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

MEMORANDUM OF LAW (1) IN FURTHER SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT AGAINST ALL DEFENDANTS AND (2) IN OPPOSITION TO THE MYRIAD DEFENDANTS' MOTION FOR SUMMARY JUDGMENT AND (3) IN OPPOSITION TO DEFENDANT UNITED STATES PATENT AND TRADEMARK OFFICE'S MOTION FOR JUDGMENT ON THE PLEADINGS

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INTRODUCTION

Contained within seven patents received by the Myriad defendants[1] are a handful of claims, challenged in this action, that are invalid under 35 U.S.C. § 101; Article I, Section 8, Clause 8 of the Constitution; and the First Amendment. The U.S. Patent & Trademark Office ("USPTO") granted the fifteen claims at issue pursuant to unconstitutional policies. Plaintiffs who challenge those actions include four national associations of medical clinicians, researchers, and pathologists,[2] six nationally recognized experts in the field of genetics, two genetic counselors, two breast cancer and women's health advocacy organizations, and six women. Plaintiffs are supported by many *amici*, including the American Medical Association, the American Society for Human Genetics, the American College of Obstetricians and Gynecologists, the American College of Embryology, and the March of Dimes, all of whom support the invalidation of the patent claims challenged. Plaintiffs' declarants, who include world-renowned geneticists such as Nobel Prize winner Dr. John Sulston and Nobel Prize-winning economist Joseph Stiglitz, support the invalidation of the patent claims challenged.[3]

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[1] "Myriad defendants," as used herein, refers to defendants Myriad Genetics and the directors of the University of Utah Research Foundation.

[2] These associations are the Association for Molecular Pathology, American College of Medical Genetics, American Society for Clinical Pathology, and College of American Pathologists, collectively representing over 150,000 professionals. Compl. ¶¶ 7-10.

[3] Plaintiffs' assertion that the patents in this case were not necessary to create incentives to research or develop the genetic testing done by Myriad, and plaintiffs' analysis of the harms caused by Myriad's enforcement of its patents, are also largely supported by Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS), which advises the U.S. Secretary of Health and Human Services and consists of a committee of distinguished experts appointed by HHS. Defendants and their *amici* cite a draft report issued by the SACGHS for several propositions. SACGHS obtained public comment on the report and has in some ways modified the conclusions of the report while proposing recommendations. James P. Evans, SACGHS Task Force on Gene Patents and Licensing Practices, Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests: Final Draft Report and Recommendations, *available at* http://oba.od.nih.gov/oba/SACGHS/meetings/October2009/Evans%20Patents%20Slides--revised%20post%20meeting.pdf [referred to herein as "SACGHS Final Draft Report and Recommendations"]. Final recommendations are due to the Secretary in early February 2010. *See* Twentieth Meeting of the SACGHS: October 8-9, 2009 Meeting Summary, *available at* http://oba.od.nih.gov/oba/SACGHS/meetings/October2009/SACGHS%20Meeting%20Summary%20October%208-9-2009.pdf.

Defendants and their *amici*[4] portray this case as portending the end of "the United States biotechnology industry" and destroying any ability to patent new drugs, therapeutic methods or devices. Myriad Br. 29.[5] That portrayal is pure hyperbole and simply not true. Defendants do not cite any evidence of the destruction of an industry as a result of section 101's rule that laws of nature and natural phenomena cannot be patented. To be sure, the fruit industry survived the 1931 Supreme Court decision striking patents on fruit and the commodities trading industry has survived the *In re Bilski* opinion striking patents on business methods, 545 F.3d 943 (Fed. Cir. 2008) (*en banc*), *cert. granted sub nom. Bilski v. Doll*, 129 S. Ct. 2735 (2009). Plaintiffs do not seek to bring down the biotech industry or to invalidate the Patent Act. Even if the claims challenged in this case are struck, the Myriad defendants will still have well over one hundred other claims in just the seven patents at issue in this case to protect their business. They will be free to continue to provide BRCA1/2 genetic testing.

Plaintiffs challenge only the patenting of fundamental natural phenomena, products and laws of nature, or of ideas themselves, and not the patentability of new drugs, new therapeutic methods, devices, or specific sequencing methods.[6] Whereas inventors and industry are free to

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[4] Amicus BIO Br. 26-27; Amicus Genetic Alliance Br. 23-24; Amici BayBio et al. Br. 14; Amici Rosetta Genomics, Ltd. et al. 3-4, 12-13; Amicus Boston Patent Law Ass'n 12; Amicus Chahine Br. 4; Amicus Noonan Br. 1, 19.

[5] "Myriad Br.," as used herein, refers to the memorandum of law in support of defendants' motion for summary judgment and in opposition to plaintiffs' motion for summary judgment filed by defendants Myriad Genetics and the Directors of the University of Utah Research Foundation.

[6] For this reason, much of the discussion by the *amici* supporting the defendants can be disregarded. *See, e.g.*, Amicus BIO Br. 18-19 (discussing the "massive" costs of bringing therapeutics to market); Amici BayBio et al. 18-20 (defending the patenting of drugs); Amicus Genetic Alliance Br. 23 (discussing riskiness of investment in biotechnology ventures); Amici Rosetta Genomics, Ltd. et al. 2, 11-13 (discussing high cost of development in the biotechnology and pharmaceutical industries); Amicus Boston Patent Law Ass'n 4-6, 12 (discussing the high cost of development and defending the patenting of drugs). Most of the profits earned and expenses borne by the industry relate to drug sales and approval by the Federal Drug Administration, not genetic testing. *See* Frederic M. Scherer, *The Economics of Human Gene Patents*, 77 Academic Med. 1348, 1351-52 (2002), *available at* http://www.aamc.org/research/sloan/scherer.pdf. Drugs like Taxol, referred to by defendants (Myriad Br. 29), could still be patented. The patentholder there did not patent "isolated bark of the Pacific Yew tree" and thereby prevent any scientist from using natural materials. The patent on Taxol does not prevent a researcher from accessing the Pacific Yew to create new and different drugs. *See also* Francis S. Collins, *The Language of Life: DNA and the Revolution in Personalized Medicine* 112 (2010) (noting that "the supposed need to provide an incentive for companies to develop DNA diagnostics is unconvincing. In that situation, many of us would argue that it would be

develop and patent new drugs, therapies, devices, and specific sequencing methods, the patent claims here give exclusive rights to examining naturally-occurring genetic sequences from anyone's body. The plaintiffs merely seek to uphold the law – set forth by the U.S. Supreme Court – that natural phenomena and laws of nature cannot be patented. Such patents violate the law and would cause more harm than good to society and technological development. In the BRCA context, the existence of the challenged patents has resulted in exclusive genetic testing, thereby limiting access to different types of testing methods and alternative laboratories for patients and their physicians, and produced a chilling effect on research.

Because these claims violate the Patent Act and the Constitution, plaintiffs' motions for summary judgment as to all defendants should be granted. As will be discussed below, the claims on "isolated DNA" cover DNA that has simply been removed from the cell, while the method claims cover the mental process of comparing genetic sequences and do not involve any transformation. As such, these claims are invalid under section 101 of the Patent Act as natural phenomena, products of nature, and laws of nature. Furthermore, the USPTO's policy of granting these patent claims and the University of Utah defendants' acquisition of the patents is unconstitutional because these claims violate the First Amendment and Article I, Section 8, Clause 8 of the U.S. Constitution. The defendants' counter-motions should be denied, both because plaintiffs are entitled to challenge the constitutionality of the USPTO's policy of granting these patents, and because the Myriad defendants cannot establish that they are entitled to summary judgment as a matter of law in light of the evidence submitted by plaintiffs.

While the parties in this case have submitted thousands of pages of declarations and attachments in support of their respective motions for summary judgment, and while there are

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better for the public to have competition in the marketplace, in order to provide an incentive for higher quality and lower price").

some disagreements about the science underlying the patent claims at issue in this case, there is no serious dispute about any material facts or the fundamental issues in this case. The parties appear to be in agreement that a naturally-occurring metal, mineral, or plant is a natural phenomenon and unpatentable. Myriad Br. 21 (citing *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980)). *Chakrabarty* explained that a claimed product must have "markedly different characteristics" from the natural phenomenon, and that the use of the claimed product must be a result of the inventor's effort, not "nature's handiwork." 447 U.S. at 309-10. Similarly, the parties agree that laws of nature and ideas are not patentable subject matter. Myriad Br. 21, 41.

The dispute arises when these principles are applied to the patent claims at issue. Rather than accurately describing their claims and applying the relevant precedent, defendants attempt to obscure the true scope of their claims and rely on lower court cases – cases that either did not examine subject matter eligibility or improperly focused on novelty and utility. For the claims on "isolated DNA,"[7] they gloss over the fact that those claims cover DNA that has simply been removed from the cell, and thus are not "markedly different," and that the claims preclude anyone from accessing his or her own genetic information, the result of "nature's handiwork." *See Chakrabarty*, 447 U.S. at 309-10. Instead, they try to distract the court with discussions of standard tools of molecular biology, such as probes and primers, which are covered in other patent claims that have not been challenged in this case. For the process claims,[8] the defendants import new terms and steps into the claims, flagrantly violating basic rules of claim construction.

[7] See Claims 1, 2, 5, 6, and 7 of Patent '282; Claims 1, 6, and 7 of Patent '492; Claim 1 of Patent '473. References in this brief to "product" or "composition" claims refer to all of these claims unless otherwise indicated. Compl. ¶¶ 55-67; Decls. of Grody, Leonard, Sulston, Mason, Nussbaum, and Klein, and Mason Supp. Decl..

[8] See Claim 1 of Patent '999, Claim 1 of Patent '001; Claim 1 of Patent '441; Claims 1 and 2 of Patents '857, and Claim 20 of Patent '282. References in this brief to "process" or "method" claims refer to all of these claims unless otherwise indicated. Compl. ¶¶ 68-80; Decls. of Grody, Leonard, Sulston, Mason, Nussbaum, and Klein, and Mason Supp. Decl.

The plain language of the claims requires only the mental process of comparing or analyzing already-given sequences and do not involve any machine or any transformation of genes.

A few analogies illustrate how defendants have erred. Under defendants' view, any naturally-occurring thing that is "isolated" from its natural environment becomes patentable. Myriad Br. 7-9. Thus, "isolated" gold, i.e. gold removed from the streambed, would become patentable because it is structurally different – no longer integrated into the gravel or sand – and functionally different – potentially useful for jewelry-making. But even if all of these distinctions are true, the "isolated" gold is still gold and a natural phenomenon. Defendants additionally argue that "isolated DNA" cannot perform some of the same functions as DNA. But "isolated" gold can no longer be part of the sediment that influences the stream's channel, flow, and ecology once it is removed from the stream. However, it is still gold, and if it is redeposited into the water, it will settle and reintegrate into the streambed. Similarly, "isolated" DNA remains DNA even after it has undergone standard processes of isolation – it has simply been removed from its natural environment, and the genetic information it embodies remains the same. If reinserted into the cell, "isolated" DNA could function again. While a new and improved goldpan that is used to extract the gold from the streambed, like a new type of DNA-analyzing machine, could be patented, the extracted gold or isolated DNA cannot.

As for the process claims, defendants' construction of the claims requires importing possible steps such as "isolating" and "sequencing" that appear nowhere in the text of the patent claims. Under this theory, a claim to "comparing two pieces of gold" necessarily includes the processes of buying and using a goldpan and extracting the gold flakes and nuggets from the other minerals and materials before one examines them. Importing these terms and steps into the claims, as defendant urge, would violate every tenet of claim construction. The plain language

of the claims only requires the mental process of comparing sequences. Whether the imported "steps" involve complicated or simple technology is irrelevant when the claims simply cover "comparing" or "analyzing" without specifying the machine or requiring a transformation.

These simple analogies vividly illustrate the error involved in granting the patent claims at issue here. The defendants have made numerous factual allegations, primarily related to claim construction. The ultimate construction of the term "isolated DNA" and of the claims as a whole are questions of law, and this Court need not accept defendants' legal arguments. Even if defendants' construction of the claims is adopted by the Court, the DNA and the methods at issue are not patentable subject matter. It was both contrary to both the Patent Act and the Constitution for the USPTO to grant patents on them. That said, the conclusions the defendants draw about the basic scientific facts are also wrong.[9]

FACTUAL BACKGROUND

> *"The information contained in our shared instruction book is so fundamental, and requires so much further research to understand its utility, that patenting it at the earliest stage is like putting up a whole lot of unnecessary toll booths on the road to discovery."*
>
> -- Francis S. Collins, Director of the National Institutes of Health, *The Language of Life: DNA and the Revolution in Personalized Medicine* 113 (2010).

