11-725

IN THE

Supreme Court of the United States

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,

Petitioners,

—v.—

MYRIAD GENETICS, INC., ET AL.,

Respondents.

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

BRIEF OF *AMICI CURIAE*, INFORMATION SOCIETY PROJECT AT YALE LAW SCHOOL SCHOLARS IN SUPPORT OF THE PETITION

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INTEREST OF *AMICI CURIAE*[1]

Amici are scholars with the Information Society Project at Yale Law School (ISP),[2] an intellectual center addressing the implications of new information technologies for law and society: **Wendy Seltzer,** a Senior Fellow at the ISP, writes on law and technology of free expression and user innovation, including digital copyright, software patent, and information privacy. She founded and leads the Chilling Effects Clearinghouse, exploring legal threats to online expression at https://www.chillingeffects.org/; **Margot Kaminski**, Research Scholar in Law and Executive Director of the ISP, writes on privacy, information politics and First Amendment issues; **Priscilla Smith**, Senior Fellow of the ISP, **Jennifer Keighley**, Resident Fellow of the ISP, and **Genevieve Scott**, Visiting Fellow of the ISP, research and write on reproductive rights, with a particular focus on information policy and new technologies.

SUMMARY OF ARGUMENT

As this Court has explained clearly, the grant of a patent is a narrowly tailored exception to our free market system, a "carefully crafted bargain"

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[1] No counsel for a party authored this brief in whole or in part, and no person or entity other than *amici* and their counsel made any monetary contribution toward the preparation or submission of this brief. Pursuant to Supreme Court Rule 37.3, an email indicating the Respondent's consent to the filing of this *amicus* brief has been submitted to the Clerk. The Petitioners filed a consent to the filing of amicus curiae briefs with the Court on December 15, 2011.

[2] The Fellows participate in this case in their personal capacity; titles are used only for purposes of identification.

designed to strike a balance between the avoidance of monopolies that stifle competition and the need to encourage innovation. *Bonito Boats, Inc. v. Thunder Craft Boats,* 489 U.S. 141, 146 (1989).

In this brief, *Amici* argue, first, that the Court should grant the Petition because Myriad's monopoly on the information contained in Breast Cancer Susceptibility Genes 1 and 2 (hereafter "BRCA 1/2")[3] undermines the careful balance struck by the patent rules. The evidence establishes that by limiting research on the BRCA 1/2 genes, and in the field of genetics more broadly, Myriad's patents stifle innovation and prevent information about natural phenomenon from being used in research to improve diagnosis and treatment of deadly diseases.[4]

Second, *Amici* argue that this Court should grant the Petition to closely examine these patents, which harm public health and undermine the exercise of fundamental rights. Myriad's patents create significant health risks for women, limit access to life-saving information about naturally occurring aspects of their own genomes, thereby undermining

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[3] BRCA1 and BRCA2 "belong to a class of genes known as tumor suppressors. Mutation of these genes has been linked to hereditary breast and ovarian cancer." National Cancer Institute Fact Sheets, *BRCA1 and BRCA2: Cancer Risk and Genetic Testing*, (Mar. 29, 2009), *http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA* .

[4] Dep't of Health & Human Serv., Sec'y's Advisory Comm. on Genetics, Health, and Soc'y, *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* (April 2010), *available at* http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_patents_report_2010.pdf (hereinafter SACGHS report) (hereinafter SACGHS report).

their liberty rights to decisional autonomy, bodily integrity, and procreation.

ARGUMENT

I. The Petition Should Be Granted Because The BRCA 1/2 Patents Stifle Innovation And Create a "Double Monopoly," Thereby Undermining The Goals Of The Patent System In Conflict With This Court's Precedent.

Because "imitation and refinement through imitation are both necessary to invention itself and the very lifeblood of a competitive economy," *Bonito Boats*, 489 U.S. at 150, the central concern of patent law is "the difficult business 'of drawing a line between those things which are worth to the public the embarrassment of an exclusive patent and those which are not.'" *Id.* at 148 (quoting 13 Writings of Thomas Jefferson 335 (Memorial ed. 1904)). The "stringent requirements for patent protection seek to ensure that ideas in the public domain remain there for the use of the public." *Id.* at 150. This is especially true for "[p]henomena of nature, though just discovered, . . . as they are the basic tools of scientific and technological work." *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972).

To protect their public domain status and encourage scientific progress, this Court recognizes that "discoveries" of laws of nature or physical phenomena, including discoveries of an existing scientific relationship, are excluded from the category of patentable subject matter under Title 35

U.S.C. §101. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). As this Court explained:

> The underlying notion is that a scientific principle, . . . reveals a relationship that has always existed. . . . "Such 'mere' recognition of a theretofore existing phenomenon or relationship carries with it no rights to exclude others from its enjoyment. . . . There is a very compelling reason for this rule. The reason is founded upon the proposition that in granting patent rights, the public must not be deprived of any rights that it theretofore freely enjoyed."

