UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

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,

-against-

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.

No. 09 Civ. 4515 (RWS)

ECF Case

MYRIAD DEFENDANTS' MEMORANDUM OF LAW (1) IN SUPPORT OF THEIR MOTION FOR SUMMARY JUDGMENT AND (2) IN OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

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I. INTRODUCTION

Almost 30 years ago, an impassioned group of scientists, "among them Nobel laureates," urged the U.S. Supreme Court that, if genetic technology were allowed to be made the subject of a patent, a "gruesome parade of horribles" would follow. *Diamond v. Chakrabarty*, 447 U.S. 303, 316 (1980). The Court wisely rejected such arguments. Instead it endorsed an "expansive" construction of 35 U.S.C. § 101, and affirmed the patent-eligibility of the genetic technology at issue there. *Chakrabarty*, 447 U.S. at 317. The gruesome parade never materialized. Instead, the biotechnology industry has grown up and flourished under this legal regime.

As 2010 approaches, the language of Section 101 has not changed, yet plaintiffs sound essentially the same alarms. Plaintiffs have deluged the Court with declarations and *amicus* briefs claiming another "parade of horribles" if the seven DNA patents at issue in this case are upheld. Specifically, plaintiffs allege the patents at issue hinder research and limit patient access to important genetic testing.

Unlike thirty years ago, however, this Court has the benefit of experience, and that experience dispels these fears as unfounded. The *BRCA* patents have not stifled research—in fact, Myriad has consistently promoted and subsidized research on the *BRCA* genes. Over 18,000 scientists (including eight of the plaintiffs or their declarants) have conducted research on the *BRCA1* and *BRCA2* genes, and have published more than 7,000 papers on those genes since Myriad's patents were issued.

And these *BRCA* patents have catalyzed improved patient access to *BRCA* testing. Myriad has performed over 400,000 BRAC*Analysis*® tests for *BRCA* mutations for patients in all 50 states. Over 40,000 healthcare providers have used the test. As to the cost of the test, more than 90% of the BRAC*Analysis*® tests are covered by insurance at an average reimbursement rate of over 90%. All of these accomplishments are directly attributable to Myriad's investment of

more than $200 million towards developing insurance coverage and, more importantly, in raising patient and physician awareness and understanding of *BRCA* testing. Myriad could not possibly have made these investments without the protection provided by the patents plaintiffs are challenging.

If this Court were to conclude that these patents do not claim patent-eligible subject matter under 35 U.S.C. § 101, it would essentially overrule *Chakrabarty*. Perhaps more fundamentally, however, such a ruling would lead to the invalidity of thousands of biotechnology patents, and effectively unravel the foundation of the entire biotechnology industry. Numerous therapeutic drugs and diagnostic tests in development would be jeopardized. The very existence of the fledgling personalized medicine field would be threatened.

The Court should uphold the Myriad patents and reject the three legal challenges offered by plaintiffs.

II. SUMMARY OF THE ARGUMENT

The Court should grant the Myriad Defendants' cross-motion for summary judgment and hold: (i) that the challenged patent claims cover patentable subject matter under 35 U.S.C. § 101; (ii) that the challenged claims do not violate the First Amendment to the U.S. Constitution; and (iii) that the challenged patent claims are constitutional under Article I, Section 8, Clause 8 of the U.S. Constitution. It follows, then, that the Court should also deny the plaintiffs' motion on these same grounds.

A. Section 101 of Title 35, United States Code, was intended to be construed broadly to encompass "anything under the sun that is made by man." *Chakrabarty*, 447 U.S. at 309 (quoting S. Rep. No. 82-1979, 82d Cong., 2d Sess., 5 (1952); H.R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952)). "[A]ny new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof," is patent-eligible unless it falls within one

of three limited exceptions recognized by Supreme Court case law: laws of nature, natural phenomena and abstract ideas. *Chakrabarty*, 447 U.S. at 308-309. The categories of patent claims at issue in this case—one set covering isolated DNA (which is a "composition of matter" under Section 101); the other set covering diagnostic methods using such isolated DNA ("process[es]" under Section 101)—do not fall into any of these three limited categories. Thus, the inventions set forth in these claims are patent-eligible.

As to the composition claims, the law is clear, and has been for a hundred years or more, that isolated or purified products, even if they originate from "natural" sources, are patent-eligible. Plaintiffs' misguided approach is illustrated by the fact that their argument depends upon convincing this Court that this long and consistent line of authority was the product of legal error after legal error after legal error. For example, plaintiffs say that Learned Hand's holding that a purified natural substance (adrenaline) was patent-eligible subject matter was "erroneous." *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 Fed. 95 (S.D.N.Y. 1911), *aff'd in relevant part*, 196 F. 496 (2d Cir. 1912).[1] *See* ACLU Br. 25.[2] Plaintiffs also seek to convince this Court that the Court of Customs and Patent Appeals ("CCPA"), one of the Federal Circuit's predecessor courts, "committed this same error" in finding purified prostaglandin hormones, purified

[1] The late Judge Giles Rich, who was the principal author of the 1952 Patent Act, and who served as a judge of the CCPA and the Federal Circuit from 1956 to 1999, wrote that "Judge Learned Hand . . . knew as much patent law as any judge ever has." Giles S. Rich, *The Vague Concept of "Invention" as Replaced by Sec. 103 of the 1952 Patent Act*, 46 J. Pat. Off. Soc'y 855, 860 (1964). Indeed, the Second Circuit panel affirming District Judge Hand's ruling in *Parke-Davis* went out of its way to praise his opinion as "most exhaustive," and as dealing with "the difficult chemical questions presented" with "the greatest clearness." 196 F. 496 (2d Cir. 1912). *See generally* G. Gunther, LEARNED HAND 307 (Alfred A. Knopf 1994) (describing the *Parke-Davis* case as an example of Learned Hand's "legendary," "intense absorption in the factual tangles and his untiring effort to make sense out of the legal rules" in patent cases).

[2] "ACLU Br.," as used herein, refers to the memorandum in support of summary judgment filed by plaintiffs, Association For Molecular Pathology; American College Of Medical Genetics; American Society For Clinical Pathology; College Of American Pathologists; Haig Kazazian, M.D.; Arupa Ganguly, Ph.D.; Wendy Chung, M.D., Ph.D; Harry Ostrer, M.D.; David Ledbetter, Ph.D; Stephen Warren, Ph.D.; 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.

strawberry essence, and isolated bacteria all to be patent-eligible under Section 101. *See In re Bergstrom*, 427 F.2d 1394, 1400-02 (C.C.P.A. 1970); *see also In re Kratz,* 592 F.2d 1169, 1174 (C.C.P.A. 1979) (claim to a substantially purified chemical compound naturally occurring in strawberries was patent-eligible); *In re Bergy*, 596 F.2d 952, 960 (C.C.P.A. 1979) (upholding patent-eligibility of cultured microorganisms). *See* ACLU Br. 24. These cases, like *Parke-Davis* and others that came before, likewise establish that purified or isolated natural products are patent-eligible under Section 101, and patentable if they differ in kind from their natural counterparts.

Ultimately, the plaintiffs seek to convince this Court that the U.S. Patent and Trademark Office ("USPTO") engaged in an "erroneous analysis" and reached an incorrect conclusion when it issued guidelines affirming the patentability of genetic inventions. *See* Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001). *See* ACLU Br. 24. This of course ignores the extensive study, and the conclusions reached after a vigorous notice-and-comment process, that led to the USPTO's guidelines. In short, the Court should view plaintiffs' legal arguments with a skeptical eye since they ignore the statutory language, Congressional policy, a long line of consistent judicial precedent, and the USPTO's expert conclusions.

The composition-of-matter claims—covering isolated *BRCA1/2* nucleic acids—are patent-eligible because they do not exist in pure form in nature. In addition, they differ in kind from native (naturally occurring) *BRCA1/2* genes. Specifically, the claimed isolated nucleic acids have new properties and functions not found in the native genes, resulting in "ample practical differences" from the native genes. *Parke-Davis*, 189 Fed. at 103. The Fourth Circuit, which relied on Learned Hand's *Parke-Davis* decision, phrased it well: "There is nothing in the language of the Act which precludes the issuance of a patent upon a 'product of nature' when it

is a 'new and useful composition of matter' and there is compliance with the specified conditions for patentability." *Merck & Co., Inc. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156, 161 (4th Cir. 1958).

As to the method claims, the Supreme Court and the Federal Circuit have held that the key to determining the patent-eligibility of a method or process claim is that it transforms an article "to a different state or thing." *Gottschalk v. Benson*, 409 U.S. 63, 70 (1972); *see also Diamond v. Diehr*, 450 U.S. 175, 192 (1981); *Prometheus Labs, Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1345 (Fed. Cir. 2009). In *Prometheus*, the Federal Circuit found that claims to a diagnostic method that utilized a correlation were not a mere "law of nature," but a patent-eligible application of a law of nature in a transformative fashion. Similarly, the method claims in this case are also patent-eligible because they involve the same type of transformations recognized by the *Prometheus* court.

B. Plaintiffs' novel First Amendment argument is premised upon the false assumption that the challenged patent claims cover "information" and pure thought or speech. The "isolated DNA" claims cover chemical compositions, not mere information, and the diagnostic method claims cover physical laboratory testing. These claims do not prevent anyone from thinking, speaking, or disseminating information.

C. Finally, plaintiffs argue that "the patent claims in this case can be held as a matter of law to impede rather than promote the progress of science" under Article I, Section 8, Clause 8 of the U.S. Constitution. ACLU Br. 38. But that Clause only addresses *Congress's* power to enact necessary and proper laws to protect intellectual property; it imposes no restrictions on the

USPTO's determinations to grant any individual patent.[3] However, even if Article I, Section 8, Clause 8 *did* apply to the USPTO's actions, plaintiffs' argument would be foreclosed by *Eldred v. Ashcroft*, 537 U.S. 186, 212-13 (2003), which recognized Congress's considerable latitude in deciding whether specific intellectual-property determinations promote the progress of science and useful arts. Here, the USPTO had ample bases for concluding that these patents advanced those causes: The availability of patents incentivized Myriad not only to discover the *BRCA* genes but also to invest heavily in disseminating *BRCA* testing to the public. Moreover, since publishing its discoveries, Myriad has consistently promoted and subsidized research on the *BRCA* genes: More than **18,000 scientists** have researched *BRCA1* and *BRCA2*, and published over **7,000 papers** on the genes. Myriad has invested more than **$200 million** in promoting patient access to *BRCA* testing. As a result, over **400,000 patients** have been tested for *BRCA* mutations throughout the United States. Plaintiffs' anecdotal allegations ring hollow in the face of all of the scientific progress that has been spurred by the *BRCA* patents.

This Court should uphold the patent eligibility of Myriad's patent claims. The law requires it, and good policy demands it.

III. TECHNICAL BACKGROUND

This case involves 15 claims in seven patents issued by the USPTO after examination for compliance with the prerequisites of the U.S. patent laws, including the requirements of subject-matter eligibility and utility (35 U.S.C. § 101), novelty (*id.* § 102), and nonobviousness (*id.* § 103). Generally, the involved claims include claims to compositions and methods for diagnosing and treating cancer. The novel compositions and methods resulted from the

[3] Article I, Section 8, Clause 8 of the U.S. Constitution gives Congress the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."

identification and isolation of two genes, "*BRCA1*" and "*BRCA2*" (collectively referred to as "*BRCA1/2*"), which are associated with cancer. Shattuck Decl. ¶ 3; Skolnick ¶¶ 16-18; Tavtigian Decl. ¶¶ 3-4. Using the elaborate processes detailed in the patents, the inventors precisely mapped the locations of these genes on human chromosomes and identified mutations within these genes that correlate with an increased breast and ovarian cancer risk. *See generally* Shattuck Decl. ¶¶ 4-5; Tavtigian Decl. ¶¶ 3-4; Skolnick ¶¶ 16-18.

It is critical that the Court understand that the involved patent claims **do not cover human genes in the body**. Nor do they cover mere information, or laws of nature, or abstract ideas, or any substance present in the human body. Rather, the challenged patent claims cover **isolated** *BRCA1/2* DNA molecules and methods for diagnosing cancer using such **isolated** *BRCA1/2* DNA molecules. Based on the discovery and isolation of these vitally important molecules, the inventors conceived new diagnostic tools and methods useful for identifying DNA mutations associated with an increased risk of cancer. The claimed inventions are a set of tools and diagnostic methods, more akin to a medical instrument that a doctor uses to diagnose a broken bone.