[9] That there is little real disagreement about the actual facts is illustrated by the responses of the defendants to Plaintiffs' Statement of Material Facts ("SMF"). The USPTO denies very few facts, relying largely on legal arguments that the facts are irrelevant or characterizations. USPTO Counter-SMF. Myriad admits ¶¶ 11, 16, 19, 21-27, 29-39, 70, 86, 151 of the Plaintiffs' SMF. For many other facts set forth in plaintiffs' SMF, Myriad relies solely on legal arguments that these facts are unsupported, irrelevant, or otherwise inadmissible, and offers no disputing evidence: Myriad Counter-SMF ¶¶ 9, 46, 51, 57, 77, 79, 80, 82, 83, 89, 129, 141, 180, 181, 195. Myriad offers disputing evidence for some facts that it argues are unsupported, irrelevant, or otherwise inadmissible. Plaintiffs assert that these disputing facts are unresponsive to the facts in question: Myriad Counter-SMF ¶¶ 1-3, 12, 16, 40, 66, 74, 75, 78, 81, 84, 85, 88, 90, 91, 94, 95, 99, 100, 109, 121, 124, 126-128, 130, 131, 133-138, 140, 144-146, 148, 152, 161, 163, 166, 170-172, 182, 186-190, 194, 196-200, 202, 203, 205, 208, 210. Myriad disputes other facts without legal objection, but the disputing evidence is unresponsive to the facts in question: Myriad Counter-SMF ¶¶ 6, 8, 17, 18, 44, 49, 52-56, 60, 64, 68, 71-73, 87, 92, 93, 97, 132, 142, 143, 149, 150, 154, 156, 158, 159, 162, 164, 165, 167-169, 176, 178, 185, 201, 206, 207, 209. Myriad did not dispute or was unresponsive to some portion of these facts: Myriad Counter-SMF ¶¶ 41, 43, 45, 103, 116-118, 122, 130, 139, 153. *See also* Plaintiffs' Counter-Statement to Myriad Defendants' Rule 56.1 Statement of Material Facts. Accordingly, the defendants have not created any genuine issue of material fact in opposition to plaintiffs' motion for summary judgment.

Despite the voluminous filings in this case, there is no material dispute about the nature of DNA. Plaintiffs never suggested that DNA is "merely information," Kay D. ¶ 126, as defendants assert. Rather, plaintiffs argued that the patents at issue exclude all others from accessing the information stored in DNA. The defendants agree with plaintiffs that DNA does, in fact, embody information – whether "isolated" or not. Myriad Br. 32-33.

DNA is a chemical; however, to suggest that it is a chemical like any other, as defendants do, is simply incorrect. DNA is foremost an informational molecule. Klein D. ¶ 8.[10] No other known molecule has the ability to store vast quantities of information and to transmit that information through self-replication. Nussbaum D. ¶ 29; Klein D. ¶¶ 8-9; Sulston D. ¶¶ 11, 13. Its method of transmitting information is through transcription to create RNAs and translation to create proteins. Mason Supp. D. ¶¶ 10-12; Klein D. ¶¶ 11, 13. The information is stored through the sequence of nucleotide bases within the DNA strand. Nussbaum D. ¶¶ 35-39; Mason D. ¶¶ 6-7, 13; Mason Supp. D. ¶ 21; Klein D. ¶ 8; Sulston D. ¶¶ 16-17. The order of the nucleotides is of prime importance, because within this order is contained the genetic code, the information that directs human cells to grow, to differentiate into specialized structures, to divide, and to respond to environmental changes. Klein D. ¶ 12. A human DNA sequence embodies an order of nucleotides that is a blueprint for all of the cells of the human body. For example, H_2O, HOH and OH_2 all describe and represent the exact same water molecule; conversely, TAA, ATA and AAT encode entirely different amino acids. Mason Supp. D. ¶ 21. DNA is not described according to the sugars and phosphates that make up its backbone. *Id.* It is this instructional capacity of DNA that renders it both a product of nature and a law of nature. The treatise on which defendants rely emphasizes the informational quality of DNA. "Today the idea that DNA carries genetic information in its long chain of nucleotides is so fundamental to biological

[10] "___ D." refers to an expert's declaration.

thought that it is sometimes difficult to realize the enormous intellectual gap that it filled….DNA is relatively inert chemically." Bruce Alberts, *Molecular Biology of the Cell* 98, 104 (1994).

The essence of DNA is that it instructs the growth and operation of all of the cells of the human body, including cancer cells. Indeed, Myriad's entire business plan is based on obtaining the information contained in DNA, not in using its chemical properties. When a patient submits a sample, Myriad sends back a report that says it has examined the genetic information in the sample and, based on that, has concluded that the patient has (or does not have) X mutation on his or her BRCA1/2 genes. The report further explains if the mutation is correlated with breast and/or ovarian cancer, or whether Myriad does not know whether it is correlated with cancer. *See* Girard D. ¶ 4; Limary D. ¶¶ 5-6. The fact that the information comes from something that can be described, in part, as a chemical is essentially irrelevant to Myriad's business. Indeed, Myriad described itself as a "genetic information business." Kevin Davies & Michael White, *Breakthrough: The Race to Find the Breast Cancer Gene* 166 (1996) (quoting Myriad Genetics' April 1994 press release). Most significantly for this case, the patents that have been granted and obtained allow Myriad to preclude all others from obtaining information about individuals' BRCA1/2 genes. Its claims over "isolated" BRCA1/2 DNA reach the DNA of 6.7 billion people.

"Isolated" DNA

Defendants claim that the composition patents do not cover DNA but only "isolated" DNA.[11] Their expert, Dr. Kay, quotes the definition of "isolated" found in the patents. Kay D. ¶ 17. "Isolated" DNA is "substantially separated from other cellular components which naturally accompany a native human sequence" and "embraces a nucleic acid sequence … which has been removed from its naturally occurring environment, and includes recombinant or cloned DNA

[11] Use of "isolated DNA" in drafting claims on genes has been referred to as a "lawyer's trick" by some academic commentators. *See* John M. Conley & Roberte Makowski, *Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents*, 85 J. Pat. & Trademark Off. Soc'y 301, 305 (2003).

isolates and chemically synthesized analogs or analogs biologically synthesized by heterologous systems." *See* '282 patent, col. 19:10-12, 14-18, '473 patent, col. 19:8-10, 12-15; '492 patent, col. 17:64-66, col. 18:1-5.[12]

Myriad interprets this language to mean that "isolated DNA" includes DNA that is "extracted from a cell or chromosome, or DNA that is chemically synthesized." Myriad Br. 13. As interpreted by Myriad, "isolated" DNA thus includes: (1) DNA removed from a cell and from cellular components such as proteins, but not separated from other DNA, *see* Myriad Br. 13; Kay D. ¶ 17; (2) DNA removed from a cell and cellular components such as proteins but that includes only the BRCA gene sequence, *see* Myriad Br. 13-15; Kay D. ¶¶ 17, 133 (appearing to define "excised" as cutting the DNA to include the full sequence of the BRCA genes); (3) DNA that is the BRCA gene without the non-coding regions or introns, *see, e.g.,* Kay D. ¶ 187 (using the phrase "extracting and excising" without specifying whether the "excision" includes separating the BRCA1 DNA from other DNA or also involves removing the BRCA1 introns); Myriad Br. 14, 26 (arguing that "extracted … products that originate in nature are patent-eligible"); (4) cDNA, a form of DNA that does not include introns; (5) recombinant DNA, Myriad Br. 14; (6) cloned DNA, *id.*; (7) chemically synthesized analogs of DNA, *id.*; and (8) biologically synthesized analogs if synthesized by heterologous systems, *id.* The first four categories of DNA clearly constitute natural phenomena and thus render their claims invalid. Additionally, Myriad claims all of these substances whether in the double- or single-stranded form of DNA, both of which occur naturally in the body. *See, e.g.*, patent '441, col. 20:61-65; patent '282, col. 20:58-62.

[12] This patent definition of "isolated DNA" tracks the USPTO's regulations stating that "A patent claim directed to an isolated and purified DNA molecule could cover, e.g., a gene excised from a natural chromosome or a synthesized DNA molecule." Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

Myriad claims all sequences of "isolated" DNA. If one person has a BRCA1 DNA sequence that includes GAGC at a given position and another person has a BRCA1 DNA sequence that includes GATC at that same position, Myriad asserts that its patent claims cover both once isolated. Because people's DNA varies, whether in the body or isolated, Myriad's claims extend to every form of the DNA found in anyone's BRCA1/2 genes. These variations were created in nature, not by the defendants; yet, the patents give the exclusive right to "isolate" all of these naturally-occurring sequences and to claim them, even if they have never previously isolated a particular sequence.

For these reasons, the patent claims cover DNA that is not "markedly different" from natural phenomena. If the Court concludes that any of these forms of "isolated" DNA as covered by the patents is a natural phenomenon and therefore unpatentable, the Court need not address any of the other forms because a claim is invalid if it covers anything precluded by the Patent Act, even if it also covers permissible subject matter. *See, e.g., Titanium Metals Corp. of Am. v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985). Defendants argue that "isolated DNA" is "different-in-kind" because of its structure and functions. Myriad Br. 30-32. Defendants' formulation is not the controlling legal test, and these distinctions are baseless. "Isolated DNA," like the "isolated gold" discussed above, is not markedly different in structure or function from natural phenomena.

"Isolated DNA" does not have "markedly different characteristics" from DNA in the body.

1. "Isolated" DNA is not "markedly different" in structure from DNA in the body.

Defendants' expert defines DNA to mean "repeating units that are connected to form a strand…." Kay D. ¶ 14. The "repeating units" are "known as nucleotides." *Id.* Thus, he defines DNA to be the nucleotide sequence. The nucleotides have a chemical structure. Kay D. ¶ 125,

Fig. 1. That chemical structure is identical whether the nucleotides are in the body or in a test tube. Klein D. ¶¶ 27-28; Mason D. ¶¶ 29, 32; Mason Supp. D. ¶ 22; Nussbaum D. ¶¶ 22-23, 35.

Despite their expert's opinion, defendants argue repeatedly that DNA or "isolated" DNA is not a nucleotide sequence. *See, e.g.*, Myriad's Statement of Material Facts ("SMF") ¶¶ 6-7. As their expert notes, the patents define "isolated" to "embrace [] a nucleic acid sequence…." Kay D. ¶ 17. The claims themselves repeatedly refer to a "nucleic acid sequence." *See, e.g.*, patent '282, cl. 2. The method claims all refer to comparing "sequences." *See, e.g.*, patent '001, cl. 1. Because the definition for purposes of the claims is the "sequence," the critical question is whether the "sequence" is different when the DNA is isolated. It is not, and defendants present no evidence to the contrary. Indeed, Myriad in effect concedes that they are the same. Kay D. ¶ 187 ("**native** DNA is analyzed to determine if the structural composition is the same or different from the normal **native** gene") (emphasis added).

In arguing that "isolated DNA" is different structurally from DNA in the body, defendants note that DNA in its "native" state "is protected in the cell, always surrounded by proteins and stably embedded in chromosomes." Myriad Br. 30. But the DNA surrounded by or linked to proteins as a component of chromatin inside a cell is not structurally different from DNA after it has been separated away from the other cellular substances. Nussbaum D. ¶¶ 17-35; Klein D. ¶¶ 26-27. Any differences are between chromatin and DNA, not between DNA in a cell and DNA outside a cell. Nussbaum D. ¶¶ 19-20; Klein D. ¶¶ 26-28.[13]

Finally, defendants wrongly suggest that DNA in the body is always chemically linked to other elements. The body unwinds DNA and separates its strands when it replicates the DNA during cell division, and when it transcribes the genes during protein synthesis. Nussbaum D. ¶

[13] At other points, defendants point to "methylation" that occurs within a cell and involves additions to the cellular DNA. *See, e.g.*, Myriad SMF ¶ 12. However, DNA appears in the body in non-methylated states, so this argument is at best diversionary. Mason Supp. D. ¶ 22.