Parker v. Flook, 437 U.S. 584, 593 n.15 (1978) (quoting P. Rosenberg, Patent Law Fundamentals, § 4, p. 13 (1975)). Granting patents on the recognition of existing relationships in nature, such as the nucleotide sequence on a strand of DNA, prevents the use of these natural phenomenon to conduct additional research, "discover" other natural relationships, and develop innovations in disease treatments.

The BRCA 1/2 patents have imbalanced the patent system.[5] The patents are on basic scientific knowledge, "the very instructions inside each of our cells that determine what proteins are produced."[6] Because "knowledge itself is what is patented in a

[5] Stiglitz Decl. ¶¶ 15, 19. 25, Jan. 19, 2010.
[6] *Id*. at ¶ 25.

gene patent," the tradeoff that normally occurs in the patent system is undermined.[7]

Ordinarily, patents leave room for competitors to "invent around."[8] For example, with chemical compounds, a patent does not prevent competitors from manufacturing a different chemical compound with a functionally similar result. Because the human genome contains a finite number of genes, it is impossible to invent around a genetic patent to create an equivalent, but non-infringing invention.[9] "One cannot invent around the sequence if it is patented because each gene and each gene sequence is unique in its kind."[10] Moreover, researching and acquiring a patent on human genetic information does not impose the same financial costs as the development of pharmaceutical patents.[11] Pharmaceutical drug development costs are increased due to "salaries for research and development scientists, the great expense of animal research and human clinical trials, and the cost of

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[7] *Id.* at. ¶¶ 10, 12. 25.

[8] *See WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1355 (Fed. Cir. 1999).

[9] Andrew S. Robertson, *The Role of Genetic Patents in Genetic Test Innovation and Access*, 9 Nw. J. Tech. & Intell. Prop. 377 at *10 (2011) (*citing* Stephen A. Merrill & Anne-Marie Mazza eds., *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* Nat'l Research Council, Nat'l Acad. Of Scis. (2006)).

[10] Gert Matthijs, *The European Opposition Against the BRCA Gene Patents*, 5 Familial Cancer 95 (2006).

[11] Lori B. Andrews, *The Gene Patent Dilemma: Balancing Commercial Incentives with Health Needs*, 2 Hous. J. Health L. & Pol'y 65, 77 (2002); *see also* SACGHS report. at 34 ("The cost of developing these laboratory-developed tests appear to be relatively modest."); Cho Decl. ¶¶ 17, 23, Aug. 17, 2009.

obtaining FDA approval."[12] In contrast, technological developments in the area of genomic screening can be accomplished in much less time, using known techniques, and is not regulated by the FDA.[13]

By securing a patent on the genetic information in the BRCA 1/2 genes, Myriad has left no alternative for genetic testing on those genes, creating a powerful "double monopoly."[14] "When the uniqueness of the genetic code is combined with the exclusive rights of patents, a truly unbreakable monopolistic right is generated."[15] In such an environment, patentees are dissuaded from performing additional research, charging reasonable prices, or cross-licensing technology.[16] "Profit maximizing behavior and progress-maximizing behavior" are "at odds."[17]

This is the precisely the environment that has allowed Myriad to abuse its monopoly power by inflating prices, delaying researchers' access to information, and inhibiting the progress of genetic testing. The BRCA 1/2 patents place restrictions on

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[12] *Id.*
[13] *Id.*
[14] Gert Matthijs, *The European Opposition, supra,* at 5.
[15] Gert Matthijs & Dicky Halley, *European-Wide Opposition Against The Breast Cancer Gene Patents*, 10 Eur. J. of Hum. Genetics 783 (2002).
[16] Maureen E. Boyle, *Leaving Room For Research: The Historical Treatment of The Common Law Research Exemption in Congress and the Courts, and Its Relationship To Biotech Law And Policy*, 12 Yale J. L. & Tech. 269 (2010) (*citing* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 6918 (1998)).
[17] *Id.*

facts of nature that distort the efficient allocation of resources; the tremendous rewards granted to Myriad do not correspond to the social returns.[18]

II. Myriad's Monopoly In Facts of Nature Was Unnecessary To Incentivize Research On The BRCA 1/2 Genes, and Inhibits Innovation.