As noted above, the patents in this case broadly contain two categories of challenged patent claims: (i) claims directed to isolated *BRCA1/2* DNA molecules,[4] and (ii) claims directed to cancer-diagnosing methods and cancer-therapeutic screening methods that utilize those isolated DNA molecules.[5] Linck Decl. ¶¶ 43, 79, 81; Doll Decl. ¶¶ 37-42. The isolated DNA molecules are distinct from any substance found in the human body—indeed, in all of nature.

[4] Claims 1, 2, 5, 6 and 7 of U.S. Patent No. 5,747,282 ("the '282 patent"); claim 1 of U.S. Patent No. 5,693,473 ("the '473 patent), and claims 1, 6 and 7 of U.S. Patent No. 5,837,492 ("the '492 patent").

[5] Claim 1 of U.S. Patent No. 5,709,999 ("the '999 patent"); claim 1 of U.S. Patent No. 5,710,001 ("the '001 patent"); claim 1 of U.S. Patent No. 5,753,441 ("the '441 patent); claims 1 and 2 of U.S. Patent No. 6,033,857 ("the '857 patent"); and Claim 20 of the '282 patent.

Kay Decl. ¶¶ 137, 173; Linck Decl. ¶¶ 48, 51, 54, 57, 59, 64, 77. The methods involve steps that transform a deleterious gene buried among over 25,000 known genes in the patient's chromosomes to make it detectable using modern diagnostic methods and machinery. Kay Decl. ¶¶ 178, 183-187.

Isolated DNA is *different in kind* from any composition found in nature. Kay Decl. ¶ 138; Linck Decl. ¶¶ 47, 48, 51, 54, 57, 59, 64, 77; Schlessinger Decl. ¶¶ 27, 30; Doll Decl. ¶¶ 27-29, 33. Isolated DNA acquires new properties not shared by its native (naturally occurring) counterpart. Kay Decl. ¶ 134; Schlessinger Decl. ¶¶ 27, 30; Doll Decl. ¶¶ 27-29; Linck Decl. ¶ 48. These new properties impart isolated DNA molecules with new characteristics and new utilities. Kay Decl. ¶¶ 134-139; Doll Decl. ¶ 29; Linck Decl. ¶¶ 51, 54-55, 57. Unlike native DNA, the isolated form can be used as a probe, a diagnostic tool that a molecular biologist uses to target and bind to a particular portion of DNA, allowing it to be detectable using laboratory machinery. Kay Decl. ¶ 138; Linck Decl. ¶¶ 45, 51, 54-55, 57, 77; Schlessinger Decl. ¶¶ 27-29; Doll Decl. ¶ 29. Native DNA cannot possibly be used this way. Kay Decl. ¶ 138; Schlessinger Decl. ¶¶ 27, 30; Doll Decl. ¶ 29.

Isolated DNA may also be used as another diagnostic tool, a "primer," which can be used in "sequencing" DNA. Kay Decl. ¶ 136. Sequencing is a method used by molecular biologists to determine the primary structure of a DNA molecule. Kay Decl. ¶ 138. A primer is used in a sequencing method to bind to (or "hybridize" with) a DNA target, such as an isolated *BRCA1/2* gene, DNA, or a synthetic DNA complementary to mRNA ("cDNA") to form a hybridization product that acts as a substrate for the enzymes used in the sequencing reaction. Kay Decl. ¶ 138.

Native DNA does not have the chemical, structural, or functional properties that make isolated DNA so useful to the molecular biologist. Kay Decl. ¶ 139; Linck Decl. ¶¶ 48, 51, 54-

55, 57, 59, 64, 77. Native DNA cannot be used as a molecular tool, such as a probe or primer, and cannot be used to detect mutations. Kay Decl. ¶ 139; Schlessinger Decl. ¶¶ 27, 30; Doll Decl. ¶ 29. Nor can native DNA be used in sequencing reactions to determine the structure of a DNA molecule. Kay Decl. ¶ 139. Excision, extraction, and purification from cellular components, or synthesizing DNA directly from its nucleotide components, is essential to be able to use isolated DNA molecules, *e.g.*, as primers or probes. Kay Decl. ¶ 139; Linck Decl. ¶¶ 45, 48, 51, 54, 55, 57, 64, 77; Sulston Decl. ¶ 25. *Only* isolated DNA molecules have the required chemical, structural and functional properties important for use as diagnostic tools and in the claimed diagnostic methods. Kay Decl. ¶ 139; Linck Decl. ¶¶ 45, 51, 54, 55, 57, 77; Schlessinger Decl. ¶¶ 27, 30; Doll Decl. ¶ 29.

The method claims at issue are directed at detecting *BRCA1/2* mutations in an individual and screening for potential cancer therapeutics. *See* '282 patent at col. 156:13-24; '999 patent at col. 161:17-25; '001 patent at col. 155:2-17; '441 patent at col. 155:17-26; '857 patent at col. 169:40-54. The claimed diagnostic methods transform a deleterious gene buried among the over 25,000 other known genes in the human genome and make it detectable in the clinic. Kay Decl. ¶ 187; Linck Decl. ¶ 81.

None of the method claims involves "looking" at genes. Kay Decl. ¶ 187. In fact, one cannot detect or determine the nucleotide sequence of a human subject's genes by mere inspection. Kay Decl. ¶ 187. Even a microscope would be of no use for determining the nucleotide sequence of a gene. Kay Decl. ¶ 176. Detection of a gene marker requires breaking open the cells of a tissue sample, and extracting and excising the native DNA. Kay Decl. ¶ 187; Linck Decl. ¶¶ 82, 90-91. Using a set of molecular tools, such as a diagnostic probe or a primer that can specifically bind to a *BRCA1/2* DNA molecule in a tissue sample, the now-isolated DNA

is analyzed to determine if the structural composition is the same or different from the normal native gene. Kay Decl. ¶ 187. These molecular diagnostic tools were designed based on their ability to bind to and form a stable chemical structure with a target DNA. *See*, *e.g.*, '473 patent at col. 28:23-30. Thus, the claimed diagnostic methods are not mere abstract ideas, and cannot be performed by merely looking at a gene. Kay Decl. ¶ 187; Linck Decl. ¶ 105.

IV. MYRIAD'S DECLARANTS

Myriad's submission is supported by declarations from the following individuals:

- **Richard Baer, Ph.D.**, Professor of Pathology & Cell Biology at Columbia University and Deputy Director, Institute for Cancer Genetics; Dr. Baer explains his research on *BRCA1* and Myriad's support for his research.

- **Melanie K. Bone, M.D.**, private practitioner providing breast-cancer risk assessment, describes how the BRAC*Analysis*® test helped her develop a medical management plan appropriate for dealing with her own cancer and how it has helped her own patients manage their risk of getting cancer.

- **Gregory C. Critchfield**, President of Myriad Genetic Laboratories, Inc., describes Myriad's policies regarding research conducted on *BRCA1/2* by other institutions, the increasing awareness and availability of BRAC*Analysis*® test to detect breast and ovarian cancer, and other institutional policies.

- **John J. Doll,** former Acting Director of the USPTO (2008-2009), former Commissioner for Patents of the USPTO (2005-2009), and Director of the Patent Examination Technology Center 1800, which examined patent applications claiming biotechnological inventions (1995 to 2005), explains the USPTO's policies and Examination Guidelines with respect to claims to isolated DNA molecules.

- **Richard P. Frieder, M.D.,** Assistant Clinical Professor in the UCLA Dept. of Obstetrics and Gynecology, sets forth the importance of the BRAC*Analysis*® test to the medical treatment and medical management of his patients, and the high quality and accuracy of that test.

- **Mark A. Kay, Ph.D., M.D.,** Professor and Director of the Program in Human Gene Therapy at Stanford University School of Medicine, provides an explanation of the technology involved in the Myriad patents and the meaning of the claim terms in those patents from the perspective of one of ordinary skill in the art in 1994-95.

- **Jenny Lessman, P.A.-C.,** a Physician Assistant in Obstetrics and Gynecology at MeritCare in Detroit Lakes, Minnesota, explains her personal and professional experience using the BRAC*Analysis*® test.

- **Rong Li, Ph.D.,** Professor, Department of Molecular Medicine/Institute of Biotechnology at the University of Texas Health Science Center, describes his research on *BRCA1* without impediment from Myriad.

- **Nancy Linck, Ph.D.**, former Solicitor of the USPTO and former Administrative Patent Judge at the USPTO, provides historical and legal perspective on the development of the USPTO's policies and Examination Guidelines with respect to patenting of isolated DNA molecules.

- **Todd Ogaard**, Vice President of Customer Services at Myriad Genetic Laboratories, Inc., offers a helpful explanation of certain insurance-coverage issues and Myriad's policies in helping low-income individuals to obtain the BRAC*Analysis*® test.

- **Jeffrey D. Parvin, Ph.D., M.D.,** Professor, Department of Biomedical Informatics at the Ohio State University, provides testimony regarding the absence of any negative impact from Myriad's patents upon his research on *BRCA1*.

- **Philip R. Reilly, J.D., M.D.**, a noted Bioethicist and Venture Partner at Third Rock Ventures in Boston, Massachusetts—a venture capital company—elaborates upon the role of patents and the patent system in creating incentives for new scientific and medical research and developments.

- **William Rusconi**, Senior Vice President of Marketing at Myriad Genetic Laboratories, Inc., explains Myriad's policies regarding insurance payments and educating health professionals and the general public about hereditary breast and ovarian cancers.

- **John Franklin Sandbach, M.D.,** a physician board-certified in hematology and oncology, provides testimony regarding clinical research studies he conducted involving *BRCA1/2* screening in hereditary breast and ovarian cancers, the lack of any negative impact on his research from Myriad's patents, and the positive impact of the contributions made by Myriad's researchers.

- **Joseph Schlessinger, Ph.D.**, Chairman of the Department of Pharmacology at Yale University School of Medicine and William H. Prusoff Professor, and co-founder of SUGEN, Plexxikon and Kolltan; Dr. Schlessinger explains the differences between isolated or synthetic nucleic acid molecules and native genes.

- **Donna Shattuck, Ph.D.**, a named co-inventor on several Myriad patents (the '473, '999, '001, '282, and '441 patents) relating to the invention of isolated *BRCA1* DNAs, sets forth the state of the art and the process leading to the discovery of the *BRCA1* gene and its DNA structure.

- **Mark Skolnick, Ph.D.**, founder and Chief Scientific Officer of Myriad Genetics, Inc., personally involved in the identification and characterization of the *BRCA1* and *BRCA2* genes, and named co-inventor of the '001, '282, and '441 patents, explains the *BRCA1* invention and the importance of private funding in the development of *BRCA1* tests.

- **Joseph Straus**, Director Emeritus of the Max-Planck-Institute for Intellectual Property, discusses treatment of patents on isolated DNA molecules in Europe, and studies on the effect of patents on research in Europe and the United States.

- **Sean V. Tavtigian, Ph.D.**, Associate Professor in the Department of Oncological Sciences at the University of Utah School of Medicine, and a named co-inventor of the '999 patent, the '001 patent, the '282 patent, the '441 patent, the '492 patent and the '857 patent, explains the discovery of the *BRCA2* gene, and the invention relating to isolated *BRCA2* DNA molecules.

V. ARGUMENT

A. Claim Construction

1. The Legal Standard

Before considering the patent-eligibility of a patent claim, it is critical for the Court to properly construe disputed terms in the claims so that their scope is accurately assessed. *See, e.g.*, *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1354 (Fed. Cir. 2005) ("[A] utility patent protects 'any new and useful process, machine, manufacture, or composition of matter, or any new or useful improvement thereof,' 35 U.S.C. § 101 (2000), the scope of which is defined by the patent's written claims."). Patent claim terms are construed as a matter of law by the Court, and their terms are given their ordinary and customary meaning, as they would be understood by a person of ordinary skill in the art as of the effective filing date of the patent. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (*en banc*). The intrinsic evidence, *i.e.*, the claims, the specification, and the prosecution history, is the most significant source of the legally operative meaning of claim language. *Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1370 (Fed. Cir. 2005).

2. Claim Construction

With respect to the critical issues in this case, plaintiffs' arguments are premised on two legally erroneous conclusions: (1) that isolated DNA molecules are merely "products of nature"

or "information" (ACLU Br. 9-15); and (2) that the claimed methods represent only abstract ideas, knowledge, or mental thought processes. ACLU Br. 15-19.

