No. 2010-1406

United States Court of Appeals for the Federal Circuit

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, THE AMERICAN COLLEGE OF MEDICAL GENETICS, THE AMERICAN SOCIETY FOR CLINICAL PATHOLOGY, THE 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, and KATHLEEN RAKER,

Plaintiffs-Appellees,

v.

UNITED STATES PATENT AND TRADEMARK OFFICE,

Defendant,

and

MYRIAD GENETICS, INC.,

Defendant-Appellant,

(caption continued on inside cover)

Appeal From The United States District Court
For The Southern District of New York
In Case No. 09-CV-4515, Senior Judge Robert W. Sweet

BRIEF FOR THE APPELLANTS

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and

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-Appellants.

CERTIFICATE OF INTEREST

Counsel for the appellants, 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, certifies the following:

1. The full name of every party or amicus represented by me is:

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

2. The name of the real party in interest represented by me is:

Myriad Genetics, Inc.; the University of Utah Research Foundation

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

None.

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

Jones Day (Gregory A. Castanias; Brian M. Poissant; Laura A. Coruzzi; Barry R. Satine; Eileen Falvey; Lynda Q. Nguyen; Israel Sasha Mayergoyz).

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Parties

Myriad	The Myriad Defendants (Defendants-Appellants 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), unless the context suggests that it refers only to Defendant-Appellant Myriad Genetics, Inc.
Plaintiffs	Plaintiffs-Appellees, collectively
PTO	United States Patent and Trademark Office

Patents-in-Suit

the ’473 patent	U.S. Patent No. 5,693,473 (composition claim 1 at issue)
the ’999 patent	U.S. Patent No. 5,709,999 (method claim 1 at issue)
the ’001 patent	U.S. Patent No. 5,710,001 (method claim 1 at issue)
the ’282 patent	U.S. Patent No. 5,747,282 (composition claims 1, 2, 5, 6, and 7, and method claim 20, at issue)
the ’441 patent	U.S. Patent No. 5,753,441 (method claim 1 at issue)
the ’492 patent	U.S. Patent No. 5,837,492 (composition claims 1, 6, and 7 at issue)
the ’857 patent	U.S. Patent No. 6,033,857 (method claims 1 and 2 at issue)

Defined Terms

A___	Joint Appendix page(s)
BRCA1/2	Two genes (*BRCA1* and *BRCA2*) associated with a predisposition to breast and ovarian cancers

court	United States District Court for the Southern District of New York, the Honorable Robert W. Sweet, presiding
Court	United States Court of Appeals for the Federal Circuit, or the Supreme Court of the United States, according to context
DNA	Deoxyribonucleic acid
native DNA	DNA as it exists, unisolated and unpurified, and integrated with chromosomes, in the human body
PTO	United States Patent and Trademark Office

All emphasis in this brief is added unless otherwise indicated.

STATEMENT OF RELATED CASES

Pursuant to Federal Circuit Rule 47.5, appellants provide as follows:

(a) There have been no previous appeals in this case.

(b) They are aware of no other case that will be directly affected by the Court's decision in this case.

STATEMENT OF JURISDICTION

Myriad contests the district court's subject-matter jurisdiction. Plaintiffs invoked district-court jurisdiction under 28 U.S.C. § 1338(a). Final judgment was entered on April 19, 2010. Myriad timely appealed on June 16, 2010 (Fed. R. App. P. 4(a)(1)(A)). This Court has appellate jurisdiction under 28 U.S.C. § 1295(a)(1).

STATEMENT OF THE ISSUES

1. Whether, under *MedImmune*'s jurisdictional standard—requiring that "all the circumstances . . . show that there is a substantial controversy, *between parties having adverse legal interests*, of *sufficient immediacy and reality to warrant the issuance of a declaratory judgment*"—the district court erred by finding a case or controversy based on decade-old events and events not involving the plaintiffs in this case?

2. Whether the district court erred by holding that Myriad's composition claims, drawn to isolated DNA molecules that are undisputedly compositions of matter, were nonetheless ineligible for patenting under 35 U.S.C. § 101?

3. Whether the district court erred by holding that Myriad's method claims, drawn to diagnostic methods that transform human samples and compositions of matter, were ineligible for patenting under § 101?