28; Mason Supp. D. ¶ 23; Klein D. ¶ 29. At those times, it is free-floating. *Id.*; s*ee also* Kay D. ¶¶ 148 (DNA "typically" is not free-floating), 150.

2. "Isolated" DNA is not "markedly different" in function from DNA in the body.

Defendants' argument that "isolated" DNA is functionally distinct from DNA in the body is flawed both legally and scientifically. Even if there are some functional differences between DNA in the body and isolated DNA, it does not follow that those differences render isolated DNA patentable. The patent defines the function of isolated DNA according to how DNA in the body functions – i.e., coding for a polypeptide. '282 patent, cl.1 ("An isolated DNA coding for a … polypeptide"). Whether inside the body and surrounded by other cellular components or removed from the body and separated from other cellular components, DNA performs the same function of storing the instructions that code for a polypeptide. If DNA in the body and isolated DNA did not perform this same function, isolated DNA would be useless in diagnosing human predispositions, because it is precisely this sameness that allows doctors and scientists to infer what exists within the human body. Klein D. ¶¶ 28, 34. Thus, it is nonsensical to argue that isolated DNA has "markedly different characteristics" from DNA in the body, when their sameness makes isolated DNA useful in the field of genetic diagnosis.

Rather than address this fundamental scientific truth, defendants instead argue that "native" DNA and isolated DNA are different because (1) "native" DNA can perform functions that isolated DNA cannot, such as passing on hereditary traits or creating proteins, and (2) isolated DNA can perform functions that "native" DNA cannot, such as being used as probes and primers (segments of DNA that are usually synthesized by machines for use in sequencing or testing). *See, e.g.*, Kay D. ¶¶ 100, 132-36, 168-169, 174. None of the challenged claims in this case are limited to particular functions of isolated DNA that might distinguish it from "native"

DNA. Thus, while there may be differences between isolated DNA and "native" DNA with respect to what humans can or cannot do with them, the claims are to be analyzed according to their limits. Arguing that isolated DNA is different from "native" DNA by citing some functional distinctions not mentioned in the patent claims themselves cannot rescue an invalid claim. Even if there are differences between the limits of what has been claimed and DNA as it exists in the body, those differences are not "markedly different." 447 U.S. at 310.

The functions that defendants describe as unique to "native" DNA are not so. For the reasons stated in Dr. Nussbaum's declaration and *supra* p. 11 those functions depend on interactions between DNA and other things, such as surrounding proteins.

As to the three functions of "isolated" DNA cited by defendants, they first assert that "isolated" DNA can be sequenced and read to determine if there are mutations[14] in the DNA in the body. Kay D. ¶¶ 134-35. However, "native" DNA also has the potential to be sequenced and read. It is only humans' inability – currently – to sequence DNA while it is in the body that requires scientists to isolate it. No technique has yet been invented to enable scientists to sequence and read DNA while it exists in the body. But such is theoretically possible and may very well be invented in the future. DNA, whether in the body or outside the body, has the potential to be sequenced so that one can determine what polypeptide it encodes. Returning to the analogy above, only once gold is extracted from the sediment can it be seen and appreciated for its shininess. The shininess is an inherent property of the gold, just like the coding information is an inherent property of the DNA.

Second, defendants claim that "isolated" DNA can be used as a primer. Myriad Br. 8; Kay D. ¶ 136. With respect to some of the challenged claims, which plaintiffs argue are limited

[14] Defendants do not deny that the mutations covered by their claims reflect naturally-occurring variations in the gene and are not created by scientists. *See, e.g.*, Mason D. ¶¶ 18-21.

to an entire BRCA gene (i.e. '282 patent, cl. 1), this assertion is simply not true. Only small portions of a gene can be used as a primer. *Compare* Kay D. ¶ 183 (primer is 15-30 nucleotides) *with* Kay D. ¶ 178, n. 13 (BRCA1 cDNA is 5914 nucleotides); Nussbaum D. ¶ 40; Mason Supp. D. ¶¶ 16-17. Kay also notes that "[i]n the real world, virtually only synthetic DNA is used as primers and probes." Kay D. ¶ 162. Further, even for those challenged claims that could be read to cover portions of a gene (*e.g.* '282 patent, cl. 5), none of the claims that is challenged in this case is limited to the use of isolated DNA solely as a primer. It is the whole breadth of a claim that is the proper focus of the legal issues here, not some subset of what the claims may cover. In fact, defendants' patents do indeed have claims directed just to use of isolated DNA segments as primers, but plaintiffs have not challenged any of those claims. Claim 29 of patent '492, for example, claims "a pair of single-stranded DNA primers," where primers are defined as segments of the isolated BRCA2 DNA as short as 15 nucleotides. Plaintiffs have only challenged claims that have not been limited to DNA used as primers, and thus this "function" is not a basis for defending the validity of those claims.

The third function claimed to be exclusive to "isolated" DNA is its use as a probe. Myriad Br. 8; Kay D. ¶ 135. While it is theoretically possible to use the full BRCA1 DNA as a probe, it is never used this way for clinical applications. Nussbaum D. ¶ 40. *Cf.* Kay D. ¶¶ 135, 162. A probe is necessarily labeled, usually radioactively, so that it fluoresces. Accordingly, "isolate" DNA, or even a fragment thereof, cannot be used as a probe without further altering it. *Id.*; Mason Supp. D. ¶ 14. Thus, defendants are asserting that they can patent one thing because if that thing is further altered into something else, the resulting product has a different function. Furthermore, probes are typically made by machines, not from isolated DNA. Kay D. ¶ 162. As with primers, defendants specifically claim probes as separate claims (none of which is

challenged here) and thus appear to recognize that probes are distinct from the full isolated BRCA DNA sequences as claimed in their primary claims.

With respect to defendants' claims that DNA has functions that "isolated" DNA does not, it is inaccurate to say that "isolated" DNA cannot be used to create proteins. Nussbaum D. ¶¶ 30, 35. *See also* Kay D. ¶ 163. Defendants claim that isolated DNA that codes for the BRCA genes is distinct from "native" DNA because it does not contain any of the regulatory sequences and proteins that are involved in determining the expression of the BRCA gene. Here, they confuse a gene with the machinery that regulates gene expression. Nussbaum D. ¶ 35. Defendants agree that a gene can be defined as a unit of heredity that carries the information necessary to pass a trait or function from one generation to the next. Kay D. ¶ 142. That unit of heredity is composed of a segment of DNA and not the chromatin or other regulatory proteins. In the process of reproduction, it is the DNA – and only the DNA – that is responsible for the transmission of traits from one generation to the next. Nussbaum D. ¶ 29.

Classic experiments demonstrated that isolated DNA, once introduced into other cells and incorporated into chromosomes, would perform the very same function as it did while in the body. Nussbaum D. ¶¶ 30-34. The physical embodiment of a gene is DNA and the information contained within that gene is comprised of the arrangement of the bases in the DNA. This is the same whether DNA is inside the cell or isolated in a test-tube. Nussbaum D. ¶¶ 35-39.

3. Isolated DNA with the introns removed and/or cDNA

Defendants do not distinguish any of their claims by asserting that they consist solely of DNA with the introns removed or cDNA (cDNA, or "complementary DNA" is a form of DNA that does not include the introns, the regions that do not code for proteins). The claims must,

therefore, not be so limited.[15] The practice of genetic testing confirms this, given that routine methods of genetic testing uses DNA, not cDNA. Klein D. ¶ 35. If all of Myriad's claims encompass DNA that includes the introns, the Court need not consider the patentability of DNA with the introns removed and/or cDNA. Regardless, even if some claims are limited in this way, they are unpatentable subject matter.

Defendants first assert that cDNA never appears in the body. Kay D. ¶¶ 161-172. Whether cDNA appears only in the body is legally irrelevant to the question of whether it constitutes natural phenomena. Factually, the assertion is incorrect, for cDNAs do occur naturally in the human genome in the form of "processed pseudogenes" – double-stranded DNA sequences in the human genome that are substantially homologous, or similar, to the nucleic acid sequence of a processed mRNA. Nussbaum D. ¶ 42; Mason Supp. D. ¶ 18. A portion of the BRCA1 cDNA does appear in the body, made entirely without human intervention. Mason Supp. D. ¶ 18.

The key question is whether cDNA has markedly different characteristics from natural phenomena. It does not. cDNA is generated because of its complementary, biologically-determined relationship to naturally-occurring mRNA. Mason Supp. D. ¶ 18; Mason D. ¶¶ 28-29. Both DNA and cDNA are described by the same series of nucleotide bases. These bases are the same chemical structure in both DNA – whether "isolated" or not – and cDNA; thymine (T) in cDNA is the same as thymine in DNA. Mason D. ¶ 29. The exonic (protein-coding) sequences of cDNA are the same as those of "native" DNA, whether "isolated" or not. Nussbaum D. ¶¶ 41-42. To confirm this, one could compare what is listed as a cDNA sequence in the '282 patent, SEQ ID NO:1, to Figure 10A of the '282 patent, which lists the BRCA1 DNA

[15] One of the *amici*, BIO, does argue that some of the claims are limited to pure cDNA. Amicus BIO Br. 16. That purported claim construction is wrong and has not been adopted by the USPTO or the patentholder. Thus, the claim construction of this *amicus* and other *amici* who argue alternative constructions should be ignored.

sequence with introns and exons. The sequence of SEQ ID NO:1 and the sequence of exons in Figure 10A (represented by capitalized letters) are the same (the lower-case letters in Figure 10A represent the introns that do not code for protein).

To the extent the patent claims describe cDNA "inventions," they do so solely by describing the identity and sequence of the exons, both of which are identical to the DNA in the body. Defendants may claim that the structure of cDNA is different because the exons are attached to each other rather than the intervening introns. But there is nothing in defendants' claims that requires the cDNA be fully attached, each nucleotide to the next. Indeed the process by which DNA is sequenced usually results in the creation of fragments of the full gene, not the entire structure. Kay D. ¶¶ 166, 181; Mason Supp. D. ¶ 19.

Method Claims

Myriad did not invent any "medical instruments" or specific diagnostic methods as they claim (Myriad Br. 7). Routine, automated methods are used to perform DNA extraction, gene amplification, and sequencing analysis. Klein D. ¶ 32. The patent claims at issue are not analogous to medical instruments because they claim exclusive rights to compare genetic sequences irrespective of method.

Defendants' method claims consist of comparing or analyzing two DNA sequences to see if they are the same or different, a process that is also claimed with respect to RNA and cDNA sequences. In some instances, they additionally require the person engaged in the comparison to think that the differences have clinical significance. The language of the claims covers the comparing of sequences, not genes. *See, e.g.*, patent '001, cl. 1. Defendants' only justification for patenting what is solely a mental process is to argue that the mental process cannot begin until certain non-mental processes are completed. Specifically, defendants argue that one cannot

compare a DNA sequence until one "isolates" and "sequences" it and therefore the "isolation" and "sequencing" processes are inherent in the claims. Kay D. ¶¶ 64-71, 186. Beyond being a contorted reading of the plain language of the claims, which contain no language whatsoever regarding isolating or sequencing a gene, this justification is problematic for additional reasons.

First, none of the claims identifies any of the comparisons as requiring "isolated" DNA sequences or RNA sequences or cDNA sequences. The precise language of the claims is broader. If a scientist invented a method for viewing DNA, RNA, or cDNA sequences without isolating them, use of that method to compare or analyze a person's BRCA genetic sequence would still infringe the terms of the patent.

Second, none of the claims identifies any of the steps necessary to compare. Defendants' expert suggests that the prior steps can be found in the explanations of the patents. Kay D. ¶ 115. But that explanation explicitly defines a method that "may" be used, not all of the methods known or unknown.

Sweeping Nature of Defendants' Claims

Defendants' claims are sweeping. As noted, they claim all forms of the "isolated" BRCA1/2 DNA – whether simply extracted or excised from a sample or chemically synthesized in the lab, whether containing naturally-occurring mutations correlated with cancer or not, and both single-stranded and double-stranded forms. As experts have noted, broad patent claims on genes are particularly detrimental for follow-on innovation. Stiglitz D. ¶¶ 34-35; Murray D. ¶¶ 15, 19.