In this section, Myriad sets forth the correct constructions of only those claim terms that are both in dispute and necessary for the Court to decide the legal issues presented by plaintiffs' complaint.[6] In brief, as set forth below, the term "isolated DNA" means a DNA molecule that is extracted from a cell or chromosome, or DNA that is chemically synthesized. (In either case, "isolated DNA" is a chemical compound distinct from any composition found in nature.) Additionally, each of the properly construed method claims involves physically transformative steps central to its purpose. Thus, none of the methods can be said to involve mere "mental" acts or claim a law of nature *per se*.

Plaintiffs' proffered constructions of certain claim terms ignore the principles of claim interpretation established by Federal Circuit precedent as articulated in, most notably, that Court's *en banc* decision in *Phillips*. For one, the plaintiffs look principally to *extrinsic* evidence (in particular, expert testimony) as the primary source for definitions of all claim terms; this is contrary to *Phillips*, which emphasized that the patent documents themselves are to be given primacy, and that the specification of the patent is "the single best guide" to claim interpretation. 415 F.3d at 1315.

For another, plaintiffs ignore terms which the patentees explicitly defined in the specification, preferring (again) to rely upon extrinsic evidence of meaning. Such extrinsic evidence is irrelevant: "[W]hen a patentee explicitly defines a claim term in the patent

[6] For purposes of this motion, Myriad proffers its construction of only certain claim terms that are material to the pending cross-motions for summary judgment. Failure to include a construction of any other claim term is not an admission that Myriad agrees with ACLU's proffered construction of any other claim term. If further proceedings are needed after this Court rules on the pending cross-motions, Myriad will likely seek a *Markman* hearing so that all of the relevant claims and claim terms may be properly construed by the Court as a matter of law before trial.

specification, the patentee's definition controls," and extrinsic evidence "is simply irrelevant." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380, 1382 (Fed. Cir. 2009).

Plaintiffs have presented the Court with over 30 declarants. Only two, however—Grody and Leonard—have even reviewed the claims of the Myriad patents. The remaining declarants discuss DNA sequencing in general but do not address the subject matter of the patent claims. Their opinions are therefore irrelevant to claim construction. The Grody and Leonard declarations (which parrot each other almost word-for-word) rely principally on extrinsic evidence in defining claim terms, which Federal Circuit case law holds to be erroneous. Perhaps most tellingly, though, plaintiffs' proffered constructions of the claim terms are riddled with commentary insinuating that the terms should be construed to cover "naturally" occurring substances. ACLU Br. 10-15. That is not what the claims say.

The proper constructions of relevant claim terms are set forth below.

(a) "Isolated DNA" Claims

The term "**isolated DNA**" or "**isolated DNA molecule**" is expressly defined in the patents as a DNA molecule (*i.e.*, a chemical composition) "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." '473 patent, col. 19:12-15; '282 patent, col. 19:14-18; and '492 patent, col. 18:1-5. (emphasis supplied). That express definition is "controls." *Martek*, 579 F.3d at 1380.

The term "DNA" stands for deoxyribonucleic acid. This "acid" is a real and tangible molecule, a chemical composition made up of deoxyribonucleotides linked by a phosphodiester backbone. Kay Decl. ¶ 125; Linck Decl. ¶ 45; Schlessinger Decl. ¶ 12; Doll Decl. ¶ 13. (Even plaintiffs' declarants admit that "All DNA is a molecule…" Grody Decl. ¶ 10; Leonard Decl. ¶30.) The patents thus explain that *isolated* DNA is "substantially separated from other cellular

components which naturally accompany" a gene. '473 patent, col. 19:8-9; '282 patent, col. 19:10-11; and '492 patent, col. 17:64-65.

Plaintiffs, however, contend that DNA is mere information. ACLU Br. 26-29. To support that contention, plaintiffs ignore the fact that DNA is a chemical composition (it is, after all, an "acid"), and instead proffer a definition that equates DNA to merely a sequence of nucleotides—or a sequence of letters. According to the plaintiffs, "'DNA' means a sequence of … nucleotides… A, C, T or G. … Determining the precise arrangement of A's, C's T's and G's in … DNA… is called 'sequencing.'" ACLU Br. 10. Plaintiffs' erroneous construction of "DNA" appears calculated to convey the notion that the sequence of a DNA molecule is mere information that can be determined by mere inspection. It cannot. In order to obtain a DNA sequence, a scientist, using the tools of modern molecular biology, must break open the cells of a patient's tissue sample, extract the DNA, and then isolate and purify that DNA before sequencing it. Kay Decl. ¶¶ 178, 186-187; Linck Decl. ¶ 53.

"DNA" thus cannot mean a "nucleotide sequence," as plaintiffs contend. ACLU Br. 10. 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, in the same way that H_2O represents the water molecule as two atoms of hydrogen and one atom of oxygen. Kay Decl. ¶¶ 126, 127; Schlessinger Decl. ¶ 19; Doll Decl. ¶ 31. Such shorthand is "simply a means of describing a compound; it is not the invention itself." *Regents of Univ. of N. M. v. Knight*, 321 F.3d 1111, 1122 (Fed. Cir. 2003) (citing *In re Papesch,* 315 F.2d 381, 391 (C.C.P.A. 1963)). Thus, a DNA or nucleotide "sequence" is a description of the linear order of nucleotide units that make up the polynucleotide; it is not, itself, a chemical compound. Deoxyribonucleic acid, on the other hand, *is* a chemical compound—a particular and defined

"acid," as its name demonstrates. Kay Decl. ¶ 125; Linck Decl. ¶¶ 45-46; Schlessinger Decl. ¶ 12; Doll Decl. ¶¶ 26-27, 31. Put another way, while every DNA molecule *has* a nucleotide sequence, it is not accurate to say that every DNA molecule is *just* a nucleotide sequence.

Plaintiffs' proposed definition of "isolated DNA" as synonymous with a "fragment" of DNA (ACLU Br. 10) is also erroneous. This proffered construction implies that fragments of DNA exist in cells in the body ready for the picking—*i.e.*, that DNA "fragments" can be removed from the cell with no change in structure or function. ACLU Br. 10. But genes in cells are part of larger structures called "chromosomes," and cannot simply "break off" from the chromosomes. Kay Decl. ¶¶ 131, 142; Linck Decl. ¶ 48. The patents' specifications define "isolated DNA" as requiring excision from the chromosome and extraction from the cell, or chemical synthesis. That definition controls. *Martek*, 579 F.3d at 1380. *See* Kay Decl. ¶ 17; Linck Decl. ¶ 53. As shown below, this is key to understanding why the composition-of-matter claims satisfy Section 101.

"***BRCA1***" and "***BRCA2***" each are defined in the patents as a cancer-predisposing gene, some alleles of which cause susceptibility to breast and ovarian cancers. *See*, *e.g.*, '282 patent, col. 1: 22-23, and 4:34-35; '492 patent, col. 1: 20-21, and col. 4:28-29. This explicit definition "controls." *Martek*, 579 F.3d at 1380.

Plaintiffs' proffered construction of these terms, as "a particular fragment of DNA found on chromosome …" (ACLU Br. 11, 14), is improper: It does not adopt, and indeed is inconsistent with, the explicit definition provided by the patents. But even if the patents had omitted that explicit definition, one of ordinary skill in the art would understand that *BRCA1/2* are genes, not "a fragment of DNA." Kay Decl. ¶ 27. Genes are integrated into the entire

chromosome and not (as the term "fragment" would suggest) broken or detached, or easily "picked" from the chromosome. Kay Decl. ¶¶ 27, 131, 142; Doll Decl. ¶ 27.

(b) Method Claims

(i) Diagnostic Method Claims

The diagnostic method claims each relate to a method for detecting an alteration in a *BRCA1/2* gene in a human sample. ('999 patent, claim 1; '001 patent, claim 1; '441 patent, claim 1; and '857 patent, claims 1 and 2). Each claim requires *comparing or analyzing the nucleotide sequence of* ***a BRCA1 or BRCA2 gene, RNA, or a cDNA obtained or prepared from a human patient tissue sample or samples.*** These claims further specify the patient sample used: a human sample ('999 patent); a tumor and a non-tumor sample from a human subject ('001 patent); a tissue sample from the subject ('441 patent); or from a suspected mutant allele, a region of the patient's chromosome. ('857 patent, claims 1 and 2). Linck Decl. ¶¶ 82-83.

In each of the claimed methods, the critical DNA molecule represented by the nucleotide sequence must be obtained from the patient's sample before it can be compared or analyzed. Kay Decl. ¶¶ 64-67, 70; Linck Decl. ¶¶ 82-83. This requires something much more than mere "inspection." Rather, a transformative step is required in which the patient's sample is processed so that it can be analyzed, using a molecular diagnostic tool such as a probe or primer—*i.e.*, the isolated *BRCA1* and *BRCA2* DNA molecules of the invention.

The nucleotide sequence of the gene, mRNA, or cDNA cannot be determined by mere inspection. Kay Decl. ¶¶ 186, 187. The gene, mRNA and allele are all within the patient's body and must be isolated from a patient's tissue sample in order to be sequenced. Kay Decl. ¶ 186. To this end, the cells of the tissue sample must be broken open, and a sample of the DNA or RNA must be extracted. Kay Decl. ¶ 186. Sequencing is accomplished using a diagnostic probe or primer to hybridize to the target DNA or RNA extracted from the sample to initiate a

sequencing reaction. Kay Decl. ¶¶ 138, 177, 183, 187. Where a cDNA is used for sequencing, the cDNA must first be synthesized using mRNA obtained from the patient sample and a primer to form the hybridization product. Kay Decl. ¶¶ 70, 179, 186. Each of these steps is "transformative"—as a result of these steps, the sample no longer resembles a tissue or tumor sample, the cDNA no longer resembles a native RNA molecule, and the hybridization product no longer resembles the native gene. Kay Decl. ¶¶ 138, 170, 185, 186.

The dependent claims confirm the nature of the transformative steps used. In the '999 patent, dependent claims 3-10 each require elaborate molecular diagnostic techniques to perform the steps of determining and analyzing the sequence of the *BRCA1* gene, RNA, or cDNA obtained or prepared from the patient's sample. Linck Decl. ¶¶ 91-92. In claim 3, for example, this step involves "hybridizing a *BRCA2* gene probe …. to RNA isolated from the human sample and detecting the presence of a hybridization product." Linck Decl. ¶¶ 91-92. This "hybridizing and detecting" step involves the transformation of the patient sample into a hybridization product detectable by molecular diagnostic techniques. Linck Decl. ¶¶ 91-92. The same is true for claims 4-10, each of which require the use of *BRCA1*-specific primers or probes resulting in the transformation of the patient's sample into something completely different, ***i.e.***, a "hybridization product." Linck Decl. ¶¶ 91-92.

The claim language also confirms that the transformative steps required to determine the patient's *BRCA1/2* sequence are central to the purpose of each of the claimed methods—***i.e.,*** detecting, screening, or identifying an alteration or mutation in the *BRCA1/2* genes of the human subject. For example, the claims cover a "method for detecting a germline alteration in a BRCA1 gene … in a human" ('999 patent, claim 1); a "method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene" ('001 patent, claim 1); a

"method for screening germline of a human subject for an alteration of a BRCA1 gene" ('441 patent, claim 1); a "method for identifying a mutant BRCA2 nucleotide sequence in a suspected mutant BRCA2 allele" ('857 patent, claim 1); and a "method for diagnosing predisposition for breast cancer … wherein an alteration in the germline sequence of the BRCA2 gene or … mRNA of the subject indicates a predisposition to said cancer" ('857 patent, claim 2).

Thus, contrary to plaintiffs' contentions (ACLU Br. 15-19; 29-32), these claims do not cover merely "looking at" and "comparing" sequences. Kay Decl. ¶¶ 64-67, 70. Instead, each of these methods require the transformative use of the novel *BRCA* molecules, primers, or probes central to the purpose of the claims, and does not presume that these tools are already provided. Kay Decl. ¶¶ 64-67, 70; Linck Decl. ¶¶ 90, 105.

(ii) Cancer Therapeutic Screening Method Claim

Claim 20 of the '282 patent is a cancer therapeutic screening method using *BRCA1*. The method comprises four steps: (1) growing a ***transformed*** eukaryotic host cell; (2) growing said ***transformed*** eukaryotic host cell in the absence of **said compound**; (3) determining the rate of growth of said host cell in the presence of **said compound** and the rate of growth of said host cell in the absence of said compound; and (4) comparing the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic. Linck Decl. ¶ 84.