STATEMENT OF THE CASE

A. Preliminary Statement

The disputed claims relate to isolated BRCA DNA molecules, and methods of using them to identify patients at risk of breast and ovarian cancers. Twenty recruited plaintiffs brought this declaratory-judgment action against Myriad and the PTO, alleging that 15 claims plaintiffs selected from seven patents-in-suit exclusively licensed to Myriad were not patent-eligible under 35 U.S.C. § 101, and that their issuance violated the First Amendment and the Patent and Copyright Clause, Article I, Section 8, Clause 8. Plaintiffs did not allege, and thus no issue is presented, that Myriad's claims are invalid under any other provision of the Patent Act.

On November 1, 2009, the district court held that the assortment of plaintiffs recruited to join this lawsuit could properly mount this declaratory-judgment action. On April 2, 2010, the court issued another order holding each disputed claim non-patent-eligible under § 101. Both rulings were in error.

The district court's conclusion that there was a sufficiently ripe case-or-controversy under Article III and the Declaratory Judgment Act would, if upheld, allow virtually anyone to challenge virtually any patent. The court admitted that its jurisdictional ruling was influenced by this "unique" case posing "questions of difficult legal dimensions" with "far-reaching implications."

The court's merits ruling, holding that the disputed claims were not patent-eligible, was also erroneous. For Myriad's composition-of-matter claims, the court divined a broad, unbounded prohibition on patenting "products of nature," which in its view forbade Myriad's composition claims covering isolated BRCA DNA molecules. For the method claims, the court misconstrued those claims and failed to recognize the methods' transformative nature, requiring the extraction, processing, and analysis of human tissue or blood samples.

The isolated DNA molecules, which are undisputedly compositions of matter, and the methods of utilizing them, are patent-eligible. Their discovery, isolation, and disclosure has added greatly to our understanding and prevention of hereditary cancers, and thus merit patent-eligibility. Without the incentives provided by the Patent Act, many biotechnology-based advances in the diagnostic, therapeutic, agricultural, and other fields, including (but scarcely limited to) Myriad's BRCA DNA testing, could not even have gotten off the ground.[1] The future of diagnostic and personalized medicine promises new ways of identifying and curing genetic disorders and other diseases, resulting in incalculable societal

[1] Over the past 29 years, the PTO has issued some 2,645 patents with claims to "isolated DNA," and over 50,000 patents containing at least one claim directed to a nucleic acid sequence, including those derived from humans, other animals, plants, bacteria, and so on. (A3467; A3710; A3719-3877; A5321.) Among them, U.S. Patent No. 4,703,008, claiming an "isolated DNA" encoding human erythropoietin, led to the successful commercialization of the blockbuster therapeutic, Epogen®. (A3876; A5316-17.)

benefits. (A3488; A4546; A5700-02; A5811-75.) If this judgment is not reversed, and the important incentives of the patent laws not restored to these critical inventive activities, valuable future developments will slow or cease, or be driven underground so that their developers can maintain trade-secret protection without disclosing them. (A3488; A4530-4701; A5674-75; A5702-07.)

B. Procedural History

Plaintiffs filed a complaint for declaratory judgment and injunction on May 12, 2009, alleging that 15 patent claims selected by them from seven Myriad patents are invalid and unconstitutional. (A1034-1064.)

On July 13, 2009, defendants Myriad and the PTO filed motions to dismiss on various jurisdictional grounds. (A1101-19; A1120-78.) Those motions were denied on November 1, 2009. (A1-88.)

On August 26, 2009, plaintiffs filed a motion for summary judgment, and, on December 23, 2009, Myriad opposed and filed its own summary-judgment motion. After a February 4, 2010 argument, the Court issued a summary-judgment order on March 29, 2010 (amended on April 2, 2010) that each of the 15 claims selected for challenge by plaintiffs are not patent-eligible under § 101. (A89-247) Final judgment was entered on April 19, 2010. (A248-58.) Myriad timely appealed on June 16, 2010. (A7840-43.)

STATEMENT OF FACTS

The seven patents-in-suit relate to human genetics. The composition claims at issue each claim an "isolated" BRCA1 or BRCA2 molecule. ("BRCA" is shorthand for breast cancer; *BRCA1* and *BRCA2* are two genes associated with a predisposition to breast and ovarian cancers.) (*E.g.*, A785:2:54 to A786:4:21; A3444-45; A3454-55; A4292-96.) The method claims set forth methods for using those isolated molecules as diagnostic tools for identifying patients at risk for these cancers. (A965:169:47-54; A3455-54.)