The evidence in this case establishes that the promise of a patent grant did not act as the incentive for the original research on the BRCA genes; and rather than encouraging innovation and scientific progress, the BRCA 1/2 gene patents stifle advances in medical testing. As a result, the patents prevent research into relationships between the BRCA genes and other cancers as well as other genetic diseases, delaying the discovery of life-saving information about breast cancer, ovarian cancer, and other diseases.

These limitations on innovation are not a normal consequence of the patent system; they are a consequence of the overextension of the patent system to cover the discovery of scientific fact, creating a monopoly on the "basic tools" of scientific research. *Gottschalk*, 409 U.S. at 67. Given the fundamental nature of the information contained in a human gene, it is unsurprising that the BRCA 1/2 patents on human genes have retarded innovation and stifled competition.

[18] Stiglitz Decl. ¶¶ 19, 26, Jan. 19, 2010.

A. The Monopoly Granted To Myriad Was Unnecessary To Incentivize the Identification of the BRCA 1/2 Genes.

In its report entitled *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* (hereinafter "SACGHS report"), the Secretary's Advisory Committee on Genetics, Health and Society conclude that patents are not necessary to ensure that genetic tests come to market,[19] finding significant evidence that most gene discoveries are in fact not patent-driven.[20] The "inventor class" in genetics and biotechnology are academic and industry researchers whose primary motivations are "the desire to advance understanding, help their patients by developing treatments for disease, advance their careers, and enhance their reputations."[21] Gene patents serve only to prevent alternative, and potentially more accurate, tests from being shared in the market.[22]

Moreover, advances in genetics have been and continue to be significantly funded by the publically financed human genome project and U.S. federal funds.[23] According to the SACGHS report, although

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[19] SACGHS report at 26.
[20] *Id*. at 2.
[21] *Id*. at 21-22.
[22] *Id*. at 34.
[23] *Id*. at 26; Ledbetter Decl. ¶ 13 , Aug. 20, 2009; *See also* Cho Decl.¶ 22, Aug. 17, 2009 (a study of gene patents in the US on genetic diagnosis showed that 67% were for discoveries funded by the U.S. government) (*citing* Schissel, A., Merz, JF, Cho, MK., *Survey Confirms Fears About Licensing of Genetic Tests*, 402 Nature 118 (1999); *see also* Cho Decl. ¶¶ 17, 23, Aug. 17, 2009 ("the majority of patented gene discoveries were supported by the federal government.")).

a patent or exclusive license may at times stimulate its holder to develop a genetic test, SACGHS found no cases in which possession of exclusive rights was necessary for the development of a particular genetic test, including test kits and tests for both common and rare genetic diseases.[24]

This case proves the point. As the District Court Opinion discusses at length, the discovery of the BRCA 1/2 gene patents received significant federal funding through the National Institutes of Health and was made possible by the use of known sequencing techniques[25] and the scientific contributions of various teams of researchers, including those who were staunchly opposed to patenting the BRCA 1/2 gene sequences.[26]

B. Myriad's Patents Stifle Advances in Testing and Research.

Plaintiffs in this suit include researchers at Yale University, the University of Pennsylvania, and Georgetown University who would like to offer a broader range of testing and services to their

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[24] SACGHS report at 2.

[25] *Ass'n for Molecular Pathology et. al v. United States Patent and Trademark Office,* 653 F.3d 1329, 1373 (Fed. Cir. 2011) (Circuit Judge Bryson concurring in part and dissenting in part) (95a); *Ass'n for Molecular Pathology et. al. v. United States Patent and Trademark Office*, 702 F. Supp.2d 181, 201-202 (S.D.N.Y. 2010) (155a-156a).

[26] Stiglitz Decl. ¶ 26, Jan. 19, 2010; *Ass'n for Molecular Pathology et. al.,* 702 F. Supp.2d at 201-202 (154a-158a) (*citing* Jeff M. Hall et al., *Linkage of Early-Onset Familial Breast Cancer to Chromosome 17q21*, 250 Science 1684 (1990); Richard Wooster, et. al, *Identification of the Breast Cancer Susceptability Gene BRCA 2*, 378 Nature 789-92 (1995)).

patients but fear they will be sued for infringement by Myriad.[27] By threatening litigation and sending cease and desist notices, Myriad prevents researchers and specialists at top academic institutions from researching alternative and less costly means of testing for mutations in the BRCA 1/2 genes.[28] In addition, because of its patents, Myriad controls all test data in the United States, but fails to make this data readily available to researchers, limiting their ability to conduct research on breast cancer, ovarian cancer, and other cancers and diseases.[29]

a. The Patents Prevent Research To Improve Myriad's Test, Which Contains Numerous Ambiguities And Fails to Detect Some Mutations.