Contrary to plaintiffs' proffered construction (ACLU Br. 18-19; 31-32), this claim does not cover any sort of "natural process." The claim language itself requires growing a "transformed" cell. Kay Decl. ¶¶ 57, 63. Indeed, many transformative steps are involved in the steps of the method. For example, the transformed eukaryotic host cell used in the "growing" steps must be "transformed," *i.e.*, manipulated to contain an altered *BRCA1* gene. In another transformative step, potential cancer therapeutics are added to the growth media to assay their

effect on cell growth rate. Linck Decl. ¶ 84. Thus, the claim, when considered as a whole, cannot be construed to simply cover a mental act.

B. The "Isolated DNA" Claims Cover Patent-Eligible Subject Matter Under 35 U.S.C. § 101

1. Isolated Natural Products That Are Different-in-Kind From Products of Nature Are Patentable Subject Matter Under 35 U.S.C. § 101

Section 101 of Title 35 provides:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

These "expansive terms"—in particular, Congress's use of the terms "*any* new and useful process, machine, manufacture, or composition of matter, or *any* new and useful improvement thereof"—reflect that "Congress plainly contemplated that the patent laws would be given wide scope." *Chakrabarty*, 447 U.S. at 308. Indeed, similar "broad language" has existed in every version of the U.S. patent laws dating back to 1793, and "embodie[s] Jefferson's philosophy that 'ingenuity should receive a liberal encouragement.'" *Id.* (quoting 5 Writings of Thomas Jefferson 75-76 (Washington ed. 1871)). The Supreme Court has thus acknowledged Section 101's breadth, quoting the Committee Reports accompanying the 1952 Patent Act, which "inform us that Congress intended statutory subject matter to 'include anything under the sun that is made by man.'" *Chakrabarty*, 447 U.S. at 309 (quoting S. Rep. No. 82-1979, at 5 (1952) and H.R. Rep. No. 82-1923, at 6 (1952)). As the Supreme Court more recently noted, after noting these aspects of the *Chakrabarty* decision, "we are mindful that this Court has already spoken clearly concerning the broad scope and applicability of § 101." *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 131 (2001).

The fact that Section 101 is broad and expansive does not mean that it imposes no limits on patent eligibility, however. The Court has recognized three narrow categories of subject-matter that fall outside the scope of Section 101: "The laws of nature, physical phenomena, and abstract ideas have been held not patentable." *Chakrabarty*, 447 U.S. at 309. The Court gave, as examples of patent-ineligible subject matter, "a new mineral *discovered in the earth* or a new plant *found in the wild*," as well as Einstein's "celebrated law that $E=mc^2$" and Newton's discovery of the law of gravity. *Id.* (emphasis added). One thing that is important to note about these modest limitations on patent-eligibility are the qualifiers "discovered in the earth" and "found in the wild." The courts have consistently distinguished between "something preexisting and merely plucked from the earth and claimed as such" (which would not be patent-eligible), and, for example, "a biologically pure culture produced by great labor in a laboratory and so claimed," which is patent-eligible under Section 101. *In re Bergy*, 596 F.2d at 976. Or, to put it in the terms adopted by the CCPA in *In re Bergstrom*, "naturally occurring" compounds that "do not exist in nature in pure form" are patent-eligible. 427 F.2d at 1401. Thus, naturally occurring iron ore "discovered in the earth," or a dandelion plant "found in the wild" may not be patent-eligible, but human manipulations of iron ore, into purified forms or into other products, or sexually reproducing plants, of course may be patented. *Plummer v. Sargent*, 120 U.S. 442, 445 (1887) (claim for "iron ornamented in imitation of bronze by the application of oil and heat"); *J.E.M. Ag Supply*, 534 U.S. 124 (upholding patent-eligibility of patent claims to corn plants).

Plaintiffs, when they recite their version of the law, contend that the Supreme Court has, in addition to "[t]he laws of nature, physical phenomena, and abstract ideas," also excluded "natural products" from the scope of patent eligibility. ACLU Br. 19. The case law does not support such a claim. *See generally AT&T Corp. v. Excel Comme'ns, Inc.*, 172 F.3d 1352, 1355

(Fed. Cir. 1999) ("[T]he Court has specifically identified *three categories* of unpatentable subject matter: 'laws of nature, natural phenomena, and abstract ideas.'") (emphasis added) (quoting *Diehr*, 450 U.S. at 185). "Natural products" are not *per se* patent-ineligible under Section 101 (Linck Decl. ¶ 23); were the law otherwise, the corn plants in *J.E.M. Ag Supply* (just as an example) would have fallen outside the scope of patent-eligible subject matter. Rather, it is well-settled that isolated or purified products, even if they originated in nature prior to being isolated or purified, *are* patent-eligible under Section 101. Linck Decl. ¶¶ 14-17, 29-34, 43, 49; Doll Decl. ¶¶ 26, 34; Straus Decl. ¶ 26, 29-34.

In the seminal *Parke-Davis* case ("erroneously" decided by Judge Learned Hand, according to plaintiffs (ACLU Br. 25)), Judge Hand, then sitting as a member of this Court, found claims to an adrenalin compound that had been isolated and purified from animal suprarenal glands to be patent-eligible. *Parke-Davis & Co. v. H. K. Mulford Co.*, 189 F. 95, 103 (S.D.N.Y. 1911). It had been known that suprarenal gland in powdered form had hemostatic, blood-pressure-raising and astringent properties, but could not be used for those purposes in gross form. The isolated and purified form of adrenaline had the desired characteristics, and differed "in kind" from the prior extracts, resulting in "ample practical differences" from those prior extracts. *Id.* Judge Hand held:

> even if [the adrenaline] were merely an extracted product without change, *there is no rule that such products are not patentable.* [The Patentee] was the first to make [adrenaline] available for any use by removing it from the other gland-tissue in which it was found, and, *while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically.* That was a good ground for a patent.

Parke-Davis, 189 F. at 103 (emphasis added). The Second Circuit affirmed, praising District Judge Hand's "most exhaustive" opinion, which dealt with "the difficult chemical questions presented" with "the greatest clearness." 196 F. 496 (2d Cir. 1912). *See also* n.1, above.

Likewise, in *Merck & Co., Inc. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958) (another "error," according to plaintiffs—ACLU Br. 24-25), the Fourth Circuit held that a Vitamin B_{12} composition useful for treating pernicious anemia was patent-eligible. *Id.* at 157-58. Although naturally occurring Vitamin B_{12} produced in cows had known therapeutic properties and was commercially available, the court found *Merck*'s composition, which was obtained from a microorganism, patent-eligible because the purified product had enhanced utility. *Id.* at 164.

The Fourth Circuit's holding in *Merck* was premised on the language of Section 101, and it relied at some length upon Judge Hand's opinion in *Parke-Davis*. *Id.* at 162, 163-64. As that court properly noted, "[t]here is nothing in the language of the Act which precludes the issuance of a patent upon a 'product of nature' when it is a 'new and useful composition of matter' and there is compliance with the specified conditions for patentability." *Merck*, 253 F.2d at 161.

The principles set forth in the *Parke-Davis* and *Merck* decisions were followed by the Court of Customs and Patent Appeals (CCPA), one of the Federal Circuit's predecessor courts whose decisions remain binding precedent in patent cases.[7] In *In re Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970) (yet another "error," according to plaintiffs, ACLU Br. 24), the prostaglandins PGE_2 and PGE_3, which were extracted from human or animal prostate glands, were found patent-eligible under Section 101. A patent examiner had rejected the claims on the basis that "inasmuch as the 'claimed compounds are naturally occurring' . . . they therefore, are not 'new'

[7] *See South Corp. v. United States*, 690 F.2d 1368, 1370-71 (Fed. Cir. 1982) (*en banc*) (adopting "[t]hat body of law represented by the holdings of . . . the Court of Customs and Patent Appeals" as "precedent" for the then-new Federal Circuit so as to "continu[e] the stability in those areas of the law previously within the jurisdiction of our predecessor courts").

within the connotation of the patent statute.'" *Id.* at 1397. The CCPA reversed the examiner and stated:

> what appellants claim—pure PGE_2 and PGE_3—is not 'naturally occurring.' Those compounds, as far as the record establishes, do not exist in nature in pure form, and appellants have neither merely discovered, nor claimed sufficiently broadly to encompass, what has previously existed in fact in nature's storehouse, albeit unknown, or what has previously been known to exist.

Id. at 1401. It bears noting that the examiner's rejected reasoning—that the applicants could not obtain a patent on "naturally occurring" compounds—is in all relevant respects identical to the arguments offered by plaintiffs here; those arguments should likewise be rejected in this case.

Similarly, in *In re Kratz*, 592 F.2d 1169 (C.C.P.A. 1979), the CCPA found patent-eligible a claim to a substantially purified chemical compound naturally occurring in strawberries, called 2-methyl-2-pentenoic acid (2M2PA). The inventors had discovered that this chemical compound imparted a strawberry flavor when added to food. Their claim to 2M2PA in "substantially pure" form was upheld even though "2M2PA is a naturally occurring constituent of strawberries and is not 'per se' novel,. . ." "since the claims do not encompass natural compositions in that 'substantially pure' 2M2PA does not apparently occur in nature." *Id.* at 1174. The CCPA in *Kratz* relied favorably upon *Bergstrom*, as well as upon the Fourth Circuit's decision in *Merck*. *Id.*

Likewise, in *In re Bergy*, 596 F.2d 952 (CCPA 1979), the CCPA upheld, under Section 101, Bergy's patent for a "[m]icrobiological process for preparing the antibiotic lincomycin at temperatures ranging from 18° C. to 45° C. using the newly discovered microorganism Streptomyces vellosus." *Id.* at 967 (quoting patent). The examiner, and then the Board of Patent Appeals, rejected claim 5 of the Bergy application, which claimed a "biologically pure culture of *Streotomyces vellosus*," ostensibly because it "claims a product of nature." *Id.* at 972. The

CCPA reversed the Board's ruling, holding Bergy's product claim for a "biologically pure" microorganism to be patent-eligible, based, *inter alia*, on the *Parke-Davis* and *Merck* decisions cited above. *Id.* at 974-75 & n.13.[8]

Plaintiffs have little response to this long line of decisions other than to urge, based largely upon the declaration of their expert Jackson, that they were "erroneously" decided. Instead, they rely upon a handful of other decisions, which they characterize as supporting their position that products of nature are not patent-eligible. ACLU Br. 20-26. But most of plaintiffs' cases were decided not on the ground of patent-eligible subject-matter under what is now known as Section 101, but on the ground that the patents sought to cover old products that had long been known and used in their respective industries. *See, e.g.*, *Am. Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566, 596 (1874) (fact that paper pulp was in "common use" and "in no sense new" rendered the patent "void for want of novelty"); *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884) (holding "artificial" alizarine synthetically produced unpatentable for being an "old article" used from "time immemorial" in the dye industry); *Ex Parte Latimer*, 1889 Dec. Comm'r Pat. 123, 125 (1889) (holding cellulose fiber not a "new" product where it had been used in the textile industry for years); *General Elec. Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d Cir. 1928) (holding tungsten unpatentable and not "new" because it had been isolated since the 1700s and was in common use in metallurgy); *In re Marden*, 47 F.2d 957 (C.C.P.A. 1931) ("*Marden I*") (nothing "new" or "inventive" about uranium, which had been discovered in 1789); *In re Marden*, 47 F.2d 958 (C.C.P.A. 1931) ("*Marden II*") (holding "pure vanadium [] not new in the inventive sense"); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*,

[8] The companion case decided with *Bergy* by the CCPA was the *Chakrabarty* case, in which the Supreme Court upheld the CCPA's judgment regarding the scope of Section 101; the *Bergy* case had become moot in the interim, *see Chakrabarty*, 447 U.S. at 307.

333 U.S. 127 (1948) (combination of six non-inhibitive strains held to be an obvious combination of known, commercially available products). And plaintiffs' principal Section 101 case, *American Fruit Growers, Inc. v. Bogdex Co.*, 283 U.S. 1 (1931), held that a claim to borax-treated oranges did not constitute a "manufacture" within the meaning of the predecessor statute to 35 U.S.C. § 101, because "there must be transformation," and the orange was not transformed by a coating of borax—indeed, coating an orange with borax to preserve it "lack[ed] novelty" because it "had been revealed . . . twenty years earlier." *Id*. at 13-14 (internal quotation omitted). *See generally* Linck Decl. ¶¶ 36-42, 60-69.

