germany and The Netherlands. I also did archival research, and conducted ethnographic observation and scientific, medical, legal, and policy meetings, related to the history and contemporary politics of breast and ovarian cancer genetic science and technology in the US and Europe.

7. My current research focuses on the development of contemporary controversies over patenting biotechnology in the United States and Europe, with special focus on the patenting of living organisms and traditional knowledge.

8. 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. Ovarian cancer is the eighth most common cancer in women and causes more deaths in the Western world than any other gynecologic cancer. While considerable funding on the part of governments and medical charities has been dedicated to look for a cause and to develop prevention and treatment strategies for these diseases, neither an unequivocal cause nor a completely effective prevention, detection or treatment strategy has yet been found for either breast or ovarian cancer.

9. The BRCA genes are susceptibility genes, which means that individuals who have mutations in either the BRCA1 or BRCA2 genes have an increased risk, but not a certainty, of contracting breast and/or ovarian cancer during their lifetime.¹ Women with inherited BRCA1 mutations have from 3.2-85% cumulative risk of breast cancer, while women with inherited BRCA2 mutations have from 4.6-86% cumulative risk of getting the disease. In the case of ovarian cancer, women with inherited BRCA1 mutations have a 40-52% cumulative risk, while women with inherited BRCA2 mutations have a 15-25% cumulative risk. Furthermore, only 5-10% of all breast and ovarian cancers are thought to be caused by a BRCA1 or BRCA2 gene mutation. In sum, the relationship between mutations in the BRCA1 and BRCA2 genes and breast and ovarian cancer incidence is extremely complex.

10. Beginning in the 1970s, women began to articulate their discontent with treatments for breast cancer. By the 1980s, breast cancer patients had begun to mobilize in large numbers around the goals of increasing public and government attention to the breast cancer epidemic. Largely as a result of significant advocacy efforts on the part of organizations such as Breast Cancer Action (a plaintiff in this case) and the National Breast Cancer Coalition, in 1991 the US Department of Defense created a \$210 million research program devoted to breast cancer research. The US government's funding for breast cancer research increased from less than \$90 million in fiscal year 1990 to more than \$2.1 billion by fiscal year 2008.²

¹ Nancie Petrucelli, Mary B. Daly, Julie O Bars Culver, and Gerald L. Feldman, "BRCA1 and BRCA2 Hereditary Breast/Ovarian Cancer—GeneReviews—NCBI Bookshelf," Website: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=brca1>, Downloaded August 24, 2009.

² National Breast Cancer Coalition, "Overview of NBCC/NBCCF's Major Accomplishments since its inception in 1991," Website: http://www.stopbreastcancer.org/index.php?option=com_content&task=view&id=259&Itemid=131, Downloaded: August 24, 2009.

11. The finding of the BRCA1 and BRCA2 genes arose out of this context of increasing scientific, medical, and public interest in breast cancer. Starting in the 1980s, scientists from the United States, England, France, Germany, Japan, and other countries participated in what was often referred to as an international “race” to identify the nucleotide sequences linked to breast cancer. In 1989, various European and American research laboratories participated in the International Breast Cancer Linkage Consortium (the Consortium), and by 1990, they had achieved their first success, when a group of researchers led by Mary-Claire King at the University of California, Berkeley announced that they had determined that the Breast Cancer Susceptibility Gene 1 (BRCA1), the first gene linked to breast cancer, was located on chromosome 17. Soon afterwards, research intensified as teams around the world focused in on this region of the genome. Multiple contenders emerged, including King, Mark Skolnick (co-founder of Myriad Genetics), and Mike Stratton (Institute for Cancer Research, London). In September 1994, a group led by scientists at Myriad Genetics and including researchers from the National Institute for Environmental Health Sciences (NIEHS), a subdivision of the National Institutes of Health (NIH), announced that they had sequenced the BRCA1 gene.