The best means to ensure the quality of genetic tests is to independently verify test results and use proficiency testing, a method in which multiple labs scrutinize the same sample.[30] However, due to its active enforcement of its patents, Myriad is the exclusive provider of BRCA 1/2 tests for mutations

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[27] Myriad aggressively enforces its patent against private research labs, nonprofits research institutions, and universities. *Ass'n for Molecular Pathology et. al.,* 702 F. Supp.2d at 204-206 (163a-166a) (including University of Pennsylvania, Cancer Genetics Network Project sponsored by the National Cancer Institute, Georgetown University, Yale University, and Oncormed); SACGHS report at 33.

[28] Ledbetter Decl. ¶¶ 13, 16, Aug. 20, 2009.

[29] Swisher Decl. ¶¶ 14, 15, 19, Aug. 19, 2009.

[30] SACGHS report at 48.

associated with breast or ovarian cancer in the United States.

Since 2002, the standard test offered by Myriad is its Comprehensive BRACAnalysis, which consists of the full sequencing of the BRCA 1/2 genes with a large rearrangement panel for detecting five common large rearrangement mutations.[31] In 2006, a study on the spectrum of mutations in BRCA genes revealed that Myriad's full sequencing test contains serious inaccuracies: 12% of women with negative test results carry cancer-predisposing genomic deletions or duplications in the BRCA 1/2 genes.[32] The study further revealed significant numbers of previously undetected mutations in BRCA 1/2 genes, including 22 different genomic rearrangements.[33]

It is well-known that the cause of these ambiguities lies in the limitations of the sequencing test itself. Simply sequencing the coding region of the BRCA 1/2 genes will not reveal all known causative mutations that have been associated with an increased risk of developing ovarian or breast cancer.[34] Sequencing only uncovers approximately 70% of known causative mutations. Of the remaining 30%, a significant portion are structural

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[31] *Ass'n for Molecular Pathology et. al.*, 702 F. supp. 2d at 203 (160a).

[32] Tom Walsh et al., *Spectrum of Mutations in BRCA 1, BRCA 2, CHEK2, and TP53 in Families at High Risk for Breast Cancer*, 295 J. Am. Med. Ass'n 1379 (2006); Swisher Decl.¶¶ 25-26, Aug. 19, 2009; Andy Pollack, *Flaw Seen In Genetic Test For Cancer Risk*, N. Y. Times, Mar. 22, 2006, *available at* http://www.nytimes.com/2006/03/22/health/22breast.html.

[33] Walsh et al., *Spectrum of Mutations, supra*, at 11.

[34] Ledbetter Decl. ¶ 16, Aug. 20, 2009.

mutations, which are primarily large rearrangements in the gene that disrupt its function.[35] In order to test for structural mutations, an additional method of testing must be used.[36] In Europe, testing has been done using Multiplex Ligation-dependent Probe Amplification (MPLA), an alternative test that can identify cancer-predisposing genomic deletions and duplications that Myriad's sequencing test does not.[37] Despite knowledge of this methodology, until 2006, Myriad continued to employ a partial testing strategy. As a result, a significant number of women were receiving false negative testing results.[38] In 2006, Myriad finally began offering a supplemental test called the BRACAnalysis Rearrangement Test (BART) which Myriad claims can detect all large rearrangement mutations in the BRCA 1/2 genes.[39] To this day, however, Myriad does not automatically test for structural mutations in the event of a negative sequencing test result.[40] Moreover, while Myriad asserts that BART is the gold standard for structural testing, Myriad has not released any formal comparison of BART with MLPA.[41]

In addition to limiting who gets tested, Myriad also fails to engage in proficiency testing or sample

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[35] *Id.*
[36] Walsh et al., *Spectrum of Mutations, supra*, at 11; Swisher Decl. ¶ 27, Aug. 19, 2009.
[37] Swisher Decl. ¶ 24, Aug. 19, 2009.
[38] Ledbetter Decl. ¶ 16, Aug. 20, 2009.
[39] *Ass'n for Molecular Pathology et. al.*, 702 F. supp. 2d at 203 (160a).
[40] Ledbetter Decl. ¶ 16, Aug. 20, 2009.
[41] *Id.* at ¶¶ 32-33.

exchange programs.[42] These programs allow multiple researchers to act as a check on each others' work, an important aspect of quality control that is "jeopardized when one lab controls all diagnostic testing for a disease."[43] In sum, without competition, Myriad fails to provide an optimal level of testing services, creating serious health risks for individual women as well as the public health.

b. The BRCA 1/2 Gene Patents Place Limits on Multiplex and Full Human Genome Testing that Prevent Researchers From Investigating Complex and Life-Threatening Diseases.