Prior to these inventions, unraveling the genetics of breast cancer was formidable. Although breast cancer was considered to have inherited or "familial" components, no gene responsible for that disease had been identified or isolated. (A279-80.) Thus, prior to the Myriad discoveries and inventions, patients at risk of breast and ovarian cancer had no way of knowing whether they might carry a potentially harmful genetic mutation.

In view of the summary-judgment posture of the case, the facts set forth here are either undisputed or taken in the light most favorable to Myriad.

A. The Structure And Function Of DNA

Human genetics is the science of heredity and variation in human beings. The basis of inheritance is a "gene." (A3523; A4325; A4723; A4837.) There are about 25,000 known genes in the entire human genome. (A3447; A4342; A4838;

A5308.) In humans, genes reside on chromosomes. (A3454; A4320-25; A4412; A4723; A5301-03; A5869.) Each chromosome contains proteins wrapped in a single integral DNA molecule. (A3468; A4320-25; A4723; A5301-03.) Thus, neither genes nor their DNA components float freely in the body. (A3494; A3707-08; A4321.) Rather, they are physically bound to other genes, nucleic acids, and proteins integral to the chromosome that play important roles in the structure and function of DNA in the body. (A3493-94; A4320-22; A4325-26; A4723-24.)

Chemically, DNA is made up of "nucleotides," linked to each other by a phosphodiester backbone. The four commonly occurring nucleotides in DNA are Adenosine, Guanosine, Thymidine, and Cytidine (A, G, T, and C, for short). (A3493; A3709; A4290; A4317-20; A4723-24.) The term "sequence" refers either to the precise linear order or structure of these nucleotides in each DNA strand, or, as in the Myriad method claims, to the DNA molecule itself possessing that linear structure. (A3453; A3493; A3526; A4313-14; A4318.) Determining the precise structure of A's, G's, T's and C's in a DNA molecule is called "DNA sequencing." (A3453; A3497; A3500-03; A3529; A4338-43.)

DNA's "double helix" structure is formed by the bonding of nucleotides on one strand of DNA to nucleotides on a second strand of DNA according to a simple rule: A binds to T, and G binds to C. This is known as "complementary base pairing." (A4319-20; A5300.)

Cells use DNA molecules in a chemical process to produce the proteins that make up the human body. DNA is also a hereditary molecule, copies of which are passed from generation to generation. Isolated DNA cannot, on its own, make protein, nor can it pass its genetic code from generation to generation. (A4321-26.)

An "isolated" DNA molecule has been removed from its naturally occurring environment. (A3452-54; A4290-91; A4322-26.) This involves chemical extraction and isolation of the DNA molecule from the thicket of genetic material in the genome. (A4322-23.) Such molecules include recombinant or cloned DNA isolates as well as chemically synthesized analogs or analogs synthesized using biochemical systems. (A4291.) Isolated DNA, separated from its native environment, is structurally distinct from native DNA, and has different properties and utilities. (A3446-47; A4322-26; A4335.) For example, a strand of isolated DNA can be used to target and bind to a complementary sequence in a tissue sample. (A4322-26.) Thus, isolated DNA can be used as a "probe," a diagnostic tool that can be detected using laboratory machinery; native DNA cannot be so used. (A3446-47; A3497; A3708; A4322-24; A4335; A4728-29.)

Isolated DNA can also be used as another diagnostic tool, a "primer," which can be used to sequence DNA. In sequencing, a primer binds to, or "hybridizes" to a DNA target, such as a BRCA DNA, to form a hybridization product that acts as a substrate for the enzymes used in the sequencing reaction. (A4322-26; A4728-29.)

Sequencing primers may be used to determine whether a mutation or variation exists in a targeted DNA sequence, such as chromosomal DNA of a patient's tissue sample; native DNA cannot be used in this way, either. (A3455-57; A4322-26.)

B. Myriad's Research And Patents

Based on an innovative population-based study of cancer in a Utah Mormon community, the inventors of the patents-in-suit were able to unravel the genetic basis of *BRCA1*- and *BRCA2*-related cancer. By studying thousands of members of large families with clusters of cancer, the inventors amassed a large data collection, and then developed new techniques for mapping genetic polymorphisms to home in on the precise location of the *BRCA1* gene within the human genome. (A4769-99; A4801-03.) The Myriad inventors were the first to isolate the BRCA1 DNA molecule, and they obtained patents covering their invention and associated methods for diagnosing a predisposition to breast and ovarian cancers. (A4769-99; A4803-06.) Myriad was then able to discover and isolate the BRCA2 molecule. (A4803-05; A5192-5232.) The inventors obtained patents directed to this invention, and associated methods, as well. (A259-967.)