12. Many scientists believed there was at least one additional gene linked with breast cancer, and continued their research. In December 1995, a group of investigators led by Mike Stratton at Britain’s Institute for Cancer Research announced that they had mapped and sequenced the BRCA2 gene, which was linked to incidence of ovarian cancer and female and male breast cancer. Concerned that Myriad could gain a monopoly on research and testing on both BRCA genes and wanting to ensure that BRCA2 would remain in the public domain, Stratton’s team applied for British and European patents

covering the gene (eventually, they applied for patents in the US as well). The day before the Stratton group published the BRCA2 gene sequence in the scientific journal, *Nature*, however, Myriad announced that it too had found the gene and submitted its sequence to GenBank, an international depository of gene sequence information. It also applied for patents on the BRCA2 gene, in both the US and Europe.

13. Although both the Myriad Genetics and Stratton groups claimed priority in finding BRCA2, a citation network analysis, based on bibliometric data, demonstrates that the scientific community, worldwide, tends to believe that Mike Stratton and his colleagues mapped and sequenced the BRCA2 gene first.³ Research has shown that scientists in the breast cancer genetics community tend to cite Stratton's *Nature* article announcing the BRCA gene sequence, as opposed to the article written by Myriad Genetics' scientists.

14. There has been considerable opposition to and controversy around Myriad's patents around the world. Many scientists have opposed the patents publicly, especially those from the cancer research community in Britain, who felt especially aggrieved as a result of the BRCA2 controversy. They credited Mike Stratton, not Myriad, with finding the BRCA2 gene. Sir Walter Bodmer, a British scientist who had been involved in early research on the BRCA1 gene, said: "Myriad is claiming it contributed far more than it actually achieved. As a result...there is a lot of feeling of unfairness among British scientists."⁴

15. Myriad cannot claim to be the sole "inventor" of the BRCA genes, since uncovering the genes entailed a collective effort involving researchers, families with

³ Robert Dalpé, Louise Bouchard, Anne-Julie Houle, and Louis Bédard, "Watching the Race to Find the Breast Cancer Genes," *Science, Technology, and Human Values*, 28: 187-216.

⁴ Emma Ross, "Scientists object to gene patent," *Guardian (London)*, January 17, 2000.

histories of breast and ovarian cancer who had contributed blood to research around the world, and studies done by multiple labs that contributed to the overall body of knowledge about breast cancer genetics. Not only did researchers who were not part of the Myriad-led team make important contributions (as noted above), but the Myriad-led team itself included important contributions from a variety of researchers.⁵ The search for the BRCA1 gene sequence was conducted by a team of forty-five researchers spread across the University of Utah, Myriad, Eli Lilly, McGill University in Montreal, and the National Institute of Environmental Health Sciences (NIEHS) in North Carolina.⁶

16. The six NIEHS researchers, who were funded by the National Institutes of Health (NIH), were initially excluded as co-inventors on the BRCA patents, and NIH was denied a share of the royalties.⁷ NIH, however, argued that its NIEHS researchers conducted some of the most important work leading to the sequencing of the gene, including identifying the sequences of two of the BRCA1 gene's fragments and helping "to cull vital pieces of genetic DNA and fit them together like a puzzle."⁸ It filed a concurrent BRCA1 patent application, adding the names of its researchers as co-inventors, arguing that Myriad's patent applications were not complete and therefore were likely to be disallowed. Eventually, Myriad agreed to add the NIEHS inventors' names to their patent application, and NIH withdrew its application. Myriad also agreed to pay the NIEHS inventors royalties, but the NIEHS inventors had not received any payments as of 2005.

⁵ Jordan Paradise, "European Opposition to Exclusive Control Over Predictive Breast Cancer Testing and the Inherent Implications for U.S. Patent Law and Public Policy: A Case Study of the Myriad Genetics' BRCA Patent Controversy," 59 *Food & Drug Law Journal* 133-154, 143 (2004) (citing Press Release, Institut Curie, The Key Dayes (Sept. 26, 2002), *available at* http://www.curie.fr/home/presse/actu_list.cfm/actu/presse/affaire/3lang/_fr.html (last visited Feb. 19, 2004)).