Their claims also cover small segments of "isolated" BRCA DNA. Claims 5 and 6 of '282, which neither the Myriad defendants nor the USPTO discusses, encompass any DNA having at least 15 nucleotides of the BRCA1 DNA. Furthermore, defendants seem to assert that

the other claims, though not as explicit, could also cover small segments of "isolated" DNA.[16] First, defendants' emphasis on the use of their patented composition as a primer makes no sense if the composition does not include small segments of DNA. Myriad Br. 8. Second, Kay notes that the composition claims use the term "encode for" or "code for." Kay D. ¶ 20. Thus, claim 1 of the '282 patent is for "isolated DNA coding for a BRCA …." As Kay notes, "coding for" means it can be used to create mRNA and/or a polypeptide "or a fragment thereof." Kay D. ¶ 20. Thus, defendants seem to claim any "isolated" DNA that can create even a fragment of a BRCA polypeptide or a fragment of mRNA.

If the defendants' claims all include very short segments of "isolated" DNA (or comparing very short segments of a DNA sequence), then it is difficult to overemphasize the sweeping nature of the claims. A careful, scientifically valid analysis done by Thomas Kepler and his co-authors of one of the claims being challenged in this case, claim 5 of patent '282, makes this clear. Cook-Deegan Ex. 2; Kepler Ex. 2. Claim 5 covers "an isolated DNA having at least 15 nucleotides of the DNA of claim 1." While claim 1 is defined as an isolated DNA coding for a polypeptide having an amino acid sequence of 1,863 amino acids (or 5,589 nucleotides), '282 patent, SEQ ID No:2, claim 5 is limited to DNA of as few as 15 nucleotides. The Kepler study took each 15-nucleotide sequence found within the BRCA1 gene, which is located on chromosome 17, and attempted to determine whether that exact sequence can be found elsewhere in the human genome. Cook-Deegan Ex. 2; Kepler Ex. 2. They limited their inquiry to only one of the 23 human chromosomes (chromosome 1) and found that a 15-nucleotide sequence from the BRCA1 gene was found 340,000 times on chromosome 1. This

[16] Defendants carefully never discuss that question, but hint that their claims do not cover fragments. Myriad Br. 16-17. *See also* Leonard D. ¶ 48; Grody D. ¶ 28 (a person skilled in the art would conclude that the patents generally define the entire gene and not segments thereof). While plaintiffs argue that these claims cover natural phenomena when they exclude fragments, the claims are even broader in scope if they do cover fragments.

translates into 14 sequences on each gene that fit the definition of Claim 5 of patent '282, and therefore "infringe." Cook-Deegan Ex. 2; Kepler Ex. 2. Plaintiffs' expert did a similar analysis for claim 6 of '282. Mason Supp. D. ¶¶ 6-9.[17] Both of these studies would apply to the other isolated DNA claims if fragments of DNA are covered by them.

Treating "isolated DNA" merely as a chemical means that any sized segment should be able to qualify as patentable subject matter; yet, these segments appear along the entire human genome. Because DNA is an informational molecule, each segment of DNA embodies a genetic code and a law of nature.

Defendants' method claims are even more wide-ranging. Defendants seem to claim any comparisons of the sequence of any segment of the BRCA1 DNA (or RNA or cDNA) with the sequence of another segment of the BRCA1 DNA (or RNA or cDNA). *See, e.g.,* '441 patent, col. 20:10-11, 37-38 (segments as short as 15 nucleotides). In addition, claim 1 of patent '441 includes looking for an "alteration of a BRCA1 gene" by, in part, comparing the "sequence of the BRCA1 gene" with the sequence of the "wild-type" (non-mutated) BRCA1 gene. As defendants' expert notes, the "BRCA1 gene . . . [is] defined in the [] patent [] as including "coding sequences, intervening sequences and regulatory elements." Kay D. ¶ 26 (quoting the '441 patent among others). Additionally, it includes any stretch of nucleic acid that encodes "a BRCA1 polypeptide, fragment, homolog or variant." *Id.* A "homolog" is a stretch of the BRCA1 gene that is "at least about 60%" similar to the original. '441 patent, col. 24:15-22. Thus, the patent can be read to include comparing any nucleotide sequence that encodes any "fragment" or "variant" of the BRCA gene or that is 60% similar to that "fragment" or "variant." *See also* Kay D. ¶ 42 (quoting the '492 patent defining homologous as "at least about 50%").

[17] Thus, claims 5 and 6 of '282 are unusual in that they are broader in scope than the independent claims on which they are based.

Therefore, in order to accomplish "comparing" as defined in the patents, one need not compare the entire genetic sequence. Claim 1 of patent '001, which involves looking for "a difference in the sequence," can be done by comparing small segments, and not the whole gene.

ARGUMENT

I. THE BRCA1/2 GENE PATENT CLAIMS VIOLATE SECTION 101.

Plaintiffs are entitled to summary judgment on the section 101 challenge to the patent claims. Patent claim construction and the issue of section 101 invalidity are questions of law. *In re Bilski*, 545 F.3d 943, 951 (Fed. Cir. 2008) (en banc), *cert. granted*, 129 S. Ct. 2735 (2009); *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1454 (Fed. Cir. 1998) (en banc). The parties have provided ample evidence in declarations to construe the claims and determine whether they violate section 101. Defendants attempt to confuse the legal questions presented by obscuring what their claims cover and mischaracterizing the legal precedent. However, once the BRCA1/2 DNA claims and process claims are construed and evaluated according to their terms and case law, only one conclusion can be drawn: they are invalid because they cover unpatentable subject matter. The DNA that has been patented clearly does not have markedly different characteristics from naturally-occurring DNA. This test was set out in *Diamond v. Chakrabarty*, the most recent Supreme Court opinion to consider the patentability of compositions, and is easily met here. 447 U.S. at 309-10. Moreover, the methods that have been patented here involve no machine and no transformation "to a different state or thing," but instead cover the mental act of comparing or analyzing given sequences. *Diamond v. Diehr*, 450 U.S. 175, 192 (1981). Thus, the select claims that have been challenged in this action must be held invalid under section 101.

A. The BRCA1/2 DNA claims are invalid because they patent natural phenomena, physical phenomena, products of nature, and laws of nature.

The patented DNA covers "natural phenomena," "physical phenomena," "products of nature," and "laws of nature" and therefore violates section 101.[18] As defined by the defendants, "isolated" means:

> An "isolated" or "substantially pure" nucleic acid (e.g., an RNA, DNA or a mixed polymer) is one which is substantially separated from other cellular components which naturally accompany a native *human sequence* or protein, e.g., ribosomes, polymerases, many *other human genome sequences* and proteins. The term embraces a *nucleic acid sequence* or protein which has been removed from its naturally occurring environment, and includes recombinant or cloned DNA isolates and chemically synthesized analogs or analogs biologically synthesized by heterologous systems.

'282 patent, col. 19:8-18, '473 patent, col. 19:6-15; '492 patent, col. 17:62-67, col. 18:1-5 (emphasis added).[19] *See also* Myriad Br. 14-15. Their expert, Kay, equates this with DNA that "has been extracted from the cell and excised from the chromosome, *or* chemically synthesized" (emphasis added), Kay D. ¶ 17. Under defendants' construction, it is clear that at least part of

[18] Unpatentable subject matter includes "laws of nature," "natural phenomena," "abstract ideas," and "physical phenomena," as defendants concede, Myriad Br. 21-22 (citing *Diehr*, 450 U.S. at 185; *Chakrabarty*, 447 U.S. at 309), as well as "products of nature." Although they do not explain the differences between "natural phenomena," "physical phenomena," and "products of nature," Defendants appear to argue that "products of nature" have not been recognized by the courts as unpatentable. Myriad Br. 21. However, *Chakrabarty* notes the key inquiry for purposes of section 101 is whether something is a "product of nature," 447 U.S. at 313 (stating that the relevant distinction is "between products of nature, whether living or not, and human-made inventions"). Numerous other cases similarly acknowledge that products of nature are unpatentable subject matter. *General Electric Co. v. De Forest Radio Co.*, 28 F.2d 641, 642 (3d Cir. 1928) (noting that "a patent cannot be awarded for a discovery or for a product of nature, or for a chemical element"); *In re Marden I*, 47 F.2d 957, 957 (C.C.P.A. 1931) (concluding that "[u]ranium is a product of nature, and the appellant is not entitled to a patent on the same, or upon any of the inherent natural qualities of that metal"); *In re Marden II*, 47 F.2d 958. 959 (C.C.P.A. 1931) (stating that "pure vanadium is not new in the inventive sense, and, it being a product of nature, no one is entitled to a monopoly of the same"). Even a case relied upon by Defendants, *Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156, 162 (4th Cir. 1958), reasons that a product of nature cannot be patentable unless it is a "new and useful composition of matter." While Defendants imply that this statement should be read as ruling that any product of nature can be patentable, the statement also echoes the principle laid out in *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948), and *American Fruit Growers, Inc. v. Brodgex Co.*, 283 U.S. 1 (1931), and other precedent when interpreting what is patentable subject matter: a product of nature is unpatentable unless it is sufficiently different to become a patentable "composition of matter."

[19] Defendants cite to this definition of "isolated" in their brief but notably omit the parts of the definition from the patents that refer to "human sequences." Myriad Br. 14-15. Throughout their papers, they attempt to hide the informational quality of isolated DNA despite the repeated descriptions in the patents of isolated DNA as a "nucleic acid sequence" – a sequence that does not change with isolation and that constitutes natural phenomena and a law of nature.

what constitutes "isolated DNA" is plainly natural phenomena – namely, DNA that "has been removed from its naturally occurring environment," Myriad Br. 14, or DNA that "has been extracted from the cell and excised from the chromosome," Kay D. ¶ 17.[20] When subject matter encompassed by a claim is unpatentable, the entire claim must collapse.[21] If a patent claim purported to cover water extracted from the ocean *or* a completely synthesized thirst quenching liquid, the claim would be invalid under section 101 because it covered a natural product – water – regardless of the fact that it may also cover subject matter that would itself be independently patentable. Similarly, the umbrella of "isolated DNA" as used in the patents covers DNA that is not markedly different in structure or function from DNA as it exists in the body. *See supra* pp. 10-17. Its removal from its naturally occurring environment, or the cell and chromosome, makes it no more patentable than the refined cellulose that was "an extract obtained by the decomposition or disintegration of material substances," the pine needle fiber "made free" from the needle, the "substantially pure tungsten," the purified uranium, the purified vanadium, and the purified ultramarine examined in precedent. *See Am. Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566, 593 (1874); *Ex parte Latimer*, 1889 Dec. Comm'r Pat. 123 (1889); *General Electric Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d Cir. 1928)*; In re Marden I*, 47 F.2d 957 (C.C.P.A. 1931); *In re Marden II*, 47 F.2d 958 (C.C.P.A. 1931); *In re Merz*, 97 F.2d 599 (C.C.P.A. 1938).

[20] In other cases relating to non-DNA patents, the term "isolated" has been defined similarly to mean "separated from." *See Mannatech, Inc. v. Glycobiotics Int'l, Inc.*, 513 F. Supp. 2d 754, 762 (N.D. Tex. 2007) (concluding that "'isolated and purified'" means "'separated from other, unwanted substances'"); *Synthon IP, Inc. v. Pfizer Inc.*, 446 F. Supp. 2d 497, 509 (E.D. Va. 2006) (noting that it was undisputed that "'isolating' (1) generally means 'separating' and (2) does not equate to 'purifying.'")

[21] Similarly, if a claim "reads on" prior art, then it is invalid, even if it also covers or "reads on" things that are not in the prior art. *Titanium Metals Corp. of Am. v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985) ("It is also an elementary principle of patent law that when, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if *one* of them is in the prior art") (emphasis in original).