The carefully considered policy of the USPTO, which has determined that isolated DNA molecules are patent-eligible under Section 101, is both correct in view of the case law (Doll Decl. ¶¶ 11-22, 26, 34; Linck Decl. ¶¶ 14-17, 47); Straus Decl. ¶¶ 28-34, and entitled to great respect. The USPTO's policy is correct because it is well established that extracted, purified, or isolated products that originate in nature are patent-eligible. Linck Decl. ¶¶ 14-17, 47; Doll Decl. ¶¶ 26, 34. Isolated DNA molecules should be treated no differently than other chemical compounds for patent eligibility. Linck Decl. ¶¶ 46, 58, 70, 76; Doll Decl. ¶¶ 28, 31. A DNA molecule isolated from its originating environment is a chemical compound and thus a "composition of matter"—one of the four classes of invention authorized by 35 U.S.C. § 101—and is patentable if all the other statutory requirements (*e.g.*, utility, novelty and non-obviousness), are met. Linck Decl. ¶¶ 43, 45-47, 49, 58; Doll Decl. ¶¶ 26, 34; Straus Decl. ¶¶ 29-34.[9]

The USPTO's policy is entitled to great respect from the courts. For one, issued patents are entitled to a presumption of validity, and it becomes a challenger's heavy burden to

[9] For example, an isolated DNA molecule may meet the statutory utility requirement if it can be used to produce a useful protein or serves as a marker for a disease. Doll Decl. ¶ 29; Linck Decl. ¶¶ 45-47, 54, 57.

overcome the presumption that this federal agency did its job and did it correctly. *See* 35 U.S.C. § 282. For another, the USPTO reached its carefully considered conclusions on the patent-eligibility of gene-related inventions only after exhaustive review of judicial precedent and after extensive notice and comment procedures. *See* Utility Examination Guidelines 66 Fed. Reg. at 1092-99 (January 5, 2001). For yet another, the Supreme Court has recognized that the USPTO's expertise—and Congress's refusal to change the law in the face of the USPTO's expert determinations—merits that respect. In *J.E.M. Ag Supply*, in considering the issue of whether plants constituted patent-eligible subject matter under § 101, the Supreme Court found it significant that the USPTO had been issuing patents on plants for over 16 years; it was unwilling to hold otherwise in the absence of any "indication from either Congress or agencies with expertise that such coverage is inconsistent with [the governing statutes]." 534 U.S. at 144-45. The Court specifically noted that "the PTO, which administers § 101 . . ., recognizes and regularly issues utility patents for plants." *Id.* at 145.

The same reasoning applies here with even greater force: The USPTO, the CCPA, and other courts "with expertise" have all ruled that patents identical in all relevant respects to the challenged claims in Myriad's patents constitute patentable subject matter under Section 101. The USPTO "regularly recognizes and issues utility patents for genes. Doll Decl. ¶¶ 26, 34-35. *See also*, Straus Decl. ¶¶ 27-28. The Federal Circuit has accepted the patent-eligibility of gene-related patents for many years now. *See, e.g.*, *In re Kubin*, 561 F.3d 1351, 1352 (Fed. Cir. 2009) (noting that "[t]his case presents a claim to *a classic biotechnology invention—the isolation and sequencing of a human gene* that encodes a particular domain of a protein" before holding the claims unpatentably obvious) (emphasis added); *In re O'Farrell*, 853 F.2d 894, 895-99 (Fed. Cir. 1988) (similar). And, significantly, the USPTO's 2001 Utility Examination Guidelines have

taken all of this into account in issuing guidelines for the issuance of gene-related patents. Those guidelines not only reflect a consistent and lengthy course of agency action (as was the case in *J.E.M. Ag Supply*), they also reflect a careful and considered judgment, and a similarly careful review of judicial precedent, made explicit after the opportunity for extensive notice and comment procedures. If Congress wants to change the law (and scuttle the biotechnology industry in so doing), that of course is the prerogative of the National Legislature.

Where Congress disagrees with the scope of patent coverage, it knows just how to step in and change the law if that is the legislative will. For example: In 1997, Congress added a new subsection (c) to 35 U.S.C. § 287, which exempts from infringement liability a medical practitioner's performance of a "medical activity" on a human or laboratory animal. Congress chose this careful legislative "fix" to the perceived problem instead of a proposed, sweeping amendment to Section 101 that would have exempted all patents covering pure medical procedures from the scope of patent-eligible subject matter. *See* H.R. 1127, § 2, 104th Cong., 1st Sess. (1995). Congress rejected that approach in favor of a more calibrated approach, which limited infringement actions and damage awards "[w]ith respect to a medical practitioner's performance of a medical activity that constitutes an infringement." *See* 35 U.S.C. § 287(c)(1). As Senator Hatch, who spoke in opposition to the proposal to amend Section 101, well put the issue: "[T]here should be a very heavy burden on those advocating change of a law that appears to be working well and has worked well for a long time." 142 Cong. Rec. S11842, S11844 (Sept. 30, 1996).

So it is here as well. Congress can consider the issue of the patent-eligibility of gene-related patents if it chooses to take up the issue, and the proponents of change will bear a "heavy burden" to make the case for legislative change: Important medical inventions such as the

anticancer drug Taxol (paclitaxel), which is isolated from the bark of the Pacific Yew tree, would not be patentable under plaintiffs' proposed legal framework. Indeed, it is no exaggeration to say that, under the regime envisioned by plaintiffs—whether implemented by congressional action or judicial decision—there would be little to nothing left of the United States biotechnology industry.

But unless and until Congress decides to make such a legislative change, there is no basis for a federal court to do so by ignoring this carefully considered and consistent agency practice, and by blithely dismissing a century of judicial decisions as "erroneous." It would be fundamentally unfair, disastrous for an entire industry, most likely a violation of the United States' treaty obligations under TRIPS (the Agreement on Trade-Related Aspects of Intellectual Property Rights),[10] and perhaps even an unconstitutional taking under the Fifth Amendment to the U.S. Constitution, for a federal court to issue a ruling that would effectively void the thousands of existing and duly issued patents on isolated nucleic acids.[11] This Court should

[10] "On January 1, 1995, the United States joined the World Trade Organization by entering the Marrakesh Agreement Establishing the World Trade Organization, which through Article II § 2 binds all of its members to the Agreement on Trade-Related Aspects of Intellectual Property Rights ('TRIPS'). 1867 U.N.T.S. 154, 33 I.L.M. 1144 (Apr. 15, 1994)." *Voda v. Cordis Corp.*, 476 F.3d 887, 899 (Fed. Cir. 2007). Article 27.1 of the TRIPS Agreement specifically states that "patents shall be available and patent rights enjoyable without discrimination as to the … field of technology …." Were Section 101 construed as plaintiffs urge, it would in effect exclude the "field of technology" of genetic inventions, which would constitute a violation of TRIPS Article 27.1's nondiscrimination command. Indeed, it would be contrary to the patent policies of virtually all industrialized nations, which recognize the patentability of isolated nucleic acids. *See, e.g.*, Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biological inventions (discussed in Straus Decl. ¶¶ 29-34).

[11] This points up yet another crucial reason why such a judgment is better left to Congress than the courts. A legislative act may be made prospective only. However, were this Court to rule as plaintiffs urge, the effect of its decision would have not only prospective but retroactive effect—it would be pronouncing that the meaning of Section 101 is, and has always been, as plaintiffs say. "The principle that statutes operate only prospectively, while judicial decisions operate retrospectively, is familiar to every law student." *United States v. Sec. Indus. Bank*, 459 U.S. 70, 79 (1982). Accepting plaintiffs' argument would surely destroy every single one of the 2,645 patents issued over the last 29 years that claim "isolated DNA"(and thousands if not tens of thousands of gene patents that do not contain that precise language, not to mention the several gene patents that the USPTO has issued to plaintiffs Chung, Kazazian, Ledbetter, and Warren). In turn, such a ruling would adversely affect the reliance that the entire biotechnology industry has placed on such patents, and that have allowed that industry to grow and flourish.

avoid all of this mischief and decline the plaintiffs' invitation to rewrite Section 101 in this fashion.

2. The Isolated *BRCA1/2* DNA Claims Are Different In Kind From Any Naturally Occurring Substance

With the proper understanding of the law, the patent-eligibility of the isolated DNA claims follows as a matter of course. Properly construed, these claims do not cover genes, gene sequences, or native human genes. Rather, they encompass isolated DNA molecules that are different in kind from any composition found in nature. Kay Decl. ¶ 138; Linck Decl. ¶¶ 51, 58, 59, 77; Schlessinger Decl. ¶ 27; Doll Decl. ¶¶ 27-29, 33. Under the proper understanding of Section 101, as set forth in the line of decisions beginning with *Parke-Davis*, and confirmed more recently by the USPTO's guidelines, an "isolated DNA" is different in kind from native genes in cells, and thus is patent-eligible subject matter.

Plaintiffs assert that "the human body does possess a natural process for isolating and purifying genes." ACLU Br. 25. Any molecular biologist knows that the body does not isolate and purify its genes. Schlessinger Decl. ¶ 11; Kay Decl. ¶ 143. No scientist would make such a claim. Genes are hereditary units of DNA contained within chromosomes in a complex with proteins. DNA is protected in the cell, always surrounded by proteins and stably embedded in chromosomes. DNA forms an integral part of, and are retained by, the chromosome in the cell. Schlessinger Decl. ¶ 11; Kay Decl. ¶¶ 131, 142-43; Doll Decl. ¶ 27. If the body were to cut up and spit out its genes, that would serve no purpose at all, and would lead to numerous illnesses. It is telling that the only one of plaintiffs' witnesses willing to make the claim that the human

body isolates and purifies its own genes was their expert Jackson, who is not a scientist of any sort, but a philosopher. *See* Jackson Decl. ¶¶ 26-29.[12]

Nor, as plaintiffs claim (ACLU Br. 5), does DNA "simply mirro[r] the RNA structure in the body." Kay Decl. ¶¶ 152, 167; Schlessinger Decl. ¶ 14. DNA is chemically and structurally different from RNA. Kay Decl. ¶ 146-147; Schlessinger Decl. ¶¶ 13-15. RNA is made up of different nucleotides as compared to DNA, and has different physical properties, including a short half-life. Kay Decl. ¶¶ 146-148; Schlessinger Decl. ¶¶ 13-15. cDNAs are more stable and less susceptible to degradation than native RNAs. Kay Decl. ¶ 171. In any event, plaintiffs' argument that DNA "simply mirrors" RNA is irrelevant, since if a chemical compound is novel and satisfies the other requirements for patentability, it is patentable. Linck Decl. ¶¶ 45-46, 49; Doll Decl. ¶¶ 26, 34.

The difference in the structural and functional properties of *isolated* DNA is critically important to the utility and function of the claimed isolated DNA molecules. Kay Decl. ¶¶ 133-134, 136, 138; Linck Decl. ¶¶ 45, 48, 51, 54, 55, 57, 64, 77; Schlessinger Decl. ¶¶ 20, 27; Doll Decl. ¶ 29. As disclosed in the patents, the claimed isolated DNAs can be used as probes and sequencing primers to identify mutations in patients and to diagnose a predisposition to cancer. *See*, *e.g.*, '473 patent, col. 28:8 to 30:21. mRNA, on the other hand, cannot be used as a sequencing primer, because its chemistry is incompatible with performing as a sequencing primer. Kay Decl. ¶ 140.

Contrary to plaintiffs' misconception (ACLU Br. 26-29), the disclosed utility of the claimed isolated DNA molecules is not as mere "information." Kay Decl. ¶¶ 127, 134, 141;

[12] Plaintiffs also cite the declaration of Dr. Mason in support of this assertion. ACLU Br. 25, citing "D. Mason ¶¶ 11-12." But Dr. Mason said no such thing in the cited paragraphs, nor, indeed, anywhere in his Declaration. The cited paragraphs of Mason's declaration discuss the process of RNA splicing, something quite different altogether from the claim in the brief that "the human body does possess a natural process for isolating and purifying genes."

Linck Decl. ¶¶ 46, 76, 97; Straus Decl. ¶ 25; Schlessinger Decl. ¶¶ 19-20; Doll Decl. ¶¶ 28, 30. As discussed above, isolated nucleic acids might *contain* information, but it does not follow that that is *all* they are. Instead, as discussed above, isolated DNA is useful as physical probes and primers to identify mutations in patients and diagnose cancer susceptibility in a patient. Kay Decl. ¶¶ 134, 138, 174, 184, 187; Linck Decl. ¶¶ 45, 48, 51, 54, 55, 57, 64, 77; Straus Decl. ¶ 25; Schlessinger Decl. ¶¶ 27-30; Doll Decl. ¶ 29, 34. Thus, the differences in the physical properties of these isolated DNA molecules versus their native counterparts are central to their ability to function in the claimed invention. Kay Decl. ¶¶ 133-134, 136, 138; Linck Decl. ¶¶ 45, 48, 51, 54, 55, 57, 64, 73, 77; Straus Decl. ¶ 25; Doll Decl. ¶¶ 27-29; Schlessinger Decl. ¶¶ 27-30. Even under plaintiffs' narrow view of the law, these differences render the claims patentable. *See* ACLU Br. 24 (asserting that in addition to isolation or purification, a product must have "properties and characteristics which [are] different in kind" from their naturally occurring counterparts to be patentable).