⁶ Rachel Nowak, "NIH in Danger of Losing Out on BRCA1 Patent," 266 *Science* 209 (1994).

⁷ Rachel Nowak, "NIH in Danger of Losing Out on BRCA1 Patent," 266 *Science* 209 (1994).

⁸ Associated Press, "U.S., Utah firm clash over rights to gene," *The Salt Lake City Tribune*, 29 October.

17. Oncormed, a company based in Gaithersburg, MD, applied for and received a patent on the “consensus sequence of the human BRCA1 gene.” The patent was issued in August 1997, four months prior to Myriad’s first patent.

18. Significant federal funds were provided toward the finding of the BRCA genes. The National Institutes of Health funded a six-person NIEHS research team. NIH also provided approximately \$2 million in research grants to the University of Utah.⁹ According to sociology professor Jane S. Zones, the NIH “contributed one-third of the funding for BRCA1’s discovery.”¹⁰

19. In addition, the process of finding the genes was identical to that by which all other genes had been found. By the time the BRCA genes were found, that process was well-understood, widely used, and fairly uniform. Many researchers have pointed out that any scientist engaged in the process of looking for any gene would have followed a process similar to Myriad’s. The British Society of Human Genetics argued in a formal statement: “The discovery of a gene sequence has for some little time been a well understood process. There is nothing novel or inventive about this in principle, and as such new gene sequences should not be patentable, even where a straightforward utility e.g., diagnostic testing has been specified, unless there has been real progress towards the design of a specific commercial product.”¹¹

20. Once the genes were discovered, medical professionals, genetics counselors, and patient advocates were very concerned about how testing for the BRCA genes would be

⁹ Rachel Nowak, “NIH in danger of losing out on BRCA1 patent,” *Science* Vol. 266, October 14, 1994, p. 209.

¹⁰ Jane S. Zones, “Profits from Pain: The Political Economy of Breast Cancer,” In Breast Cancer: Society Shapes an Epidemic, edited by Anne S. Kasper and Susan J. Ferguson, New York: St. Martin’s Press.

¹¹ British Society of Human Genetics, “Patenting of Human Gene Sequences and the EU Draft Directive,” 1997.

developed. They knew that the genes only conferred an increased susceptibility of getting breast and/ovarian cancer, rather than a certainty of getting the disease, so counseling would be tricky. Furthermore, the only effective treatment for women with a BRCA gene mutation was prophylactic mastectomy, preventive removal of the breasts, which causes not only early menopause but also serious psychological effects. As a result, people worried about how testing would be provided, who would have access, and what kind of counseling they would receive.

21. A number of organizations issued recommendations on how they believed BRCA testing should be provided, including: American Society of Human Genetics, American Society of Clinical Oncology, American College of Obstetrics and Gynecology, American Medical Association, National Breast Cancer Coalition, and Breast Cancer Action. All of them encouraged the provision of testing in the context of counseling, and more research into the relationship between the gene mutations and disease incidence and the psychological and social implications of BRCA testing.

22. Several laboratories in the United States were offering BRCA testing at the time that Myriad was awarded its patents. These included the University of Pennsylvania's Genetic Diagnostic Laboratory (GDL) and OncorMed, who both offered comprehensive testing of the genes. Together with Myriad, each of these laboratories offered its own approach to genetic testing for breast cancer as well. Because Myriad ultimately controlled patents on the BRCA genes, however, it was able to shut down these other providers—thus monopolizing diagnostic testing and dictating a single model for breast cancer genetic testing.

23. The University of Pennsylvania's GDL set up its testing services in 1995. As an academic laboratory, GDL's genetic testing services were guided by its dual priorities of research and healthcare. Starting in the early 1990s, the laboratory worked to develop a cheaper and faster alternative to DNA sequencing called *conformation sensitive gel electrophoresis (CSGE)*. By 1993, the lab had established that CSGE could be a useful, and less expensive, alternative to full sequence analysis. In setting up its BRCA testing service, GDL followed many recommendations that were made by patient advocacy groups and professional organizations in offering BRCA testing in the context of its research and requiring all clients to undergo genetic counseling.