The claims-in-suit are of two types: (i) the isolated BRCA DNA molecules themselves, and (ii) diagnostic methods and cancer-therapeutic screening methods utilizing those isolated molecules. These isolated molecules are man-made chemical compositions, structurally and functionally distinct from any substance

found in the human body—indeed, in all of nature. (A3468-72; A3707-12; A4324; A4410-13.) They are neither laws of nature, nor abstract ideas, nor mere information, but instead are useful as molecular tools (*e.g.*, primers and probes) because of their ability to target and form stable chemical structures with a BRCA DNA sequence in a tissue sample. (A3455-57; A3468-72; A4324; A4339-43.) These isolated molecules can also be sequenced in the laboratory. (A4324; A4339-43.) These differences between the claimed isolated DNA molecules and genes found in the human body are critical to their distinct functions and real-world utilities. (A4339-43.) The claims do not cover genes in the human body.

The method claims are directed at detecting BRCA mutations and screening for potential cancer therapeutics; none involves merely "looking" at genes. (A3445; A3447-48; A3455-58; A4342-43.) Indeed, one cannot detect mutations or determine the sequence of DNA by mere inspection. Detection of a gene requires molecular tools such as probes or primers; the isolated molecules are these tools, which transform a patient's sample to allow detection of mutations and sequence variations in the patient's genes. (A3455-57; A4342-43.)

The patents-in-suit disclose these advancements to the public.

C. The PTO's *Utility Examination Guidelines*

In the mid-1990's, the PTO began a careful study of the law to determine whether isolated DNA molecules were eligible for patenting under § 101. (A3703-

06; A3717-3978; A4399-4401.) After a thorough analysis of the statute and relevant case law, the PTO concluded that isolated DNA molecules were patent-eligible compositions of matter under § 101 so long as they satisfied the other statutory requirements, particularly that of utility. (A3464-66; A3703-06; A3970-78; A4399-4401.) The PTO thereafter issued interim guidelines to patent examiners for granting claims directed to isolated DNA molecules, and requested comments from the public. This effort culminated in the issuance of the revised *Utility Examination Guidelines*, 66 Fed. Reg. 1092 (Jan. 5, 2001), which addressed and responded to those comments. (A3703-06; A4241-49.) These revised guidelines set forth the PTO's practice: Isolated DNA molecules satisfy § 101 if there is a specific, substantial and credible utility for those molecules. (A3710; A3970-78.)

D. The ACLU's Filing Of This Lawsuit

The declaratory-judgment complaint, filed by 20 plaintiffs on May 12, 2009, alleged that the disputed claims are invalid under Article I, Section 8, Clause 8 of the U.S. Constitution, the First Amendment, and § 101. (A1034-64.)

The 20 plaintiffs generally fall into two categories. The first consists of organizations and individuals that share these attributes: (1) there is no allegation or evidence that any of these plaintiffs ever communicated with Myriad, or that Myriad communicated with them, regarding the patents-in-suit, let alone the

specific disputed claims selected for challenge; and (2) there is no allegation or evidence that Myriad ever evaluated any conduct of any of these plaintiffs for purposes of determining infringement. (A1034-64.) This first category includes organizations and individuals, actively recruited by ACLU to join this case, who allege they are "ready, willing, and able" to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated. (A1036-38.) This first category also includes individuals who allege they are "ready, willing, and able" to evaluate BRCA samples themselves, or find other labs to do so, if the patents are invalidated. (A1039-41.) In addition, this first category includes organizations and individuals who are neither researchers nor doctors, but who claim to be "ready, willing, and able" to use additional resources that might be developed by others were the patents invalidated. (A1041-46.)

The plaintiffs in the second category—Drs. Kazazian, Ganguly, and Ostrer—share a common attribute in that the complaint alleges, or the court found, that they had communications with Myriad more than a decade ago concerning certain of the patents-in-suit. (A11-12; A31-33; A1038-40.)

The defendants were each alleged to have some interest as an owner or licensee of the patents-in-suit. The PTO was named as a defendant for the two constitutional claims. (A1046-47.)

Plaintiffs' case is nominally directed to Myriad, but actually imperils the entire biotechnology industry—molecular diagnostics, therapeutic drugs, agricultural applications, animal husbandry, etc. Mr. Ravicher, President and Executive Director of the Public Patent Foundation, and counsel of record for plaintiffs, told CNN: "It is absolutely our intent that upon victory this will rend [sic] invalid patents on many other genes. We just had to pick one case as our case." (A7387-88.)