3. The Claimed Isolated DNAs Are Not Merely Information Or Manifestations Of The Laws of Nature

Contrary to plaintiffs' assertions (ACLU Br. 26-29), an isolated DNA molecule is not just "information," or a manifestation of the laws of nature. An isolated DNA molecule is a chemical compound, isolated (and thus "made") by man. Kay Decl. ¶ 17, 125; Linck Decl. ¶¶ 45, 46, 58, 70; Straus Decl. ¶ 25; Doll Decl. ¶ 26-27, 32-33.

Plaintiffs argue that because the function of genes both in the body and in the lab is to convey information, they should not be patentable. ACLU Br. 26-29. They are wrong. The function of isolated cDNA molecules is for use as a diagnostic tool to identify and detect disease-causing genetic mutations. Kay Decl. ¶¶ 134, 187; Linck Decl. ¶¶ 45, 48, 51, 54, 55, 57, 64, 77;

Doll Decl. ¶¶ 29, 34. Native DNA and RNA in cells cannot do that. Kay Decl. ¶¶ 134, 136, 174; Linck Decl. ¶ 48; Doll Decl. ¶ 29.

Plaintiffs argue that an important aspect of a gene is the information it contains. ACLU Br. 27. But while it is undeniable that DNA (of all kinds) conveys information, it is not the case that DNA is "pure" or "mere" information. Rather, DNA molecules are chemical "compositions of matter," to use the terminology of Section 101. Kay Decl. ¶ 125; Linck Decl. ¶¶ 16, 20, 43, 45, 47, 70, 76; Doll Decl. ¶¶ 26-29, 34; Schlessinger Decl. ¶ 19. Indeed, unlike native DNA in cells, the claimed isolated *BRCA1/2* DNA molecules can be used as diagnostic probes and primers designed and manufactured to contain specific DNA sequences such that they interact with genomic DNA. Kay Decl. ¶¶ 134, 136, 174, 184, 187; Linck Decl. ¶¶ 45, 48, 51, 54, 55, 57, 64, 73, 77. These isolated DNA molecules then may serve as (for example) probes to detect *BRCA1/2* mutations that can predispose an individual to cancer. *See*, *e.g.*, '473 patent at col. 28:8 to 30:21. Their usefulness is based on their ability to target and interact with other DNA molecules, which is a function of their own individual structure and chemistry. Kay Decl. ¶¶ 135, 183, 187.

There is no absolute legal prohibition on the patent-eligibility of products which convey or contain information, nor should there be. The structure of *any* chemical compound carries information, yet that does not make such a compound unpatentable. Kay Decl. ¶¶ 127, 128; Linck Decl. ¶¶ 46, 76; Doll Decl. ¶¶ 28, 30, 34. The structure of a chemical compound, for example, carries information about which molecules it will interact with, and what chemical properties it possesses. Kay Decl. ¶ 127; Linck Decl. ¶¶ 46, 76; Doll Decl. ¶ 28. As any scientist knows, all chemical compounds, including natural, synthetic, and artificial drugs, contain information based on the laws of nature. Kay Decl. ¶ 127; Linck Decl. ¶¶ 46, 76; Doll

Decl. ¶ 34. Yet they are not themselves laws of nature, nor mere information. Linck Decl. ¶¶ 46, 76, 97; Schlessinger Decl. ¶ 19; Doll Decl. ¶¶ 28, 30, 34. Informational content thus does not, by itself, affect the patentability of a chemical compound. Doll Decl. ¶¶ 28, 30, 34. Whether or not such a product contains or conveys information, a chemical compound that is different in kind from a compound found in nature is patent-eligible under the law.

C. Myriad's Diagnostic Method Claims Cover Patent-Eligible Subject Matter Under 35 U.S.C. § 101

1. Applications Of Laws Of Nature Are Patentable If They Satisfy The "Machine Or Transformation" Test

Laws of nature, natural phenomena, and abstract ideas may not be patentable, but it is well established that "'an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.'" *In re Bilski*, 545 F.3d 943, 953 (Fed. Cir. 2008) (*en banc*) (quoting *Diehr*, 450 U.S. at 187), *cert. granted*, 129 S. Ct. 2735 (2009). In *Bilski*, the Federal Circuit surveyed the Supreme Court's precedents and provided a "definitive test" providing that a process is patent-eligible under Section 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.*

In *Prometheus Labs. v. Mayo Collaborative Servs.*, 581 F.3d 1336 (Fed. Cir. 2009), the Federal Circuit applied the machine-or-transformation test to methods for calibrating the proper dosage of thiopurine drugs by measuring metabolites in subjects having gastrointestinal disorders. *Id.* at 1343-50. The inventors had discovered a correlation between metabolite levels in a patient's blood and the therapeutic efficiency of a dose of the drug. Based on this correlation, the inventors invented and claimed a method to optimize therapeutic efficiency while minimizing side effects by determining metabolite levels and identifying a need to adjust drug dosage upward or downward based on the levels. *Id.* at 1339-40.

The Federal Circuit found the patent claims in *Prometheus* patent-eligible under Section 101, because they "transform an article into a different state or thing." *Id.* at 1345. Notably, the court found "the determining step, which is present in each of the asserted claims, is transformative and central to the claimed methods." *Id.* at 1347. The court found that determining levels of the metabolite in the subject "necessarily involves a transformation, for those levels cannot be determined by mere inspection." *Id.* The Federal Circuit quoted approvingly Prometheus's expert: "'at the end of the process, the human blood sample is no longer human blood; human tissue is no longer human tissue.'" *Id.*

2. Myriad's Diagnostic-Method Claims Are Patent-Eligible Because They Require A Transformation

The diagnostic-method claims in Myriad's patents satisfy Section 101 because they involve precisely the same sort of transformation that rendered the claims in *Prometheus* patent-eligible. Indeed, the facts here show an even stronger claim to patent-eligibility than in *Prometheus*: Here, the BRCA sequences were not known prior to the Myriad invention; in *Prometheus*, by contrast, the method claims' transformative step involved the detection of old, known metabolites. *See Prometheus*, 581 F.3d at 1339.

Myriad's method claims each require the transformation of a tissue or blood sample in order to isolate the patient's DNA. Further, Myriad's manipulation of the sample is "central to the purpose of the claims," *id.* at 1347, just as manipulation of the sample was crucial to Prometheus's method. Transforming the tissue or blood sample and the DNA and RNA molecules in the sample is what allows the comparison between the wild-type gene (*i.e.*, the normal, unmutated version of the gene) and the patient's gene, and the resultant detection of any germline alteration.

Plaintiffs urge that claim 1 of the '999 patent is an abstract mental process of looking at naturally occurring mutations in human genes, and therefore invalid under Section 101. ACLU Br. 29. That argument is flawed, because it is based on the legally erroneous claim construction that "analyzing the sequence of a *BRCA1* gene or *BRCA1* RNA from a human sample" or the step of "analyzing a sequence of a *BRCA1* cDNA made from mRNA from a human sample" merely requires one to look at the sequence and see if it contains one of the identified alterations (therefore making it, allegedly, a pure mental process). ACLU Br. 15-18, 30-32. The entire premise of this argument is wrong.

Claim 1 requires the step of "analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample" or the step of "analyzing a sequence of a BRCA1 cDNA made from mRNA from a human sample." Contrary to plaintiffs' contention, when this claim is properly construed, one cannot analyze a sequence of a *BRCA1* gene, *BRCA1* mRNA, or *BRCA1* cDNA made from mRNA from a human sample using a purely mental process. Rather, one of ordinary skill in the art would understand that the step of analyzing the sequence of a *BRCA1* gene, *BRCA1* RNA or a *BRCA1* cDNA made from mRNA from a human sample would require *the sequencing of the BRCA1 gene*; more particularly, the claims require processing the human sample and determining the sequence of the gene. Kay Decl. ¶ 70; Linck Decl. ¶¶ 82-83, 90. One of skill in the art would further understand that the step requires using an isolated DNA molecule specific to *BRCA1*, such as a primer specific to the *BRCA1* genomic DNA, *BRCA1* mRNA or *BRCA1* cDNA, to analyze their nucleotide sequence. Kay Decl. ¶¶ 70, 135, 136, 184, 187; Linck Decl. ¶¶ 82-83, 90. Without this isolated DNA molecule, the sequence cannot be analyzed.

Using the proper claim construction, the "analyzing" step of claim 1 of the '999 patent necessarily involves transformations that are central to the claimed method. First, the human sample must be transformed in order to analyze the sequence of a *BRCA1* gene, *BRCA1* RNA or a *BRCA1* cDNA made from mRNA of the sample. Kay Decl. ¶¶ 70, 185, 186; Linck Decl. ¶¶ 82-83, 90. Second, the DNA or RNA of the tissue sample is transformed when a primer or probe is used to bind to and "hybridize" the DNA or RNA isolated from the human sample. Kay Decl. ¶¶ 70, 138; Linck Decl. ¶¶ 82-83, 90. A new "hybrid" DNA/DNA or DNA/RNA compound is formed, allowing its sequence to be analyzed. Kay Decl. ¶¶ 70, 138. As a result, the original human sample is no longer the same human sample, and the DNA and mRNA obtained from the human sample are no longer the same DNA and mRNA molecules that were present in the original human sample. Kay Decl. ¶¶ 185, 186; Linck Decl. ¶¶ 85-90.

This is clearly a transformation within the meaning of *Prometheus*, *Bilski*, and the underlying Supreme Court decisions that set forth the "transformation" test.[13] And this transformation is central to the purpose of the claim, *i.e*., a method for detecting "germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer." '999 patent, col. 4:38-40. Analyzing the sequence of a *BRCA1* DNA or mRNA in a tissue sample is critical to detecting such a germline mutation.

Likewise, in addition to claim 1 of the '999 patent discussed above, each of the other method claims at issue in this case (claim 1 of the '001 patent, claim 1 of the '441 patent, and claims 1 and 2 of the '857 patent), when properly construed, have transformations at their core.

[13] *See Gottschalk v. Benson*, 409 U.S. 63, 70 (1972) ("Transformation and reduction of an article 'to a different state or thing' is the clue to patentability of a process claim that does not include particular machines.") (citing *Cochrane v. Deener*, 94 U.S. 780, 787-88 (1876); *Diehr*, 450 U.S. at 192 (use of mathematical formula in process "transforming or reducing an article to a different state or thing" constitutes patent-eligible subject matter); *Parker v. Flook*, 437 U.S. 584, 589 n.9 (1978) ("An argument can be made [that the Supreme] Court has only recognized a process as within the statutory definition when it either was tied to a particular apparatus or operated to change materials to a 'different state or thing.'") (quoting *Cochrane v. Deener*, *supra*).

None of them claims merely abstract mental processes. Each of the method claims involves a method for detecting, screening, or identifying mutations and alterations in the *BRCA1*/*2* genes (*e.g.*, claim 1 of the '001 patent,[14] and claim 1 of the '441 patent[15], and claim 1 of the '857 patent[16]), or for diagnosing a predisposition for breast cancer (*e.g.*, claim 2 of the '857 patent[17]). In each of these claims, a human tissue sample must be extracted and transformed in order to analyze the sequence of a *BRCA1*/*2* genomic DNA, *BRCA1*/*2* RNA or a *BRCA1/2* cDNA made from mRNA of the sample. Kay Decl. ¶¶ 64-67, 178. Additionally, the DNA or RNA of the tissue sample is transformed when the isolated *BRCA1* DNA molecule is used to bind to and "hybridize" the DNA or RNA in the human sample. Kay Decl. ¶ 70. As a result of this process, a new "hybridization product" consisting of a DNA/DNA or DNA/RNA hybrid compound is formed, allowing its sequence to be analyzed. Kay Decl. ¶ 70. After this step, the original human sample is no longer the same human sample, and the DNA and mRNA obtained from the human sample are no longer the same DNA and mRNA molecules that were present in the original human sample. Kay Decl. ¶¶ 70, 185, 186; Linck Decl. ¶¶ 82-83, 85-90.