24. OncorMed, a medium-size start-up biotechnology company, was founded in 1993. As noted above, OncorMed had been actively involved in the BRCA gene discovery research, and developed its testing service based on its own patents and licenses on the BRCA2 patents from Mike Stratton. Its licensing agreement with Stratton required the company to sublicense the patent further (to prevent a monopoly) and require counseling before and after undergoing genetic testing. OncorMed's approach to genetic testing focused on finding a gene mutation in high-risk families, so it was careful to require patients to provide family history information, in order to link the gene mutation information to the family history. It was also careful to minimize costs for patients by adopting a step-by-step testing process. The laboratory first searched for well-known, frequently occurring BRCA gene mutations. This test was priced at \$500. If no mutations were found, it would then conduct protein truncation testing, which was said to be 80 percent sensitive, for unknown mutations in regions of the gene where mutations are most likely to be found. This test was priced at \$800. If that test still resulted in no

mutations, it would sequence the rest of the gene for another \$800. Overall, this step-by-step approach was cheaper for patients and was also more efficient for the company.

25. Myriad Genetics adopted an approach to genetic testing that was considerably different from either GDL's or Oncormed's approach. Myriad, a start-up biotechnology company formed in 1991 by a scientists at the University of Utah, treated BRCA testing as a purely commercial service and as an ordinary medical test. After applying for patents on BRCA1 and BRCA2, Myriad set up its own BRCA testing service. Myriad considered issues of medical practice, such as how patients would be counseled and how results would be conveyed, as being outside of its scope, despite recommendations of patient advocates and professional organizations that the best BRCA-testing systems would be those that provided counseling and were offered through research protocols. Its only requirement was that testing be provided through a physician, but it did not require a physician to have any specialized knowledge about genetic testing or counseling whatsoever. This is particularly problematic because research has shown that primary care physicians have little understanding of genetics and are less equipped to provide counseling than their specialist counterparts.¹²

26. Myriad offered four types of laboratory analyses very soon after it applied for patents on the BRCA genes: analysis of three mutations common among the Ashkenazi Jewish population (about \$450); BRCAAnalysis, which included full sequencing of the two genes (about \$3,000); Rapid BRCAAnalysis, which provided full sequencing with results returned to the physician within 7 days (about \$4,000); and single mutation

¹² M. Escher and A.-P. Sappino, "Primary care physicians' knowledge and attitudes towards genetic testing for breast-ovarian cancer predisposition," *Annals of Oncology*, 1131-1135.; A.N. Freedman, L. Wideroff, L. Olson, et al., "US physicians' attitudes toward genetic testing for cancer susceptibility." *American Journal of Medical Genetics*. 2003, 120(1): 63-71.

analysis (about \$250), usually done after a mutation had been found in a family.

Myriad's laboratory methods reflected its corporate priorities to reap immediate revenue from a testing service and to develop a database of information on fully sequenced BRCA genes that might eventually yield insight for therapeutic developments or could be sold or licensed to other companies.

27. By 1997, the US Patent and Trademark Office had granted both Oncormed and Myriad patents five patents covering various aspects of the BRCA1 gene sequence. In May 1998, following a series of lawsuits that settled out of court, Myriad bought OncorMed's patents and testing services for an undisclosed sum.