Myriad's patents directly interfere with researchers' ability to investigate complex diseases. Current understandings of complex diseases reveal that in most cases, rather than associating a single gene with a given disease, multiple genes play a causative role.[44] For example, autism is associated with more than ten different genes.[45] Similarly, BRCA 1/2 may be associated with, and serve as a predictor for, cancers other than breast or ovarian cancer, and even other diseases.[46] "Multiplex testing" is a recent innovation in genetic testing which allows researchers to simultaneously test multiple genetic markers.[47] Such screening might eventually be done by affordable whole-genome

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[42] *Id.* at ¶ 23.
[43] *Id.*
[44] *Id.* at ¶ 24.
[45] *Id.*
[46] *Id. at* ¶ 25.
[47] SACGHS report at 49.

sequencing and may be used in various contexts, including newborn screening.[48] This testing will be essential to identifying conditions that involve multiple genetic factors or to simultaneously test for multiple conditions.[49]

However, the fact that multiplex tests involve multiple genes also raises concerns that they will violate multiple patents.[50] The number of patents protecting genes spread among various patent holders and assignees, thus far 20% of the human genome,[51] has led to a "patent thicket," described by the SACGHS report as "a dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology."[52] The SACGHS report concludes that because of the thousands of patents claiming gene molecules or methods of associating a gene with a phenotype, developing

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[48] *Id*. (*citing* The President's Council on Bioethics, *The changing moral focus of newborn screening: an ethical analysis by the President's Council on Bioethics. Chapter Three: The Future of Newborn Screening* (2008)).

[49] SACGHS report at 49.

[50] *Id*. (*citing* D Nicol, *Navigating the molecular patent landscape*, 18 Expert Opinion on Therapeutic Pat. 461, 468 (2009); S Soini, S Aymé, & G Matthijs, *Patenting and licensing in genetic testing: ethical, legal and social issues*, 16 Eur. J. of Human Genetics S10, S12 (2008); TJ Ebersole, MC Guthrie, & JA Goldstein, *Patent pools as a solution to the licensing problems of diagnostic genetics* 17 Intellectual Property & Technology Law Journal 6 (2005)).

[51] K. Huang & F. Murray, *Does Patent Strategy Shape the Long-Run Supply Of Public Knowledge? Evidence From Human Genetics*, 52 Acad. of Mgmt. J. 1193 (2006).

[52] SACGHS report at 51 (*citing* C Shapiro, *Navigating the patent thicket: cross licenses, patent pools, and standard setting*, 1 Innovation Pol'y and the Econ. 119 (2001)).

multiplex testing, parallel sequencing and whole-genome sequencing will depend upon the acquisition of multiple rights or licensees to patents on genes, which will likely be prohibitively expensive and complex under current law.[53]

A recent study performed by researchers from the Centre for Intellectual Property Rights and the Centre for Human Genetics in Belgium confirms that 64% of patents relating to genetic testing will be difficult to invent around.[54] Patents on human genes are often also difficult to interpret. For example, claim six of Myriad's patent on the BRCA 1 gene sequence is so broad that it includes at least 4% and as much as 100% of the genes in the human genome.[55] Patent claims that are difficult to circumvent can only be evaded after "a substantial investment of money and time, as well as a large amount of inventiveness."[56] Even if many of those patents are ultimately found to be invalid for anticipation or obviousness, the costs associated with litigating the scope of the patents is prohibitive.[57] As the SACGHS report discusses, under the standard set out in *eBay v. MercExchange, L.L.C.*, a multiplex developer faces the risk of an injunction and will not

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[53] SACGHS report at 51-52.

[54] *Id*. at 15-16 (*citing* I. Huys, N Berthels, G Matthijs, & G Van Overwalle, *Legal uncertainty in the area of genetic diagnostic testing*, 27 Nature Biotechnology 903 (2009)).

[55] Mason. Supp. Decl. ¶¶ 3-6, Jan. 19, 2010.

[56] SACGHS report at 16.

[57] *Id*. at 51-52 (*citing* Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 Hou. L. Rev. 1059, 1076-1080 (2008)).

learn if that injunction will issue until after lengthy and expensive litigation.[58]

The Association of Genetic Counselors concur that exclusive licenses and patents will "hinder the cost-effectiveness of genetic testing, particularly when analysis of multiple genes or the entire genome is necessary to assess the risk or existences of a disease."[59] As multiplex testing and whole-genome sequencing become commonplace medical tools, thickets of gene patents will discourage the development of advanced tests and their application to medicine.[60] If more than one gene is patented, researchers are prevented from developing a comprehensive, cost-effective test for the full panel of human genes.[61] In the case at hand, as long as the patents on the BRCA 1/2 genes remain, researchers will be unable to include these genes in tests for other disease predispositions, including other forms of cancer, as well as in tests that simultaneously test for multiple genetic conditions.[62]

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[58] SACGHS report at 53 (indicating that the lack of clarity regarding how *ebay* will be applied has a chilling effect on research) (*citing eBay v. MercExchange, L.L.C* ., 547 U.S. 388 (2006)).