Contrary to plaintiffs' contentions (ACLU Br. 26-32), none of these claims attempts to pre-empt the use of a fundamental principle or law of nature; rather, each involves a particularized *application* of a fundamental principle. The distinction is crucial and

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[14] Claim 1 of the '001 patent claims a method for screening a tumor sample from a human subject for a somatic alteration in a *BRCA1* gene by comparing a *BRCA1* gene, RNA, or cDNA made from mRNA sequences in a tumor sample with the same molecules from a non-tumor sample and identifying the differences.

[15] Claim 1 of the '441 patent claims a method for screening the germline of a human subject for an alteration of a *BRCA1* gene by comparing *BRCA1* gene, RNA, or cDNA made from mRNA germline sequences in a sample with the wild-type sequences and identifying the differences.

[16] Claim 1 of the '857 patent claims a method for identifying a mutant *BRCA2* nucleotide sequence in a suspected mutant *BRCA2* allele by comparing the nucleotide sequence of the suspected mutant *BRCA2* allele with the wild-type sequence and identifying the difference.

[17] Claim 2 of the '857 patent claims a method for diagnosing a predisposition for breast cancer in a human subject by comparing the germline sequence of the *BRCA2* gene or mRNA in a tissue sample from a human subject with the germline sequence of the wild-type *BRCA2* gene or mRNA and identifying any alterations.

demonstrates the patent-eligibility of each claim. *Diehr*, 450 U.S. at 187 (claims that foreclose others from a particular "application" of a fundamental principle are patent-eligible under Section 101; claims that "seek to pre-empt the use of" that fundamental principle are not); *Bilski*, 545 F.3d at 953 (same).[18]

Plaintiffs also argue (ACLU Br. 32) that Myriad's claims are analogous to those in *Parker v. Flook*, 437 U.S. 584 (1978). In that case, the claimed invention involved a computer program for determining when an alarm limit was reached. 437 U.S. at 585. The only novel feature of the claimed method was a mathematical algorithm. *Id*. at 585-86. The Court in *Flook* concluded: "Respondent's process is unpatentable under § 101, not because it contains a mathematical algorithm as one component, but because once that algorithm is assumed to be within the prior art, the application, considered as a whole, contains no patentable invention." *Id*. at 594. Here, again, as noted above, the invention of the Myriad patents is not a mere algorithm, but a specific and transformative diagnostic method. Like the claims in *Diamond v. Diehr*, 450 U.S. 175 (1981), Myriad's method claims are to an *application* of a law of nature—a method for detecting a germline alteration linked to breast and ovarian cancer—and would not pre-empt the law of nature itself. Linck Decl. ¶¶ 104-105.

Plaintiffs' attempt to draw support from Justice Breyer's dissent from the dismissal of the petition for certiorari in *Laboratory Corp. of Am. Holdings, Inc. v. Metabolite Labs., Inc.*, 548 U.S. 124, 126-27 (2006) (*see* ACLU Br. 19, 31), is both legally irrelevant and factually flawed.

[18] Plaintiffs seek to draw an analogy between this case and *In re Grams*, 888 F.2d 835 (Fed. Cir. 1989). *See* ACLU Br. 29, 31. But the Federal Circuit in *Prometheus* explained why *Grams* did not control that case; its reasoning applies with full force here. *See Prometheus*, 581 F.3d at 1348. In *Grams*, "the essence of the claimed process" was a mathematical algorithm. *Id.* The *Grams* court posed this critical question: "What did applicants invent?" 888 F.2d at 838. And the answer was a mathematical algorithm, since performing the clinical tests was already in the prior art and not the focus of the specification. *Id*. at 838-39. In contrast, Myriad's invention is not a mathematical algorithm but instead is a set of novel diagnostic tools and methods based on the discovery of the structure and mutations in the *BRCA1* and *BRCA2* genes that are correlated with a predisposition of humans bearing those genes to certain cancers. Based on this discovery, the inventors invented and claimed certain specific diagnostic methods for detecting, identifying and screening patients for a predisposition to cancer.

It is legally irrelevant because an order denying a writ of certiorari carries with it no precedential weight, *see, e.g., Hughes Tool Co. v. Transworld Airlines, Inc.*, 409 U.S. 363, 365 n.1 (1973), and it follows as a matter of course that an opinion *dissenting* from such a non-precedential order "is not controlling law." *Prometheus*, 581 F.3d at 1346 n.3. In any event, the *Laboratory Corp.* case "involved different [patent] claims from the ones at issue here." *Id.*

D. Myriad's Cancer Therapeutic Screening Method Claim Satisfies The "Machine Or Transformation Test"

Claim 20 of the '282 patent recites a method for screening for potential cancer therapeutics.[19] Plaintiffs argue that this claim is unpatentable because it allegedly patents the abstract idea of comparing growth rates of two cells, which, according to plaintiffs, is merely a data-gathering step that is unpatentable under *Grams*. ACLU Br. 31-32. This argument fails. Plaintiffs' argument improperly focuses on only one single method step in the claim, not the claim as a whole, which is what Section 101 looks to:

> The Supreme Court has also made clear that the patent eligibility of a claim as a whole should not be based on whether selected limitations constitute patent-eligible subject matter. *See Bilski*, 545 F.3d at 958 (citing *Diehr*, 450 U.S. at 188, 101 S.Ct. 1048; *Parker v. Flook*, 437 U.S. 584, 594, 98 S.Ct. 2522, 57 L.Ed.2d 451 (1978)). As noted in *Diehr*, the Court has specifically stated that it is "inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis." 450 U.S. at 188, 101 S.Ct. 1048. Moreover, it is improper to consider whether a claimed element or step in a process is novel or nonobvious, since such considerations are separate requirements set forth in 35 U.S.C. §§ 102 and 103, respectively. *Bilski*, 545 F.3d at 958 (citing *Diehr*, 450 U.S. at 188-91, 101 S.Ct. 1048).

Prometheus, 581 F.3d at 1343.

[19] Claim 20 provides: "A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic, growing said transformed eukaryotic host cell in the absence of said compound, determining the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cell in the absence of said compound and comparing the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic."

Claim 20 of the '282 patent meets the transformation test and is thus patent-eligible. The claim requires the use of transformed eukaryotic cells that contain an altered *BRCA1* gene that causes cancer. *See* '282 patent at col. 31:46-53. The first step, growing a transformed eukaryotic host cell containing an altered *BRCA1* gene causing cancer in the presence of a compound, involves at least two transformations central to the claimed method. Transformation of a eukaryotic host cell requires human intervention and is thus transformative. Kay Decl. ¶¶ 57, 63; Linck Decl. ¶ 84. Introduction of the test compound into the host cell also requires a transformation. Linck Decl. ¶ 84. Claim 20 plainly satisfies Section 101.

E. The Patent Claims Are Constitutional Under The First Amendment

Plaintiffs also make the unprecedented argument that the challenged Myriad patents violate the First Amendment because they allegedly "directly limit thought and knowledge" by encompassing pure thought and speech. ACLU Br. 34. The very premise of plaintiffs' argument is both false and completely coextensive with the faulty premise of their Section 101 arguments—that these patent claims simply cover information and abstract thought processes. *See* pp. 32-34, above. In short, defendant USPTO has *not* "given entire control over a body of knowledge and over pure information to a private company," as plaintiffs allege. ACLU Br. 37. The claimed isolated DNAs and diagnostic methods are not "pure information," laws of nature, or abstract ideas. They are chemical compounds and transformative methods that are useful as molecular diagnostic tools. Kay Decl. ¶¶ 125, 134; Linck Decl. ¶¶ 45, 46, 48, 51, 54, 55, 57-58, 70, 77, 90, 101; Schlessinger Decl. ¶¶ 19, 27-30; Doll Decl. ¶¶ 26-29.

Plaintiffs suggest that the "threat of the patentee locking up a substance and all its uses is far greater with gene patents than with chemicals due to the science of genes." Jackson Decl. ¶ 15. Plaintiffs apparently believe that one cannot invent around a gene, potentially allowing patent holders to enjoy a monopoly, thereby hampering further downstream diagnostic and

therapeutic research. *See* ACLU Br. 37. These same concerns were raised, and rejected as unfounded, during the implementation of the USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001). Linck Decl. ¶¶ 71-74; Doll Decl. ¶¶ 20, 21. When a patent claiming a new chemical compound issues, the patentee has the right to exclude others from making, using, offering for sale, selling, or importing the compound for a limited time. Doll Decl. ¶ 44. The patentee is required to disclose only one utility, that is, to teach others how to use the invention in at least one way. Linck Decl. ¶ 72. Because the patentee is not required to disclose all possible uses, promoting the subsequent discovery of other uses is one of the benefits of the patent system. Linck Decl. ¶ 72; *see generally* 66 Fed. Reg. at 1094 ("The incentive to make discoveries and inventions is generally spurred, not inhibited, by patents. The disclosure of genetic inventions provides new opportunities for further development. . . . Other researchers may discover higher, better or more practical uses, but they are advantaged by the starting point that the original disclosure provides."). In short, the issuance of patents in general, and these patents in particular, furthers the values inherent in the First Amendment. They certainly do not violate that Amendment.[20]

F. The Patent Claims Are Constitutional Under Art. 1, Sec. 8, Clause 8 Of The U.S. Constitution

Finally, plaintiffs urge that the patent claims here are invalid under Article I, Section 8, Clause 8 of the U.S. Constitution. There is no merit to that suggestion, either. Like plaintiffs'

[20] Plaintiffs cite no case—and the Myriad Defendants are aware of none—even suggesting, let alone holding, that a patent claim can violate the First Amendment. This is for good reason: The very premise of the patent laws encourages the free and open dissemination of information regarding inventors' scientific advances, and so it is difficult to even hypothesize a patent that could violate the First Amendment. In exchange for a limited period of exclusivity, patent owners must disclose their inventions to the world by allowing them to be published as "letters patent," a term that literally means "open letters." *See In re Bo Thuresson Af Ekenstam*, 256 F.2d 321 (C.C.P.A. 1958). The bargain of the U.S. patent laws requires inventors to disseminate the facts about their invention in exchange for those exclusive rights. *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 151 (1989) ("The attractiveness of such a bargain, and its effectiveness in inducing creative effort and disclosure of the results of that effort, depend almost entirely on a backdrop of free competition in the exploitation of unpatented designs and innovations.").

First Amendment claim, this Constitutional claim is also entirely derivative of their legally flawed Section 101 arguments. *See* ACLU Br. 38 (urging violation of Article I, Section 8, Clause 8 "[f]or the reasons stated above"). That is reason enough to reject the argument.

Article I, Section 8, Clause 8 of the U.S. Constitution provides that Congress has the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." In *Eldred v. Ashcroft*, 537 U.S. 186 (2003), the Supreme Court rejected the claim that Congress's post-creation extension of the term of a copyright violated the clause because an extension of the copyright term *after* a work was created could not, as a matter of law or fact, serve as an incentive to create that already-made work—and, therefore, the statutory extension did not "promote the Progress of Science." *Id.* at 211-13.

In rejecting that argument, the *Eldred* Court stressed "that it is generally for Congress, not the courts, to decide how best to pursue the Copyright Clause's objectives" of promoting and incentivizing progress. *Id.* at 212-13 (citing *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 6 (1966) ("Within the limits of the constitutional grant, the Congress may, of course, implement the stated purpose of the Framers by selecting the policy which in its judgment best effectuates the constitutional aim.")).

Of course, the Clause is by its terms "both a grant of power and a limitation" *on Congress's power* to create systems of intellectual-property laws. *Graham*, 383 U.S. at 5. Whatever "limitation" the Clause may impose, the limitation is on *Congress's* legislative power, not the USPTO's executive power. The Clause is *not* a free-wheeling limitation that is enforceable on the USPTO's decision to issue any individual patent (Article I of the Constitution speaks solely to congressional powers; the USPTO is an Executive Branch agency exercising

statutorily delegated powers). For that reason alone, the Clause has no application to the USPTO's decisions to grant individual patent claims, which is the basis of plaintiffs' argument: "*these patent claims* impede the progress of science." ACLU Br. 38 (emphasis added).[21]

Plaintiffs' Article I, Section 8, Clause 8 argument is thus fatally flawed as a matter of law. That said, the factual premise of that argument is also absent: The assertion that "these patent claims impede the progress of science" (ACLU Br. 38), by chilling research and clinical development, is unsupported. Patents generally promote research by providing incentives to make discoveries and inventions, and *these* patents in particular have, by their issuance and publication, extensively promoted research in this area. Disclosure of genetic inventions, furthermore, provides opportunities for further development. Reilly Decl. ¶¶ 16, 24, 26; Critchfield Decl. ¶¶ 2-18; Tavtigian Decl. ¶¶ 14-17; Linck Decl. ¶¶ 27-28, 71, 73; Doll Decl. ¶¶ 45-47; Schlessinger Decl. ¶¶ 31-32; *see generally* 66 Fed. Reg. at 1093-94 ("The patent system promotes progress by securing a complete disclosure of an invention to the public, in exchange for the inventor's legal right to exclude other people from making, using, offering for sale, selling, or importing the composition for a limited time."); *id.* at 1094 ("[P]romoting the subsequent discovery of other uses is one of the benefits of the patent system. When patents for genes are treated the same as for other chemicals, progress is promoted because the original inventor has the possibility to recoup research costs, because others are motivated to invent around the original patent, and because a new chemical is made available as a basis for future research.").