28. Armed with their patents and those it acquired from Oncormed, Myriad then sought to shut down the services of GDL as well as other remaining competitors. In early 1998, Myriad sent GDL a "cease and desist" letter, arguing that its services violated its BRCA patents by providing testing in return for payment. GDL resisted, arguing that it was only providing testing in research protocols that were exempt from Myriad's proprietary reach. Myriad disagreed, insisting that by giving results to, and receiving payments from, health-care professionals, GDL was providing a commercial service that violated its patents. GDL limited its testing service to individuals enrolled in research protocols within the National Cancer Institute's Cancer Genetics Network, a group of researchers funded by the National Institutes of Health. Myriad sent GDL another letter, stating that so long as GDL disclosed results to the patient, it was providing a commercial service rather than conducting research and violating Myriad's patent. After further negotiations, Myriad forced GDL to shut down its BRCA-testing laboratory. GDL could no longer conduct any tests (even for research purposes) that involved disclosure of

results to the client. This resolution, which arose through a combination of Myriad's patent rights and legal resources and GDL's reluctance to engage in a prolonged fight with the company, allowed Myriad to control not only the provision of BRCA testing, but also the definition of research and the boundary between research and commercial services for all those who engaged in laboratory or clinical services related to the BRCA genes. By holding patents on such fundamental findings (the BRCA genes), Myriad was able to define what counted as research and what counted as health care, and have significant influence over the kinds of studies that scientists were able to conduct. Imagine how the future of biotechnology would have been affected if Watson and Crick had decided to patent DNA and wield their patents in a similar manner.

29. Because Myriad has had a monopoly on BRCA testing in the United States, it has been able to control how it tests for the BRCA genes, and whether and how it incorporates new research findings into its testing system. For example, in 2001, researchers at the Institut Curie in France reported that they had found large cancer-causing rearrangements in the BRCA1 gene that were not being found through Myriad's testing system. Myriad initially refused to admit that its test was incomplete, and it eventually took years for the company to change its system and include analysis of these genomic rearrangements. In the interim, American clients undergoing BRCA testing assumed that Myriad's test was the "gold standard," and had no idea that the company was not analyzing these types of disease-causing genomic changes.

30. Today, Myriad's tests are available without the direct involvement of a physician or a specialized genetic counselor. Since it shut down other major testing providers in the late 1990s, Myriad has partnered with companies that offer remote access to genetic

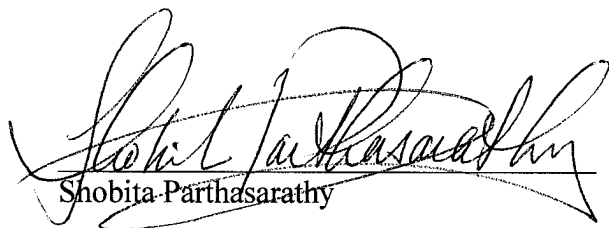
testing services. DNA Direct, for example, allows clients to provide a sample through satellite blood-draw sites.¹³ Blood samples are then sent to Myriad Genetics for testing (both full-sequence and mutation specific analyses are offered), and when results are available, clients can then review them online. This means that clients do not need to receive any type of counseling whatsoever, from any health care professional, when they undergo BRCA testing.

31. Myriad's patents on BRCA1 and BRCA2 have allowed it to monopolize clinical diagnostic BRCA testing in the United States. There are significant and obvious downsides to having a single laboratory offer a genetic diagnostic test. Women cannot get access to confirmatory testing, and the lack of competition does little to assure that the company will update its test to reflect the most up-to-date scientific knowledge or that the test will be offered at a reasonable price. Indeed, at least some of Myriad's competitors were offering testing services that were less expensive and more efficient than Myriad's test. Beyond this, clinical laboratory testing takes place in a broader context of patient care and services. By monopolizing the testing field, Myriad has also dictated the standards for patient care in breast cancer genetic testing. Other models for BRCA testing that existed prior to Myriad's assertion of its patents and included more comprehensive care, genetic counseling and an emphasis on research, are no longer available to women.

I declare, pursuant to 28 U.S.C. §1746, under penalty of perjury under the laws of the United States, that the foregoing is true

¹³ "DNA Direct, "DNA Direct@DNAdirect.com," <https://www.dnadirect.com/web/>, retrieved August 23, 2009.

and correct to the best of my knowledge and belief.



Shobita Parthasarathy

Executed on August 24th, 2009