In large part, defendants' arguments rely on the notion that only "native" DNA – DNA as it is found in one's body – can constitute unpatentable subject matter under section 101. They read far too much into a few examples of unpatentable subject matter given in *Chakrabarty* – "a new mineral discovered in the earth or a new plant found in the wild," 447 U.S. at 309 – as if these examples define the outer bounds of what is unpatentable under section 101. However, if that were the case, then surely the citrus fruit of *American Fruit Growers*, which had been chemically treated such that its "rind or skin carries borax in amount that is very small but sufficient to render the fruit resistant to blue mold decay" would have been found patentable. *Am. Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 6 (1931). While the lower court had concluded that "the complete article" – the combination of the natural fruit and a boric compound – "is not found in nature" and thus was patentable, the Supreme Court observed that "every change in an article is the result of treatment, labor, and manipulation." *Id.* at 11-12. The key question is not whether the patented thing has undergone change of any kind from its form in nature, but whether it no longer is natural phenomena or a product of nature. Thus, the combination of bacteria strains in *Funk Brothers*, though not naturally-occurring, was held unpatentable because the individual strains and their qualities in aggregate were the "work of nature." 333 U.S. 127, 130 (1948). *Diamond v. Chakrabarty* would not have presented a close question if the legal standard were whether the genetically-engineered bacterium naturally existed in the environment – it did not. 447 U.S. 303 (1980). The only conclusion that can be drawn from this precedent is that forms of DNA other than DNA existing in one's body may constitute unpatentable subject matter.

Chakrabarty instructs that to be patentable, the claimed product must "hav[e] a distinctive name, character [and] use." 447 U.S. at 309-10 (quoting *Hartranft v. Wiegmann*, 121

U.S. 609, 615 (1887)). The Court explained that the patentable man-made bacteria has "markedly different characteristics from any found in nature" and that its "discovery is not nature's handiwork, but his [the inventor's] own," when comparing the genetically-modified bacterium to the unpatentable combination of bacteria in *Funk Brothers*:

> "Each of the species of root-nodule bacteria contained in the package infects the same group of leguminous plants which it always infected. No species acquires a different use. The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect it always had. The bacteria perform in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee." 333 U.S. at 131.
>
> Here, by contrast, the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under section 101.

Chakrabarty, 447 U.S. at 310. The claimed DNA in this case does not have a distinctive name, character, and use from DNA in the body, nor does it have markedly different characteristics. Both are DNA, their chemical structures are not markedly different, the genetic code embodied by each is the same, and their use in storing and transmitting information is identical. Isolated BRCA1/2 DNA is useful because the sequence – the result of "nature's handiwork" – informs the physician or scientist about how the gene operates in one's body. BRCA1/2 sequences, with or without mutations, are the same before and after isolation. Similarly, complementary DNA, or cDNA, is the result of its naturally-occurring mirror relationship with mRNA. Because it is a function of a law of nature, cDNA can and does exist naturally in the body. *See supra* p. 16. Even if the patent claims are limited to cDNA produced in the laboratory[22] – a proposition that is difficult to reconcile with the plain language of the claims and Myriad's own suggested broad construction as discussed *supra* pp. 8-16 – the cDNA at issue here is identical to the cDNA that

[22] cDNA can be generated in the laboratory using routine, standard techniques. Mason Supp. D. ¶ 19.

is naturally-occurring. In *Cochrane v. Badische Anilin & Soda Fabrik*, the Supreme Court held that an artificial version of alizarine could not be patented because it was not a "new composition of matter." 111 U.S. 293, 311 (1884). Thus only the process, not the product, could potentially be patented.

Defendants do not deny that their patents allow them to exclude anyone from obtaining his or her own BRCA1/2 sequence. As such, the law of nature represented by a person's BRCA1/2 genetic sequence is completely preempted by their claims. *See, e.g.*, *Gottschalk v. Benson*, 409 U.S. 63, 71-72 (1972) (observing that "[t]he mathematical formula involved here has no substantial practical application except in connection with a digital computer, which means that if the judgment below is affirmed, the patent would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself"). Defendants have not patented one, or even many, specific isolated BRCA1/2 molecules. They have patented every formulation of the BRCA1/2 genes, thus obstructing access to one's own genetic information. Mason Supp. D. ¶¶ 3-4. This information is enormously different in both scope and extent from other information contained in chemical compounds. While chemical molecules like water can be described as H_2O, HOH, or OH_2 because they consist of any two hydrogen atoms and an oxygen atom, DNA is not described according to its atomic structure, i.e., the sugars and phosphates that make up its backbone. *See supra* p. 7. Instead, DNA is described by its sequence of nucleotide bases – the order of these nucleotides matters because DNA encodes the instructions for the development and functioning of each of our cells. For that reason, genes and human genetic sequences have been recognized by scientists as the most fundamental information about humanity. Sulston D. ¶ 10.

This point highlights a distinction between the claims presented here and the claim at issue in *Parke-Davis*. The compound in *Parke-Davis* involved the transformation of adrenaline into a pure form that could be administered as a therapeutic. *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95 (C.C.S.D.N.Y. 1911). Adrenaline serves no informational function whether "purified" or not – it may provide a non-specific fight or flight signal, but the compound of adrenaline is the same from person to person, whether produced internally or administered. Klein D. ¶ 10-11; Nussbaum D. ¶ 39. It does not encode for the design of human organs. It is continually produced and degraded, unlike DNA. Klein D. ¶ 11. It is at least possible for an inventor to develop another therapeutic that would perform the same functions as patented adrenaline. Moreover, the patented substance in *Parke-Davis* included "a new and inorganic substance arising from the regrouping of atoms… which have been broken from the molecules which constituted their original form…[and] by rearrangement and by addition of new atoms created new molecules" 189 F. at 98.[23]

In contrast, the DNA at issue in these patents performs the same informational function whether it is in the body or isolated. The claimed "isolated" BRCA DNA is not administered as a therapeutic; the genetic sequence contained therein is what is useful. There is no regrouping, rearrangement, or addition to the "isolated DNA" sequence – if there were, it would no longer be of practical use in the genetic testing context. Klein D. ¶¶ 28, 34. Moreover, nobody can "invent" a different formulation of DNA that serves the same function of informing a patient whether she has significant mutations on her BRCA genes. DNA is a blueprint for the creation

[23] Judge Hand construed what is covered by the Takamine, or "Adrenalin," patent claim, which is defined in part as being "free from inert and associated gland-tissue." He concluded that the "new and inorganic substance" that is part of the patented "Adrenalin" was not the original "inert and associated gland-tissue" because it had undergone rearrangement and represents the creation of new molecules. *Id.*

of proteins, cells, and the human body; at most, adrenaline is akin to a thermostat, a non-specific signal in response to environmental cues. Klein D. ¶¶ 10, 12.

Aside from the dissimilarity between DNA and adrenaline as compounds, the legal analysis of *Parke-Davis* cannot control the outcome of this case. *Chakrabarty* clearly overruled the statement upon which defendants rely: "even if [the adrenaline] were merely an extracted product without change, there is no rule that such products are not patentable." Myriad Br. 22 (quoting *Parke-Davis*, 189 F. at 103). *Chakrabarty* proclaimed that a patentable product is "a product of human ingenuity 'having a distinctive name, character [and] use.'" 447 U.S. at 309-10. A simple "extracted product without change" could not meet this test. Furthermore, while *Parke-Davis* is a lengthy opinion that examines many different claims in two patents and several different legal objections, the discussion of patentable subject matter is short and focuses on novelty and utility. 189 F. at 102-3 (finding that the "invention was therefore novel" and that "Takamine was the first to make it"). Without citing case law that dealt with natural phenomena, the court concluded that the adrenaline became a "new thing commercially and therapeutically. That was a good ground for a patent." 189 F. at 103. Yet, subsequent case law has established that "it is improper to consider whether a claimed element or step in a process is novel or nonobvious, since such considerations are separate requirements" when evaluating whether a claim is patent-eligible subject matter. *Prometheus Labs. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1343 (Fed. Cir. 2009). To the extent that *Parke-Davis* set out a test for subject matter eligibility that was based on novelty or the mere extraction of a natural product, that test has been overruled.

Beyond *Parke-Davis*, defendants rely on lower court cases to bolster their assertion that isolated DNA should be patentable. None of these cases is persuasive or binding in this context.

The patent claim on vitamin B(12) in *Merck* did not reach many forms of purified vitamin B(12), including vitamin B(12) derived from sources other than the specified fermentates. *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156, 160 (4th Cir. 1958). The same is not true of defendants' patents, which preclude examination of any and all BRCA1/2 genes. *In re Bergstrom* did not cite any precedent for its 101 analysis, and instead focused on novelty. 427 F.2d 1394 (C.C.P.A. 1970). As in *Parke-Davis*, the product could be administered as a therapeutic and thus is distinguishable from the isolated DNA at issue here; isolated DNA is not "markedly different" when it comes to its significant feature – its sequence. *Id.* *In re Kratz* involved a § 103 obviousness or anticipation challenge as well as a § 102 analysis. 592 F.2d 1169 (C.C.P.A. 1979). While the court discussed whether the composition claimed was a naturally-occurring compound, the patent was not scrutinized under section 101. *Id.* at 1174-75. Rather, the court concluded that the patent should be upheld because there was no basis in the prior art for the invention. *Id.* The patent at issue in *Bergy* primarily claimed processes for creating an antibiotic through fermentation of a microorganism. The product claim over a "biologically pure culture of the microorganism . . . being capable of producing the antibiotic lincomycin" was limited to a specific function – creating a named antibiotic that could not otherwise be produced by the microorganism. *In re Bergy*, 596 F.2d 952, 967, 972 (Fed Cir. 1979), *appeal dismissed as moot*, 444 U.S. 1028 (1908). The DNA at issue here, whether isolated or not, encodes for the same BRCA1/2 proteins and the "isolated DNA" claimed by defendants is not limited to non-natural uses such that it would exclude that encoding function. Therefore, the claims do indeed cover DNA that performs this most natural of functions.

The Supreme Court and lower court precedent cited here and in section II of the opening brief (referred to herein as "Pls. SJ Br.") establishes that natural phenomena or products of

nature, even when removed from their natural environment or purified, are unpatentable. Defendants argue that these cases involved patents that were dismissed "on the ground that the patents sought to cover old products that had long been known and used in their respective industries" and therefore do not speak to what is patentable under § 101. Myriad Br. 25. They imply that these cases, instead, centered on novelty. Oddly, defendants list *Funk Brothers* as one of these cases, even though *Chakrabarty* cites it at length in its discussion of the limits placed on patents by § 101. 447 U.S. at 309-10. A closer reading reveals the flaw in defendants' logic. There is no question that the cases do refer to an unpatentable thing as not new or inventive. One would expect nothing different when describing natural phenomena, for while natural phenomena may be recently discovered, they will have existed from time immemorial and not be truly inventive. As *Funk Brothers* explained, "there is no invention here unless the discovery that certain strains of the several species of these bacteria are non-inhibitive and may thus be safely mixed is invention. But we cannot so hold without allowing a patent to issue on one of the ancient secrets of nature now disclosed." 333 U.S. at 132. The *In re Marden II* court observed that "pure vanadium is not new in the inventive sense, and, it being a product of nature, no one is entitled to a monopoly of the same." 18 C.C.P.A. at 1059. Similarly, "[pure tungsten] existed in nature and doubtless has existed there for centuries." *General Electric Co.*, 28 F.2d at 643. References to a thing being "old" may indicate that it is a product of nature; these references do not negate the courts' conclusions that the thing is not patentable subject matter.