The specific facts surrounding Myriad's patents and business practices bear this out.

[21] The distinction can be seen by comparing the nature of the challenge rejected by the Court in *Eldred* to the challenge put forth by plaintiffs here. *Eldred* involved a facial challenge to a Congressional enactment (the Sonny Bono Copyright Term Extension Act, Pub. L. 105-298, § 102(b) and (d), 112 Stat. 2827-28 (amending 17 U.S.C. §§ 302, 304)). Plaintiffs here, by contrast, challenge no Congressional enactment, but instead simply challenge the patent-eligibility of a handful of discrete patent claims.

1. Myriad's Patents Promote Research And Advance Clinical Development, Medicine and Quality of Patient Care

As the USPTO has acknowledged, gene-related patents in general promote progress. The evidence is overwhelming that Myriad's patents have done just that.

First, there is no basis to suggest that patents, as a general matter, impede the progress of science. Reilly Decl. ¶¶ 38, 41-45, 49; Straus Decl. ¶¶ 39-48. Plaintiffs' so-called "evidence" of a negative impact of gene-related patents on basic and clinical science is at best anecdotal. Straus Decl. ¶ 39. In contrast to plaintiffs' assertion, an empirical study conducted at the University of Illinois, which included a survey of 125 academic researchers (including university, non-profit and government labs), demonstrated little to no negative impact of patents on biomedical research productivity. Straus Decl. ¶¶ 44-47. In a survey of biomedical researchers in universities, government, and nonprofit institutions published in 2005 in the journal *Science*, the vast majority of participants (381 out of 414) reported that they were not impeded by the existence of patents, and even modifications or delays in their research as a result of patents were rare. Straus Decl. ¶ 48.

These results are consistent with another empirical study, this one undertaken by the German government, to determine whether patents on DNA molecules impeded entry into particular fields of research in which isolated DNAs had been patented. Straus Decl. ¶¶ 40-41. The study found that DNA patents created no such barriers to entry. Straus Decl. ¶ 41. Interestingly, the great majority of those interviewed across the entire surveyed group clearly favored the so-called "absolute product patent protection" of genes. Straus Decl. ¶ 41. Those surveyed opposed any action to disfavor this area of research and development relative to the protections which "classical" chemical inventions have traditionally enjoyed. Straus Decl. ¶ 41. The study found no specific problems with respect to licensing or any support for a special

regime for protecting genetic inventions. Straus Decl. ¶ 41. The study also found that patents on research tools, including isolated DNA molecules, have not had a discernible effect on the cost or pace of research in Germany. Straus Decl. ¶ 43.

Nor is there any evidence of a "chilling effect" of patents on basic clinical research. Reilly Decl. ¶¶ 44-49; Critchfield Decl. ¶¶ 2-18; Tavtigian Decl. ¶¶ 14-17. Indeed, plaintiffs' own declarant, Dr. Cho, has admitted elsewhere, contrary to the position she has taken in this case (Cho Decl. ¶ 24), that there is "little evidence" that gene-related patents place any restraint on clinical medicine. Reilly Decl. ¶ 41.

Second, there is no indication that these Myriad patents, in particular, have "impeded" basic scientific research. As the volume of scholarship in the area alone demonstrates, quite the opposite is true. Reilly Decl. ¶¶ 43, 49; Critchfield Decl. ¶¶ 5, 10, 13. Since Myriad's discoveries of the *BRCA1* and *BRCA2* genes were made public in October 1994,[22] and March 1996,[23] respectively, more than **18,000 scientists** have researched the *BRCA* genes, publishing more than **5,600 research papers on *BRCA1*** and over **3,000 research papers on *BRCA2***. Critchfield Decl. ¶ 13. Myriad's *BRCA1* patents have encouraged additional academic research seeking to elucidate the various physiological roles and properties of the protein encoded by the *BRCA1* gene. *See* Parvin Decl. ¶¶ 3-6; Baer Decl. ¶¶ 3-6; Li Decl. ¶¶ 3-6; Critchfield Decl. ¶¶ 3, 13. Notably, the individual plaintiffs in this suit and their supporting declarants alone have published a total of **48 peer-reviewed research papers** on the *BRCA1* and *BRCA2* genes. Critchfield Decl. ¶ 13.

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[22] Miki *et al*., *A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene* BRCA1, 266 SCIENCE, 66 (1994).

[23] Tavtigian *et al*., *The Complete* BRCA2 *Gene and Mutations in Chromosome 13q-Linked Kindreds*, 12 NAT. GENET., 333 (1996).

Further, the incentives of the patent system were instrumental in Myriad's discovery of the correct *BRCA2* sequence and its characterization of that isolated gene's true structure; this has enhanced *BRCA2* research by its disclosure to the public. Reilly Decl. ¶ 34; Tavtigian Decl. ¶¶ 14-17. Indeed, had it not been for the period of market exclusivity provided by the patent laws, and the infusion of venture and risk capital that follows from this potential market exclusivity, Myriad never would have been created, and its *BRCA1* and *BRCA2* diagnostic tests could not have been brought to the clinic, or to patients. Reilly Decl. ¶ 51; Critchfield Decl. ¶ 25; Skolnick Decl. ¶¶ 14-16; Linck Decl. ¶¶ 27-28, 71, 73.

Myriad was founded to conduct innovative research, in particular to discover and isolate genes involved in human disease. Critchfield Decl. ¶ 2. The patent portfolio on *BRCA1* and *BRCA2* genes has provided the incentives for developing and commercializing important medical diagnostic tools. Critchfield Decl. ¶ 68. Myriad has consistently promoted and encouraged both basic and clinical research on the *BRCA1* and *BRCA2* genes by others, by (1) freely allowing academic scientists to conduct research studies on the *BRCA1* and *BRCA2* genes; (2) providing direct assistance to researchers in their studies on the *BRCA1* and *BRCA2* genes; and (3) conducting its own research on the *BRCA1* and *BRCA2* genes, publishing the research results and actively disseminating information on the *BRCA1* and *BRCA2* genes. Critchfield Decl. ¶¶ 3-12.

In short, the history of Myriad and the history of these patents demonstrate that the patent system promotes the progress of science exactly as the Founding Fathers intended.

2. Patient Access and Affordability to BRCA Testing Has Been Greatly Enhanced by the Myriad Patents

As a result of the rights granted under the patents for the BRCA genes, Myriad has made substantial investments of time and capital. Those investments have resulted in unheralded

access to affordable testing for a critical syndrome which predisposes carriers of BRCA mutations to cancer. Bone Decl. ¶¶ 10, 11; Frieder Decl. ¶ 13. Myriad has spent over $200 million in raising awareness and providing education to patients, healthcare providers, and the insurance industry about the importance of *BRCA* testing and the positive pharmaco-economics of *BRCA* testing. Critchfield Decl. ¶¶ 25, 28, 66; Rusconi Decl. ¶¶ 7-9. Based on these efforts, to date, over 400,000 individuals have received *BRCA* testing and approximately 40,000 health care providers have used *BRCA* testing for their patients. Critchfield Decl. ¶ 25. As a result of its efforts with the insurance community, Myriad has received payment for *BRCA* testing from over 2,600 distinct insurance payors (companies) under 80,000 individual group plans. Critchfield Decl. ¶¶ 25, 31; Rusconi Decl. ¶ 4; Ogaard Decl.¶ 3. There are over 130 million covered lives (lives covered by insurance plans that cover or reimburse for *BRCA* testing). Critchfield Decl. ¶ 31; *see also* Rusconi Decl. ¶ 4.

With such a high percentage of insurance coverage, testing for the *BRCA* gene is both widely accessible and eminently affordable. Over 90% of the *BRCA* testing done by Myriad is covered by insurance, which, in turn, covers over 90% of the costs of the test. Critchfield Decl. ¶¶ 32, 66; Ogaard Decl.¶ 3. Thus, most patient testing is covered by insurance. Lessman Decl. ¶ 9; Frieder Decl. ¶12. The average co-pay (out-of-pocket expense) for a patient with insurance coverage is under $100. Critchfield Decl. ¶ 32. Additionally, since Myriad first launched *BRCA* testing, Myriad has provided patient assistance programs to assist individuals without insurance and who could not afford testing. Critchfield Decl. ¶ 33; Ogaard Decl. ¶¶ 4-5; Rusconi Decl. ¶6. What is more, Myriad provides free testing to non-profit, charitable organizations so that they can make testing available to even those individuals who cannot afford testing. Ogaard Decl. ¶ 6.

Many of the individual plaintiffs have suggested, by declaration and argument, that they have been impeded from getting a "second opinion" from a second provider to confirm the test results provided by Myriad. However, since Myriad started *BRCA* testing in 1996, Myriad has never received a single request from a patient or healthcare provider to conduct a second, confirmatory test at another lab. Critchfield Decl. ¶ 61. In fact, health-care providers ordering Myriad's BRAC*Analysis*® test do not feel the need for a second, confirmatory test, largely due to the ultimate quality and reliability of Myriad's test. Critchfield Decl. ¶ 61; Frieder Decl. ¶ 11; Bone Decl. ¶ 8. In any event, plaintiffs' argument that they cannot get a second test to confirm their *BRCA* mutations test results is disingenuous: Multiple laboratories are available for confirmatory testing, and many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. Critchfield Decl. ¶ 62. For example, testing for specific *BRCA* mutations is available at both the Yale DNA Diagnostic Laboratories and the University of Chicago Genetic Services Laboratories. Critchfield Decl. ¶ 62. (In fact, one of the plaintiffs in this suit, Ellen Matloff, is at Yale and is closely connected with the testing center which does this testing.) Critchfield Decl. ¶ 62 n.40.

Based on the incentives provided by the patent system, Myriad has been able to make substantial investments to further patient care, access and affordability. All of this is directly traceable to the incentives of the U.S. patent system, and to the patents granted on the *BRCA* genes.

3. The Myriad Patents Are Prime Examples Of The Effectiveness Of The Patent System

The Patent and Copyright Clause was designed to create incentives for the development of new scientific and literary works. *Chakrabarty*, 447 U.S. at 307 ("The authority of Congress is exercised in the hope that '[t]he productive effort thereby fostered will have a positive effect

on society through the introduction of new products and processes of manufacture into the economy, and the emanations by way of increased employment and better lives for our citizens.'") (internal citations omitted; ellipses in original). Linck Decl. ¶ 25; Doll Decl. ¶¶ 45-47. Pursuant to these broad powers and its policy-making authority, Congress enacted the patent statutes which endowed the USPTO with the administrative power to issue patents when the conditions of patentability were met under 35 U.S.C. Linck Decl. ¶ 20; Doll Decl. ¶¶ 11, 35**.** Indeed, over the past 200 years, the USPTO has done just that. Linck Decl. ¶ 12; Doll Decl. ¶¶ 11, 23-25.

The successful implementation of USPTO policy and the patent laws has led to an explosion of new technologies, particularly in the biotechnology sector. Linck Decl. ¶¶ 26-27; Doll Decl. ¶¶ 45-47. Without such incentives, the many biotechnology-based medical advances, such as Myriad's *BRCA1* and *BRCA2* genetic testing, could not even have gotten off the ground. Reilly Decl. ¶ 27; Schlessinger Decl. ¶¶ 31-32; Skolnick Decl. ¶¶ 14-16. The future of personalized medicine looks bright, promising new ways of identifying and curing genetic disorders and other diseases, resulting in social and health benefits for everyone. Without patent protection, this future will not happen.

CONCLUSION

For these reasons, the Myriad Defendants' Motion for Summary Judgment should be granted, and plaintiffs' Motion for Summary Judgment should be denied.

Dated: New York, New York
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CERTIFICATE OF SERVICE

This is to certify that on December 23, 2009, a true and correct copy of the foregoing document has been served on all counsel of record via the court's ECF system.

/s/ Brian M. Poissant
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