[59] National Society of Genetic Counselors, *Position Statement on Human Gene Patenting* (2010). http://www.nsgc.org/Advocacy/PositionStatements/tabid/107/Default.aspx.

[60] SACGHS report at 62.

[61] Ledbetter Decl. ¶ 24, Aug. 20, 2009.

[62] Ledbetter Decl. ¶ 25, Aug. 20, 2009.

c. Myriad's Monopoly Limits Research On BRCA 1/2 and Other Diseases.

Researchers have intentionally avoided research on BRCA 1/2 genes despite their belief that they can provide more comprehensive and less costly tests than the test offered by Myriad.[63] The patent thicket that researchers currently face heavily directs their genetic research, forcing researches to design their business models and research around any gene that has been patented or exclusively licensed.[64] As a result, researchers are unable to provide the public with improved tests for BRCA 1/2[65] or a complete test for any other disease that BRCA 1/2 may be associated with.[66]

Additionally, patents on the BRCA 1/2 genes place severe limits on data sharing. Without competition, Myriad is slow to make research available to other researchers. Myriad has stopped providing data to the Breast Cancer Information Core, a catalogue of all mutations and polymorphisms in breast cancer susceptibility genes whose principle aim is to facilitate the detection and characterization of these genes.[67] Genetic tests often reveal genetic alterations described as "variants of unknown significance" that researchers are unable to

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[63] *Id*. at ¶ 16; *Ass'n for Molecular Pathology et. al*., 702 F. supp. 2d at 204 (162a) ("A number of researchers, clinicians, and molecular pathologists have the personnel, equipment, and expertise to sequence and analyze the BRCA 1/2 genes at a lower cost than Myriad's testing.").

[64] Ledbetter Decl. ¶ 14, Aug. 20, 2009.

[65] *Id*.

[66] *Id*. at ¶¶ 24-25.

[67] Swisher Decl. ¶¶ 15, 19, Aug. 19, 2009.

interpret. In order to determine whether these variants are benign or pathogenic, researchers need large datasets, normally pooled from many labs. By hoarding clinical data for the BRCA 1/2 gene, Myriad prevents the greater genetic community from analyzing that data and making life-saving determinations about whether "variants of unknown significance" are benign or a predictor for cancer.[68] Given the limitations set out in *Madey v. Duke University*, academic medical centers and companies are likely liable for any infringing acts they commit in the course of experiments to develop a new genetic test.[69] This view is supported by Myriad's aggressive threats of litigation, indicating that they too believe that any outside testing of the BRCA 1/2 genes infringes their patent.

Finally, studies on the impact of gene patenting on scientific progress and commercialization reveal that gene patents decrease production of public genetic knowledge by 5-17%, a trend that is exacerbated when patents are broad in scope, privately owned, or closely linked to a cancerous disease.[70] All three factors are present in this case. Myriad's patents likely had a negative impact on the accumulation of public knowledge of the BRCA1 and BRCA2 genes by between 5 and 10%.[71] These results were mirrored in a study performed by Dr. Mildred Cho, a National Human Genome funded

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[68] Ledbetter Decl. ¶ 20, Aug. 20, 2009; Swisher Decl. ¶ 18, Aug. 19, 2009.

[69] *See* SACGHS report at 73 (*citing Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2003); *Embrex, Inc. v. Service Eng'r. Corp.*, 216 F.3d 1343 (Fed. Cir. 2000)).

[70] K. Huang & F. Murray, *Patent Strategy, supra,* at 14.

[71] Murray Decl. ¶ 20, Aug. 20, 2009.

survey of all laboratory directors in the United States who were likely to be conducting genetic tests.[72] 53% reported that they decided against developing a new clinical genetic test because of a gene patent or license.[73] Two thirds, or 67% of respondents, believe that gene patents resulted in a decreased ability to perform research.[74] Dr. Cho's study also found that 25% of respondents stopped performing a clinical genetic test because of a gene patent or license.[75] 65% of labs that responded reported that they had been contacted by a patent or license holder regarding the laboratory's potential infringement of a patent by performance of a genetic test, including of the BRCA 1/2 genes.[76] Further, another study performed by the American Society of Human Genetics reported similar results, finding that 46% of respondents felt that patents had delayed or limited their research.[77] Likewise, a studying analyzing the sequencing of the human genome by the public Human Genome Project and the private firm Celera revealed a 30% reduction in subsequent scientific research and product development outcomes as a result of Celera's intellectual property.[78] This evidence confirms that