Cases that involve patents relating to natural things, but do not examine the question of whether natural phenomena have been claimed, are irrelevant to the subject matter analysis. Defendants' suggestion to the contrary should be rejected. Myriad Br. 21, 27. Neither *Plummer v. Sargent*, 120 U.S. 442, 446-50 (1887) (concluding that defendants had not infringed a patent

claim over an iron product that had an ornamental appearance), nor *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 131-32 (2001) (finding that two plant-related patent statutes did not preclude the granting of patents pursuant to section 101 and noting that the parties had not disputed whether the claims qualified as "manufacture" or "composition of matter"), focused on the question of whether the patent was invalid because it claimed natural phenomena. Furthermore, while in *Plummer*, others were free to use iron and create ornamental iron in other ways, the court limited the scope of the product to the particular process described: "the patent for the product must be limited to an article made by a particular process ...." 120 U.S. at 450. *J.E.M. Ag Supply* is also notable in that the Court reaffirmed *Chakrabarty*'s product of nature analysis and once again stressed that the product of nature doctrine is part of determining what is patentable under section 101. 534 U.S. at 130-31. *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009), and *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988), two genetics-related cases, are also inapposite. Neither case involved a section 101 subject matter challenge to the patents, and *O'Farrell* centered on a method for producing protein in a bacteria whose DNA had been transformed – quite different from the instant claims. It would be erroneous for any court to assume that a case involving genetics-related patents must be read as finding broad claims on human genes to be patentable subject matter, regardless of whether any section 101 challenge was ever brought, when the Patent Act sets out patent invalidity as an issue to be raised by the parties. 35 U.S.C. § 282 (2009). If that were so, the Supreme Court could have proceeded with its consideration of *Lab. Corp. of America Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124 (2006), after it granted *certiorari* and the parties and *amici* had fully briefed the issue of patentable subject matter eligibility. Instead, the Court dismissed *certiorari* as improvidently granted based on the parties' failure to raise the section 101 issue below. *Id.*

Both sets of defendants argue that the courts must give a high level of deference to the USPTO's policy of granting gene patents. While the USPTO may be entitled to deference in the conduct and interpretation of its own procedures, 35 U.S.C. § 2 (2009), there is no case law that establishes that courts must defer to the agency with regard to interpreting substantive provisions like section 101. Defendants do not cite to any such precedent, and in fact, the Federal Circuit has stated frequently that it owes no deference to USPTO legal determinations. *See, e.g., Arnold P'ship v. Dudas*, 362 F.3d 1338, 1340 (Fed. Cir. 2004) ("This court reviews statutory interpretation, the central issue in this case, without deference"). Instead, Congress has created a presumption of validity for issued patents. 35 U.S.C. § 282 (2009). The fact that approximately 40% of patents, once challenged in the courts, have been found invalid demonstrates that this presumption is often overcome and that the respect afforded to the USPTO is far from absolute.[24] Moreover, the lack of Congressional action to specifically prohibit gene patents hardly speaks to the deference owed to the USPTO in this context. For example, the Federal Circuit recently set out a test for the patentability of process claims that potentially will invalidate thousands of patents on business methods, despite the fact that Congress has never specifically addressed the patentability of business methods. *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008); *see also* Melissa Traynor & Tom Sawyer, *Business-Method Patent Challenge Heads to High Court*, Engineering News-Record, July 27, 2009, at 13.

Finally, Myriad makes two arguments that can be easily rejected. First, Myriad asserts that if the Court were to conclude that these patent claims were invalid under U.S. law, and

[24] Institute for Intellectual Property & Information Law, University of Houston Law Center, Patstats.org, Full Calendar Year 2008 Report, http://www.patstats.org/2008_Full_Year_Posting.rev3.htm (indicating that 40% of all validity determinations in federal court in 2008 found the challenged patent to be invalid). *See also* Paul F. Morgan & Bruce Stoner, *Reexamination v. Litigation – Making Intelligent Decisions in Challenging Patent Validity*, 86 J. Pat. & Trademark Off. Soc'y 441-461 (2004) (citing USPTO statistics showing that 74% of patents previously issued by the Patent Office later challenged through the reexamination process were either canceled or changed by the USPTO, meaning their original approval was actually undeserved).

declared them invalid, it would violate the Takings Clause of the U.S. Constitution. Myriad Br. 29. Under this theory, all patents granted by the USPTO, no matter how outlandishly invalid, must be upheld to avoid a takings issue. Given the long history of invalidation of claims by the courts, this argument seems strained at best, and to plaintiffs' knowledge, has never been raised to defend a patent's validity. Second, Myriad asserts that invalidation of the claims "most likely" would violate international law. Myriad Br. 29 & n. 10. It is not surprising that Myriad only alludes to, but does not develop, this theory. Article 27 of the treaty to which it refers, the Agreement on Trade-Related Aspects of Intellectual Property ("TRIPS"),[25] allows governments to exclude from patentability diagnostic, therapeutic, or surgical methods. TRIPS, art. 27.3. It also authorizes the denial of the patentability of a particular invention on the grounds of *ordre public* (roughly translated, the "public interest"). Furthermore, article 8.1 of TRIPS allows governments to take public health concerns into consideration within their national intellectual property laws. Accordingly, the invalidation of these patents would create neither a constitutional problem nor a conflict with the U.S. government's international treaty obligations, particularly when the law of the U.S. has been, and continues to be, that natural phenomena and laws of nature are not patentable.

B. The challenged process claims do not involve a machine or transformation and thus do not constitute patentable subject matter.

The process claims challenged in this case do not involve any machine or transformation, as required by *In re Bilski*.[26] In *Bilski*, the Federal Circuit set forth the "definitive test to determine whether a process claim is tailored narrowly enough to encompass only a particular application of a fundamental principle rather than to pre-empt the principle itself." 545 F.3d at

[25] TRIPS is available at http://www.wto.org/english/docs_e/legal_e/27-trips.pdf.
[26] They are also a far cry from "cancer-diagnosing methods" claimed by the defendants (Myriad Br. 7), as they do not set out a specific method for cancer diagnosis. Even the genetic testing offered by Myriad, while informative as to hereditary predisposition, is not a method for diagnosing whether a patient suffers from cancer.

954, *cert. granted*, 129 S. Ct. 2735 (2009). "A claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." *Id.* The Myriad defendants appear to concede that the process claims do not involve the use of any particular machine.

In order to argue that the process claims meet the "transformation" prong of the *Bilski* test, the defendants import entirely new terms and processes into the plain language of the claims. Defendants' suggestion that the process claims necessarily involve extraction, transformation, and hybridization of DNA or genes is misleading and improper. Kay D. ¶¶ 62-71. None of these steps and processes is required by the claims themselves and for that reason cannot be magically inserted into the process claims. *ASM Am., Inc. v. Genus, Inc.*, 401 F.3d 1340 (Fed. Cir. 2005) (holding that discussion of separate steps of a method in specification does not support interpreting plain claim language covering only one step to inherently include other step); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed. Cir. 2005) (*en banc*). While Myriad's brief states that claim 1 of the '441 patent and claim 1 of the '001 patent involve "comparing a BRCA1 gene, RNA, or cDNA made from mRNA sequences" (Myriad Br. 38 nn.14 & 15), the actual language of these claims cover the comparing of sequences, not genes themselves.[27] Similarly, claims 1 and 2 of the '857 patent involve the "comparing" of genetic sequences, and

[27] Claim 1 of the '441 patent states: "A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises *comparing germline sequence* of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a *sequence* of BRCA1 cDNA made from mRNA from said sample with germline *sequences* of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA1 cDNA, *wherein a difference in the sequence* of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject" (emphasis added).
Claim 1 of the '001 patent: "A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises gene *comparing a first sequence* selected form [sic] the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample *with a second sequence* selected from the group consisting of a BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, *wherein a difference in the sequence* of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample *from the sequence* of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample" (emphasis added).

claim 1 of '999 involves "analyzing" sequences.[28] Defendants conveniently blur this distinction between comparing or analyzing genes (which is not claimed) and analyzing sequences (which is claimed) in order to imply that the process of sequencing genes must be performed before comparing or analyzing sequences can take place. In fact, possession of the sequences is assumed by the claim language, and only the mental process of comparing them is what is covered. Grody D. ¶¶ 40-45; Leonard D. ¶¶ 60-65.

The absence of transformation becomes even more obvious when one examines the claim language at issue in *Prometheus*, a case heavily relied upon by Defendants. The patent claim in that case read:

> A method of optimizing therapeutic efficacy for treatment of an immune mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder
>
> wherein the levels of 6-thioguanine less than about 230 pmol per 8x108 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and
>
> wherein the levels of 6-thioguanine greater than about 400 pmol per 8x108 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

[28] Claim 1 of the '857 patent states: "A method for identifying a mutant BRCA2 nucleotide sequence in a suspected mutant BRCA2 allele which comprises *comparing the nucleotide sequence* of the suspected mutant BRCA2 allele with the wild-type BRCA2 nucleotide *sequence*, *wherein a difference between the suspected mutant and the wild-type sequence* identifies a mutant BRCA2 nucleotide sequence" (emphasis added).
Claim 2 of the '857 patent states: "A method for diagnosing a predisposition for breast cancer in a human subject which comprises *comparing the germline sequence* of the BRCA2 gene or the *sequence* of its mRNA in a tissue sample from said subject with the germline *sequence* of the wild-type BRCA2 gene or the *sequence* of its mRNA, wherein an alteration in the germline *sequence* of the BRCA2 gene or the *sequence* of its mRNA of the subject indicates a predisposition to said cancer" (emphasis added).
Claim 1 of the '999 patent states: "A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables 12A, 14, 18 or 19 in a human which comprises *analyzing a sequence* of a BRCA1 gene or BRCA1 RNA from a human sample or *analyzing a sequence* of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID No. 1" (emphasis added).

Prometheus Labs. v. Mayo Collaborative Services, 581 F.3d 1336, 1340 (Fed. Cir. 2009), *petition for cert. filed*, 78 U.S.L.W. 3254 (U.S. Oct. 22, 2009)(No. 09-490).[29] The claim in *Prometheus*, by its terms, requires the "administering" of a synthetic drug to the body, and then a "determining" of the levels of metabolites that are present after the introduction of the drug. Without the administration of the drug, the medically significant levels of metabolites would not be created, and any determination of 6-thioguanine levels would be meaningless, *see id.* at 1346 (noting that the "transformation is of the human body following administration of a drug and the various chemical and physical changes of the drug's metabolites that enable their concentrations to be determined").[30]

In the context of the BRCA1/2 process claims, the medically significant fact – the sequence of one's BRCA1/2 genes – is naturally-occurring and is not created following the introduction of an artificial compound. If, as defendants argue, a "nucleotide 'sequence' is merely a scientific notation understood by one of ordinary skill in human genetics as shorthand for the primary chemical structure of the DNA molecule," Myriad Br. 15, then the "comparing" or "analyzing" of sequences surely does not demand the numerous extrinsic steps and processes that the defendants attempt to read into their process claims. The sequence exists before the process is performed, and it remains the same afterwards. The sequence from the person's sample and the reference sequence are a given, and the only step that the claims require is the mental process of comparing them. For claim 2 of the '857 patent, the mental process includes correlating the presence of a mutation with a higher risk of cancer. Whereas the patent claim in

[29] Some of the plaintiffs in this case, as well as plaintiffs' counsel, have filed amici briefs in support of *certiorari*. *See* Br. of Amici Curiae The American College of Medical Genetics et al.; Br. of Amici Curiae AARP and Public Patent Foundation.

[30] The Federal Circuit in *Prometheus* did not consider whether the claim at issue there would also meet the "machine" requirement, 581 F.3d at 1345.

Prometheus necessarily required a transformation – namely, the administration of a synthetic drug and the subsequent change in metabolite levels – no similar transformation takes place when one compares two genetic sequences. Similarly, whereas the "determining" of metabolite levels likely requires the physical step of processing a person's blood, the plain meaning of "comparing" sequences does not inherently require sequencing.

This distinction becomes even clearer when one considers the following hypothetical: A patient obtains sequencing of her entire genome, a service not currently provided by Myriad Genetics. She brings her sequence information to a geneticist in order to determine whether there are medically significant mutations on her BRCA1/2 genes. The "comparing" of her BRCA1/2 sequence information with the reference sequence by the geneticist would violate the process claims, even though he or she had not performed the underlying sequencing or ever "isolated" the DNA.

Defendants attempt to bolster their construction of the process claims by pointing to various dependent claims, none of which is challenged by plaintiffs. Myriad Br. 18. Drawing on dependent claims to narrow the scope of an independent claim, such as claim 1 of the '999 patent, is simply wrong-headed when the language of the claim is clear. *See Edward Lifesciences LLC v. Cook Inc.*, 582 F.3d 1322, 1327 (Fed. Cir. 2009). The patent law doctrine of claim differentiation presumes that "different words or phrases used in separate claims . . . indicate that the claims have different meanings and scope." *Karlin Technology, Inc. v. Surgical Dynamics, Inc.*, 177 F.3d 968, 972 (Fed. Cir. 1999). Claim differentiation "prevents the narrowing of broad claims by reading into them the limitations of narrower claims." *Clearstream Wastewater Systems, Inc. v. Hydro-Action, Inc.*, 206 F.3d 1440, 1446 (Fed. Cir. 2000). Given that the dependent claims are not at issue, they are irrelevant to the analysis except

to further illustrate the extent to which the challenged independent claims are broader and in fact do patent natural phenomena and laws of nature.

Strikingly, the USPTO does not discuss the process claims in its brief. In light of the position taken three years ago by the United States in *Laboratory Corp. v. Metabolite* on a similar patent claim, this silence is understandable. In its brief filed prior to the granting of *certiorari*, the U.S. Solicitor General acknowledged that the claim at issue "appears to involve such a natural phenomenon, because it asserts and relies on the existence of a naturally occurring correlation between elevated levels of total homocysteine and deficiencies in cobalamin or folate." Brief for United States as Amicus Curiae on Petition for a Writ of Certiorari 6, *Lab. Corp. of America v. Metabolite Labs, Inc.*, 548 U.S. 124 (2006) (No. 04-607) (citation omitted). The claim in that case read as follows:

> A method for detecting a deficiency of cobalamin or folate in warm-blooded animals comprising the steps of: assaying a body fluid for an elevated level of total homocysteine; and correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate.

548 U.S. at 129 (Breyer, J., dissenting) (dismissed for improvidential grant of certiorari, based on parties' failure to raise the section 101 issue below). The process claims at issue here more unambiguously constitute unpatentable subject matter than even the *Metabolite* claim, because the BRCA1/2 process claims do not require an analogous step to "assaying" – described as "obtain[ing] test results" by Justice Breyer. In the BRCA context, the "test results" are already obtained, the only step is comparing or analyzing the sequence against a reference sequence.

Thus, for the reasons stated here and in plaintiffs' opening brief,[31] the challenged claims do not qualify as patentable subject matter under section 101 of the Patent Act.

[31] Plaintiffs respectfully refer the court to their opening brief for a specific discussion of claim 20 of the '282 patent. Pls. SJ Br. 30-31. While the Federal Circuit overruled the district court in *Prometheus* after plaintiffs' moving brief was filed, the legal analysis does not change. Claim 20 of '282 covers the mental process of comparing growth rates

II. THE BRCA1/2 GENE PATENT CLAIMS ARE INVALID UNDER THE CONSTITUTION.

A. The patent claims violate the First Amendment.

The challenged patent claims violate the First Amendment because they directly limit thought and knowledge, including the mental process of comparing sequences and the genetic information embodied by DNA. Stiglitz D. ¶¶ 25, 34-35, 38-40. None of the defendants specifically addresses plaintiffs' First Amendment claims except to suggest plaintiffs misunderstand the facts. That argument has already been addressed. Each set of defendants makes only one other argument that deserves a response.

The USPTO argues that the "First Amendment imposes no …substantive limitation…." on patent law. USPTO Br. 12. Not surprisingly, the USPTO provides no citation to support this sweeping proposition. The proposition that if Congress or the USPTO authorized a patent on speech, whether based on content or viewpoint, it would not be objectionable under the First Amendment borders on the frivolous. *See R.A.V. v. St. Paul*, 505 U.S. 377, 395-96 (1992) (holding that government cannot censor speech based on content or viewpoint unless there is a compelling government interest and the restriction is narrowly tailored). Even if common law patent doctrines would also invalidate such a patent, as the USPTO argues, it would still be subject to strict scrutiny and invalid under the First Amendment. Morse's telegraph and Bell's telephone did not prohibit someone from thinking a thought and conveying that thought over the devices. For the reasons stated in plaintiffs' opening brief, these patent claims do prohibit thought and knowledge. There is no compelling interest in such restrictions and the restrictions are not narrowly tailored. Accordingly, they are invalid.

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of cells. The act of comparing the growth rate of two cells does not transform the growth rate of the cells – this is dictated by nature.

The Myriad defendants' response to plaintiffs' First Amendment claim is simply to reassert that "isolated" DNA is a chemical and therefore patentable. They seemingly concede that it is impossible to "invent around" their patents, but argue the patents are nevertheless valid. Myriad Br. 41-42. The USPTO carefully distinguishes the "difficulty" in inventing around (which does not render a patent invalid) from impossibility (which they correctly suggest does render it invalid). USPTO Br. 17-18.[32] The DNA or composition claims prevent anyone from "inventing around" the claimed DNA. They thus prohibit anyone from using the concept "carburetor" or, in other words, consist of a patent on all knowledge about and using the information embodied by the claimed DNA. That is unacceptable under the First Amendment.

Defendants and their *amici* in effect argue that plaintiffs' First Amendment argument is based on the theory that all patents inhibit speech about the content of the patented thing. That argument is misplaced. A patent on a carburetor does not have anything to do with the First Amendment. Patents in general have nothing to do with the First Amendment. But here, the method claims solely describe thinking. All of the steps Myriad asserts are inherent in those claims – such as sequencing – can be performed by any laboratory; Myriad controls these steps only when they are used on the BRCA1/2 genes and solely because of its monopoly on these genes. The only novel aspect of Myriad's patent claims is thinking "these are the same," "these are different," or "these differences are significant." Patents on thought violate the First Amendment.

B. The patent claims violate Article I, Section 8, Clause 8 of the U.S. Constitution.

Plaintiffs have argued that these patent claims run afoul of Article I, Section 8, Clause 8 of the Constitution because they impede rather than promote the progress of science. *See* Stiglitz

[32] The current SACGHS report concludes that "patents on genes and associations cannot be invented around." *See* SACGHS Final Draft Report and Recommendations, *supra* note 3, at slide 43.

D. ¶ 35; Murray D. ¶¶ 7-19. While plaintiffs concede that deference is due to Congress here, Pls. SJ Br. 37-38, the relevant question is not the rationality of "composition" claims as a whole, or even an undefined category of "gene patents." The question is whether these claims and these policies are rationally linked to the purposes of Article I. *See* Stiglitz D. ¶¶ 9-22. Plaintiffs provide evidence that they are not. *Id.* The USPTO provides no evidence to the contrary.

Myriad provides some evidence that is responsive to, but largely not contradictory to, plaintiffs' evidence. For example, Myriad asserts that it has permitted research on the BRCA genes. Myriad Br. 45**.** This is not responsive to the undeniable fact that the patents permit Myriad to prevent anyone from doing research. 35 U.S.C. § 271(a) (2009). The question is not whether Myriad's practices are rationally based to advancing the purposes of the Constitution, but whether the authority granted to Myriad is. Myriad's argument that it sometimes permits research, because research is so important, in many ways reinforces the irrationality of the patent grant that permits them to bar all research. Myriad also, of course, does not deny that some research has been deterred or that more would have occurred were it not for the patents. *See* Matloff Supp. D. ¶ 6; Cho D. ¶ 10; Murray D. ¶¶ 7-20 (concluding that the patents at issue are likely to have negatively impacted the accumulation of public knowledge of the BRCA1 and BRCA2 genes).

Similarly, Myriad asserts that it has an excellent test to look for mutations in the genes. *See, e.g.,* Critchfield D. ¶ 37. This case is not challenging patents on particular tests. Furthermore, this assertion is not responsive to the evidence of plaintiffs and their declarants that Myriad has, in the past, used a test that was known to be incomplete and that alternative tests now exist that could be more comprehensive than Myriad's. *See, e.g.,* Ledbetter D. ¶¶ 16-17. These alternative tests cannot be used as a result of the patents.

For each of plaintiffs' allegations supporting their Article I challenge, Myriad provides similarly non-responsive evidence. *See infra* section IV. For that reason, plaintiffs' facts must be taken as true and the Article I claim found meritorious.

III. THE USPTO'S ADDITIONAL ARGUMENTS ARE UNPERSUASIVE.

Most of the USPTO's brief is argued at such a high level of generality as to be meaningless. *See, e.g.,* USPTO Br. 8 ("It was rational for Congress to set forth in § 101 broad categories of subject matter…"); 9 ("A patent system that allows such [gene related] patents is rationally based"); 10 ("strong patent protection is vital to the biotechnology industry"); 13 ("the patent system is compatible with free speech principles" and "the patent system …expanded the amount of knowledge available to the public"); 14, n.4 ("patents tend to level the investment playing field"); 18 ("the Framers viewed patent grants as compatible with the First Amendment.…patent law promotes First Amendment interests"); 19 ("Patents like Myriad's can normally be expected to spur competitors …"). None of these arguments has any relevance to the patent claims or policies of the USPTO being challenged in this case.

The USPTO does concede that the patents challenged in this case were granted pursuant to official policies of the USPTO. USPTO Br. 23; *see also* Doll D. ¶ 37, Linck D. ¶ 49.[33]

Strikingly, the USPTO brief never refers to or defends the "method" claims being challenged by the plaintiffs as statutorily or constitutionally acceptable nor does it directly defend its policy of granting such claims. The brief contains only a very short section defending the "composition" claims without actually referring to any of them. USPTO Br. 20-23.

The USPTO does make three arguments that deserve brief mention. First, the USPTO argues that the doctrine of constitutional avoidance should preclude this Court from reaching the

[33] For a discussion of the USPTO's approach to gene patents generally, *see* John M. Conley & Roberte Makowski, *Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents (Part II)*, 85 J. Pat. & Trademark Off. Soc'y 371, 379-88 (2003).

constitutional claims. USPTO Br. 4. But, as the USPTO itself acknowledges, the plaintiffs' arguments against Myriad under section 101 of the Patent Act are arguments that the precise patent claims at issue in this case are contrary to the statute. USPTO Br. 3-4. Plaintiffs' arguments against the USPTO are that the policies of the USPTO in granting the claims at issue and other claims that are similar are unconstitutional. That there are other such claims is indisputable. *See* Doll D. ¶ 35. Invalidation of the particular claims in this case will not necessarily invalidate the USPTO's policy. Judgment for the plaintiffs based on section 101of the Patent Act does not render moot the plaintiffs' claims against the USPTO, which are not brought under section 101. Accordingly, the doctrine of constitutional avoidance is inapplicable.

Second, the USPTO appears to argue that plaintiffs cannot challenge the constitutionality of particular policies being challenged, but must instead challenge the statutes as facially unconstitutional. USPTO Br. 8; *see also* Myriad Br. 43-33. Plaintiffs do not argue the patent statutes are facially unconstitutional. Plaintiffs' arguments with respect to both the USPTO and Myriad are that if the statutes permit the claims and policies challenged, then the statutes are unconstitutional as so applied. This "as applied" challenge is completely consistent with the Supreme Court's approval of "as applied" challenges. *See, e.g., Ayotte v. Planned Parenthood*, 546 U.S. 320 (2006).

Third, the USPTO defends its policies of granting patents on isolated DNA on the grounds that DNA is a chemical. USPTO Br. 20-23. Plaintiffs agree that some chemicals are patentable. The question is whether these chemicals constitute natural phenomena and laws of nature, a subject on which that the Patent Office devotes exactly one conclusory sentence and one footnote. USPTO Br. 23 and n.6. Because the USPTO's arguments in this connection are identical to those of Myriad, plaintiffs incorporate their response at pp. 11-13, *supra*.

IV. THE REMAINDER OF MYRIAD'S FACTS ARE IRRELEVANT AND/OR MISLEADING.

The vast majority of facts offered by the Myriad defendants in their declarations are irrelevant and/or misleading. Thus, they do not raise disputed issues of material fact.

The declarations of Baer, Li, Parvin, and Sandbach are from researchers who have engaged in research on BRCA1/2 without being sued by Myriad. First, that Myriad has not enforced its patents against these researchers does not mean that it cannot. Under the law, Myriad has the authority to stop all research on the BRCA1/2 genes. 35 U.S.C. § 271(a); *Madey v. Duke Univ.*, 307 F.3d 1351 (Fed. Cir. 2002) (narrowing experimental use exception). Second, even if some research has been permitted, Myriad Br. 46, there is strong, empirical evidence that patents on genes inhibit the production of follow-on knowledge. Murray D. ¶¶ 7-20; Stiglitz D. ¶ 38-39. Defendants point to the publication of a number of papers relating to the BRCA1/2 genes. However, this is meaningless because they offer no control group to show how many papers would have been published if the BRCA1/2 sequences had not been patented. Furthermore, many of the published papers do not involve research that requires isolating or sequencing the genes. Scientists who do want to engage in this type of BRCA1/2 research are reluctant to do so because it would infringe upon the patents. Matloff Supp. D. ¶¶ 5-8; Cho D. ¶¶ 10-16. Myriad attempts to bolster its argument by citing a German study even while conceding that in Germany, unlike the United States, compulsory licensing is available for researchers. Strauss D. ¶ 42; Myriad Br. 45. Myriad also cites a single United States study that concludes that researchers often are unaware of or knowingly infringe patents, as if the fact that some people violate the law means that the law is just. Strauss D. ¶ 47 ("firms also chose to ignore or infringe patents … to move offshore ….); Myriad Br. 45.