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[72] Cho Decl. ¶¶ 9-10, Aug. 17, 2009.
[73] *Id.*
[74] *Id.*
[75] *Id.* at. ¶ 11; Cho, MK et. al., *Effects of Patents and Licenses On The Provision of Clinical Genetic Testing Services*, 5 J. of Molecular Diagnostics 3 (2003).
[76] Cho Decl.. ¶¶ 12-13, Aug. 17, 2009.
[77] *Id.* at ¶ 10 (*citing* Rabino, I., *How human geneticists in US view commercialization of the Human Genome Project*, 29 Nature Genetics 15 (2002)).
[78] Heidi L. Williams, *Intellectual Property Rights and Innovation*, (Nat'l Bureau of Econ. Research, Working Paper

though patent law is designed to "expand the public storehouse of knowledge,"[79] gene patents, and specifically the BRCA 1/2 patents, discourage innovation and research.

III. This Court Should Grant The Petition To Consider Whether The USPTO Improperly Granted Patents, Where Those Patents Threaten Women's Lives and Interfere With the Exercise of Fundamental Rights.

Breast cancer is the most frequently diagnosed cancer worldwide and the second leading cause of cancer death for women in the United States.[80] For women in the U.S. with mutations in the BRCA 1/2 genes, lifetime risks for breast cancer are as high as 80% and lifetime risk of ovarian cancer is as high as 50%.[81] Each year, tens of thousands of women get the test offered exclusively by Myriad to make determinations about their risk for cancer.[82]

Lack of access to one's genetic information deprives patients of the ability to improve their health and reduce health risks. First, Myriad's patents on the BRCA 1/2 genes grant Myriad a monopoly on testing that directly reduces women's chances of preventing or surviving breast and

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No. 16213, 2010), *available at* http://www.nber.org/papers/w16213.

[79] SACGHS report at 2.

[80] *Ass'n for Molecular Pathology et. al.,* 702 F. Supp.2d at 200 (153a).

[81] Walsh et al., *Spectrum of Mutations, supra*, at 11; *Ass'n for Molecular Pathology et. al.*, 653 F.3d at 1339 (18a).

[82] Pollack, *Flaw Seen In Genetic Test, supra,* at 11.

ovarian cancer. The BRCA 1/2 patents allow Myriad to charge an inflated price of $3000 simply for its initial sequencing test and an additional fee for its BART large rearrangement testing.[83] Facilities in Canada, who are not bound by U.S. patent law, charge one third of Myriad's fee to test for breast cancer.[84] Myriad also refuses many forms of medical insurance, forcing women to pay out of pocket or forgo testing that could be made available at a lower cost.[85]

Reduced access to testing prevents patients from determining the likely efficacy of various cancer treatments.[86] Particularly in the case of a life threatening illness where prophylactic removal of reproductive organs is at stake, Myriad's patent poses enormous harms to women's access to medical information about their own bodies. As discussed in the amicus brief of the National Women's Health Network, these harms disproportionately impact women of color and lower income women.

Second, no other lab is permitted to perform the test, preventing patients from obtained a second opinion or review of Myriad's test results, regardless of the recommendation of a patient's doctor.[87] This is the case despite publically known ambiguities in

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[83] *Ass'n for Molecular Pathology et. al.*, 702 F. supp. 2d at 203 (160a).
[84] *Id.* at 203-204 (161a).
[85] *Id.* at 204 (161a-162a).
[86] Swisher Decl. ¶ 13, Aug. 19, 2009.
[87] *Id.* at ;*Ass'n for Molecular Pathology et. al.*, 702 F. supp. 2d at 207 (169a).

Myriad's sequencing test and the 12% failure rate of the BRCA analysis.[88]

Third, as discussed at length above, Myriad's patents have discouraged research on the BRCA 1/2 genes. Because Myriad's patent claims the information on the BRCA 1/2 gene sequence itself, and not merely one test for the BRCA gene, no other researcher is permitted to develop an alternative test for the BRCA 1/2 gene or improve upon Myriad's test. Without competition, Myriad has delayed in improving its test, despite well-documented deficiencies and the existence of a high false negative score,[89] and fails to provide data to researchers, inhibiting their ability to have the data sets necessary to make determinations about "variants of unknown significance."[90] Finally, by preventing researchers from testing on the BRCA 1/2 genes, Myriad delays not only research on breast and ovarian cancer, but also progress in identifying other cancers and deadly diseases.[91]