The Skolnick declaration consists simply of the assertions that he is a public-spirited fellow and all of the plaintiffs are motivated solely by greed. Skolnick D. ¶¶ 20-23. Ignoring the fact that academic clinicians do not profit financially from their testing, Dr. Skolnick's observations about his own motives and those of plaintiffs are both self-serving and irrelevant.

The declarations of Doll and Linck are from two people who were at the USPTO at the time the policies that plaintiffs challenge were adopted. Not surprisingly, they continue to believe they did the right thing as a matter of statutory interpretation. Doll D. ¶¶ 37-43; Linck D. ¶¶ 43-49, 78-105. These largely legal declarations are the equivalent to *amicus* briefs and the court can consider them in that context, but they are otherwise also irrelevant.

The declarations of Shattuck and Tavtigian, two of the inventors listed on the patents, claim that they worked diligently and creatively to locate and sequence the BRCA1/2 genes and that they really were the first to do so. Hard work and creativity do not justify an invalid patent. If so, the extremely hard and creative work done by Albert Einstein in developing $E=MC^2$ would be eligible for a patent; yet, all agree it is not. Myriad Br. 21.

The declarations of Bone, Frieder, Lessman, Ogaard, Rusconi all are directed at three propositions. First, some women have been helped by obtaining the information that Myriad provides as a result of its test. *See, e.g.*, Bone D. ¶ 7. Plaintiffs do not disagree. This case hopes to result in increased access to genetic testing for those who are appropriate candidates.

Second, some women can afford the test. *See, e.g.*, Rusconi D. ¶ 4. Plaintiffs do not disagree. Strikingly, Myriad admits that poor women in half of the United States cannot receive reimbursement for the test. *Id.* at ¶ 5. Myriad admits that only 130 million of America's 308 million people can receive coverage for its testing from their insurance company. *Id.* at ¶ 4. For those almost 200 million who cannot receive coverage, and the half of states that do not cover

the testing for poor women, Myriad has provided only 3,000 free tests in the last four years. Ogaard D. ¶ 4. Other labs provide up to 10% of their tests for free, which would have meant they would have done 40,000 rather than 3,000. *Compare* Myriad Br. 1 *with* Ostrer D. ¶ 8. *See also* Stiglitz D. ¶ 27 (noting that the overwhelming consensus of economists is that higher prices result from monopoly power and inevitably lead to lower utilization, especially for those without insurance). These statistics reinforce plaintiffs' assertion that the patents have prevented some (indeed many) women from obtaining critical information about their own health.

Third, these declarations argue that no patient should ever want or need a second opinion before making drastic surgical decisions. *See, e.g.*, Bone D. ¶ 8 ("I trust Myriad…") That Bone does not want a second opinion before drastic surgery does not mean that other women do not. *See, e.g.*, Compl. ¶ 23; Girard D. ¶¶ 4-11. Myriad's assertion that "second opinion" means solely having a second physician interpret the results of a test, rather than re-run the test or perform a different test, is simply wrong. Love D. ¶¶ 12-19; Ostrer D. ¶ 11; Chung D. ¶ 23; Reich D. ¶ 9. In addition, Myriad's President, Dr. Critchfield adds that some second opinions can be obtained from Yale University or the University of Chicago. He very carefully qualifies his statement by asserting that "testing for specific BRCA mutations is available." Critchfield D. ¶ 62. The word "specific" hides the fact that Yale and Chicago may do only the most limited testing for individual mutations. Myriad is not permitting those labs to do full sequencing of the genes. Matloff Supp. D. ¶¶ 9, 11. Thus, women who receive negative results from Myriad have no way of confirming the accuracy of their test results.

Strauss argues that the patents in this case would be patentable in Europe. In addition to its irrelevancy, Strauss fails to mention that the patents in Europe are far more limited in scope

than the patents in the U.S., as a result of recent litigation.[34] In addition, Strauss fails to mention that the Canadian government has refused to honor similar patents by Myriad in that country, or that the patents are not enforced in Australia due to public pressure.[35] The Brazilian government does not allow patents on genes.[36]

Critchfield (self-servingly) and others tout the Myriad test as the "gold standard." *Compare* Critchfield D. ¶ 37 *with* Swisher D. ¶ 34. Plaintiffs largely do not dispute the quality of the work currently being done by Myriad. That has nothing to do with the validity of its patents. At the same time, Myriad's test cannot be considered the "gold standard" when there is no other test on the market with which to compare it. Stiglitz D. ¶ 26. The current version of the SACGHS report finds that "proficiency testing for quality assurance purposes requires that multiple labs offer a particular test ….The competition between multiple laboratories offering a particular test can also lead to innovation in the testing method for that test." SACGHS Final Draft Report and Recommendations, *supra* note 3 at slide 39.

In addition, Critchfield does admit that in the late 1990's, Myriad knew that its tests failed to identify harmful "large rearrangement mutations" and that it did not correct that situation until 2006. Critchfield D. ¶¶ 48-51. For more than one quarter of the life of the patent, Myriad was aware that a significant portion of women whom they were reporting had no risk of cancer were in fact at risk. *See also* Swisher D. ¶¶ 22-33; Chung D. ¶ 19. In addition,

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[34] Turna Ray, *EPO's Decision to Amend Myriad's BRCA1 IP May Create More Uncertainty for Euro Labs*, Pharmacogenomics Reporter, Dec. 3, 2008, http://www.genomeweb.com/dxpgx/epos-decision-amend-myriad%E2%80%99s-brca1-ip-may-create-more-uncertainty-euro-labs.

[35] *See* Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing*, 10 Health L.J. 123, 140-44 (2002) (discussing Canada); Ian Olver, *Do We Want to Block New Cancer Treatments?*, Crikey, Aug. 4, 2009, http://www.crikey.com.au/2009/08/04/do-we-want-to-block-new-cancer-treatments-then-it%E2%80%99s-time-for-some-action-on-gene-patenting/ (discussing Australia).

[36] Lei No. 9.279, de 14 de maio de 1996, Regula direitos e obrigações relativos à Propiedade Industrial (Brazil), *available at* http://www.wipo.int/clea/en/details.jsp?id=515 (Article X (IX) states that "all or part of natural living beings and biological materials found in nature, even if isolated therefrom, including the genome or germoplasm of any natural living being, and the natural biological processes" are not considered to be inventions).

Critchfield argues that other tests are less valuable. Critchfield D. ¶ 42. However, he criticizes only one particular test used in 1999 and ignores that tests that plaintiffs would offer today if the patents were invalidated are more comprehensive than Myriad's. Ledbetter D. ¶¶ 16, 21.

Critchfield also asserts that Myriad has submitted more data to the shared BIC (Breast Cancer Information Core) database than any other entity. Plaintiffs do not disagree; because Myriad is the only entity offering full sequencing of the genes, it is the only entity in the position to provide a majority of the data to the database. At the same time, Critchfield does not deny that Myriad has in recent years stopped sharing any information with the BIC database. *Compare* Critchfield D. ¶ 11 *with* Swisher D. ¶¶ 19-20.

The Reilly declaration, like the USPTO brief, is devoted to arguing that patents, including patents in the biotechnology arena, are valuable. Plaintiffs do not disagree that many patents, including patents in the biotechnology arena, are valuable and that the patent system as a whole creates useful incentives to private investment. These general comments, however, are irrelevant to the validity of the particular patent claims at issue in this case. Plaintiffs have only challenged 15 out of 179 claims of the 7 patents in suit. Even if these 15 claims are struck, the Myriad defendants will still have numerous patent claims to protect its business and investments. Reilly's conclusion that the "incentives of the patent system were instrumental in Myriad's discovery of the correct BRCA1 and BRCA2 sequence…," Reilly D. ¶ 34, is unsupported by any facts and indeed contradicted by the presented facts. Many researchers, not motivated by the incentives of the patent system, were fully engaged in the effort to discover the correct BRCA1 and BRCA2 sequences. Parthasarathy D. ¶¶ 15-19; Cho D. ¶ 17; Leonard D. ¶ 22 (noting that much of the research that led to BRCA1/2 was federally funded); Tavtigian D. ¶¶ 14-15;

Shattuck D. ¶ 20. *See also* Stiglitz ¶ 32; Kevin Davies & Michael White, *Breakthrough: The Race to Find the Breast Cancer Gene* (1996).

The patents are also not necessary for ensuring that genetic tests come to market. The fact that plaintiffs were offering BRCA testing before Myriad was awarded the BRCA patents demonstrates that researchers develop genetic tests without having patents on genes. Ganguly D. ¶¶ 3-4; Kazazian D. ¶¶ 4-5. The current statement of SACGHS's recommendations suggests that "patents do not serve as powerful incentive to conduct genetic research, to disclose genetic discoveries, or to invest in the development of genetic tests. Sufficient incentives for research and development already exist." SACGHS Final Draft Report and Recommendations, *supra* note 3, at slide 26. And, perhaps most importantly, Myriad did not patent a specific method of "isolating" and sequencing a gene, and the incentives of the patent system did not cause Myriad to invent them. Plaintiffs have alleged, without contradiction, that they have an incentive to utilize those methods, and new methods they or others have developed, to test women. *See, e.g.*, Chung D. ¶¶ 10-13; Ledbetter D. ¶¶ 9, 16, 22; Ostrer D. ¶ 9. The undisputed evidence in this case contradicts the notion that the patents were necessary to bring testing procedures to women.

Defendants argue that were it not for the exclusivity of the patents, patient access would have suffered because Myriad would not have spent $200,000,000 to promote its testing and arrange for insurance reimbursement. Myriad Br. 1, 2, 48. This is an inappropriate and offensive notion of patient access. True patient access simply cannot be achieved when patents allow one company to control all uses of a gene. True patient access requires that patients have access to the full range of available genetic tests, multiple testing facilities, and confirmatory genetic testing, and that doctors and researchers are free to engage in scientific inquiry, relay information to their patients, and develop new and improved genetic tests. Chung D. ¶¶ 17-24;

Ostrer D. ¶¶ 4-14; Ledbetter D. ¶¶ 10-28; Matloff D. ¶¶ 4-15; Reich D. ¶¶ 3-15; Ceriani D. ¶¶ 5-11; Fortune D. ¶ 3-9; Girard D. ¶¶ 4-11; Limary D. ¶¶ 4-8; Thomason D. ¶¶ 6-11; Raker D. ¶¶ 7-11; Sulston D. ¶ 36; Love D. ¶¶ 14-19; Swisher D. ¶¶ 14-35.

CONCLUSION

For these reasons, the plaintiffs' motion for summary judgment should be granted as to all defendants. The Myriad defendants' motion for summary judgment and the USPTO's motion for judgment on the pleadings should be denied.

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Respectfully submitted,

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Association for Molecular Pathology, et al. v. United States Patent and Trademark Office, et al., 09 Civ. 4515 (RWS)

DECLARATIONS
(1) IN FURTHER SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT AND (2) IN OPPOSITION TO THE MYRIAD DEFENDANTS' MOTION FOR SUMMARY JUDGMENT AND (3) IN OPPOSITION TO DEFENDANT UNITED STATES PATENT AND TRADEMARK OFFICE'S MOTION FOR JUDGMENT ON THE PLEADINGS

	Declarations
A.	Declaration of Robert L. Nussbaum, M.D. with attached Exhibits 1-2
B.	Declaration of Christopher E. Mason
C.	Declaration of Roger D. Klein, MD, JD with attached Exhibit 1
D.	Declaration of Joseph E. Stiglitz, Ph.D. with attached Exhibit 1
E.	Declaration of Fiona E. Murray, Ph.D. with attached Exhibits 1-3
F.	Declaration of Thomas B. Kepler with attached Exhibits 1-2
G.	Declaration of Robert Cook-Deegan with attached Exhibits 1-2
H.	Declaration of Ellen T. Matloff, MS