The patents at issue in this case deny patients access to vital health information about their own bodies, inhibiting their ability to make informed decisions about treatment, including whether to engage in prophylactic surgery to remove their reproductive organs. By inhibiting patient access to accurate information about their genetic makeup, the BRCA 1/2 patents threaten women's ability to

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[88] Swisher Decl. ¶¶ 25-26, Aug. 19, 2009.
[89] Pollack, *Flaw Seen In Genetic Test, supra,* at 11; Swisher Decl. ¶¶ 25-26, Aug. 19, 2009.
[90] Ledbetter Decl. ¶ 20, Aug. 20, 2009; Swisher Decl. ¶ 18, Aug. 19, 2009.
[91] Ledbetter Decl. ¶ 23, Aug. 20, 2009.

make decisions about their reproductive lives in violation of their rights to reproductive autonomy, dignity,[92] and bodily integrity, grounded in the Fourteenth Amendment's liberty guarantee.[93]

The rights to bodily integrity and reproductive autonomy are deeply rooted in our nation's history and tradition,[94] particularly in cases such as this that "involve the most intimate and personal choices a person may make in a lifetime, choices central to personal dignity and autonomy." *Planned Parenthood v. Casey*, 505 U.S. 833, 851 (1992). Since 1891, this Court has recognized the right to bodily integrity, stating "[n]o right is held more sacred, or is more carefully guarded by the common law, than the right of every individual to the possession and control of his own person, free from all restraint or interference of others...." *Union Pacific R. Co. v. Botsford,* 141 U.S. 250, 251 (1891). This right to decisional autonomy protects a person's right "to determine what shall be done with his own body." *Cruzan by Cruzan v. Director, Mississippi Dept. of Health*, 497 U.S. 261, 269 (1990) (citations omitted).

In the area of reproductive rights, this Court has held that "personal decisions that profoundly affect bodily integrity, identity, and destiny should be

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[92]Reva B. Siegel, *Dignity and the Politics of Protection: Abortions Restrictions Under Casey/Carhart*, 117 Yale L. J. 1694 (2008). The BRCA 1/2 genes are also associated with breast cancer and prostate cancer in men.

[93] There is also a First Amendment right at stake in this case, which will be addressed on remand should this Court deny cert. *See Ass'n for Molecular Pathology et. al.*, 702 F. supp. 2d at 237-238; Pl.'s Mem.Supp. Summ. J. 32.

[94] *See Washington v. Glucksberg*, 521 U.S. 702, 720-21 (1997).

largely beyond the reach of government," and "are central to the liberty protected by the Fourteenth Amendment." *Casey*, 505 U.S. at 851 & 927. The liberty interest in procreation is likewise firmly established. *Skinner v. Oklahoma*, 316 U.S. 535, 541 (1942) (recognizing a fundamental right to procreate and refusing to allow forced sterilization procedures).

Strict scrutiny applies to any law infringing the fundamental right to procreate.[95] As this Court explained in *Washington v. Glucksberg:*

> the Fourteenth Amendment "forbids the government to infringe ... 'fundamental' liberty interests *at all,* no matter what process is provided, unless the infringement is narrowly tailored to serve a compelling state interest."

521 U.S. 702, 721 (1997). In this case, there is no compelling interest supporting the government grant of patent rights in the BRCA 1/2 genes and the infringement of patients' constitutional rights to decisional autonomy and bodily integrity.[96] Indeed, the compelling interests in public health and in promoting medical progress support patent denial. Both individual autonomy interests and the public health would be served, indeed vitally protected, by

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[95] *Skinner v. Oklahoma*, 316 U.S. 535, 541 (1942); *see also Griswold v. Connecticut,* 381 U.S. 479, 485-586 (1965); *Eisenstandt v. Baird*, 405 U.S. 438, 453 (1972); *Carey v. Populations Services*, 431 U.S. 678, 685 (1977).

[96] This right has only been curtailed in a narrow set of cases grounded in the government's interest in preserving lives and the public health. *Jacobson v. Massachusetts*, 197 U.S. 11, 26 (1905); *see also Whalen v. Roe*, 429 U.S. 589, 592 & 603 (1977).

recognizing the inherent invalidity of patenting the information within a human gene.

Myriad's intrusion into the intimate and private decisions of individual citizens should not be permitted in the name of a monopoly. Limiting a woman's ability to access the genetic information within her own body serves only to inhibit her chances of survival and the survival of countless others whose constitutional liberties and lives could be spared by overturning the USTPO's improper grant of patents on the BRCA 1/2 genes.

CONCLUSION

For the foregoing reasons, *amici* respectfully request that the Court grant the Petition for Certiorari in the present case.

Respectfully submitted,

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