E. The District Court's Ruling Sustaining Jurisdiction

On July 13, 2009, Myriad filed a motion to dismiss the complaint for lack of jurisdiction. Myriad urged there was no evidence of any real or immediate dispute between Myriad and any plaintiff. (A1120-41.)

On November 2, 2009, the court denied Myriad's motion and sustained subject-matter jurisdiction. (A1-88.) The district court identified only three of the 20 plaintiffs—Drs. Kazazian, Ganguly, and Ostrer—as ever having been contacted by Myriad, in the form of letters sent over a decade prior to the filing of the complaint. (A11-12; A31-33.) Similarly, the district court identified another old letter that Myriad sent in 1998 to the National Cancer Institute's Dr. Nayfield, who is not a plaintiff in this case, indicating Myriad's "support" for the Institute's research, "without reservation," and offering Myriad's testing services "at a substantial discount" in support of the Institute's research. (A33-34.) The district

court also made passing reference to a purported telephone call initiated by plaintiff Matloff, to an unidentified Myriad employee, regarding her laboratory conducting certain genetic screening. (A34-35.) Finally, the court also relied on two patent cases—also occurring more than a decade prior to the filing of the complaint—one initiated by Oncormed against Myriad and later dismissed; the other between Myriad and the University of Pennsylvania. (A35-36.) Neither Oncormed nor the university is a plaintiff here. (A1034.) The case involving the university did not name Drs. Kazazian or Ganguly as defendants (both had been employed at a laboratory operated by the university), and was dismissed in 1999 after Myriad failed to serve process. (A1148.)

Despite the limited, aged nature of these events, and further despite the plethora of unfettered research on BRCA1 and BRCA2 molecules (A3439; A3444; A3484-85), the court nonetheless exercised jurisdiction based on a purportedly widespread understanding that "within the research community . . . Myriad has taken the position that any BRCA1/2 related activity infringes its patents and that Myriad will assert its patent rights against parties engaged in such activity," and the plaintiffs' "ability and desire" to engage in such testing. (A63-64)

F. The District Court's Ruling That DNA Patents Are Not Patent-Eligible

Plaintiffs moved for summary judgment on August 26, 2009. (A1634-84.) Myriad opposed on December 23, 2009, and submitted its own summary-judgment

motion. (A3429-3611.) Numerous declarations from patients, doctors, and researchers accompanied both motions. World-renowned scientists weighed in on both sides.

Plaintiffs and their *amici* urged the court to invalidate Myriad's disputed patent claims under § 101, the Constitution, and for policy reasons, arguing that Myriad's patents claims impede research, and block patient access to and increase costs for the BRCA diagnostic tests. (*See, e.g.*, A1639-84; A3099-3124; A3141-70; A3188-3214; A3240-71.)

Myriad responded with evidence that its patents promote BRCA research, pointing out that over 18,000 researchers have conducted studies on BRCA, and over 7,000 relevant papers have been published, since the inventors disclosed these inventions to the public. Moreover, Myriad showed that patients now have ready access to the BRCA tests, 90% of which are covered by insurance (average co-pay: $100), and that Myriad provides patient assistance for those who cannot afford the test. (A3439-40; A3444; A3484-87.)

Plaintiffs and their *amici* also contended that the claimed isolated DNAs are non-patent-eligible products of nature, laws of nature, and natural phenomena. (A1664-77; A3112-20; A3162-67; A3196-3200; A3249-55.) They further claimed that isolated DNAs are not "markedly different" from DNA inside the human body, yet they admitted that sequencing and detection could not be performed without

those isolated molecules. (A1665-71; A1698.) Plaintiffs also urged that the claimed methods constituted mere information and thought, that the steps of the methods did not involve a transformation, that claims to "comparing" sequences cover "looking" at sequences and seeing if they are the same, and that any claims to the naturally occurring relationship between mutations and susceptibility to cancer are laws of nature and thus not patent-eligible. (A1674-76.)

Myriad and its *amici* countered with showings that isolated BRCA DNA molecules are patent-eligible new and useful compositions of matter, that the isolated molecules do not exist in the body, and that they perform substantial utilities that cannot be performed by "native" genes in the human body. (A3458-72; A3493-3500; A3707-12; A4320-43; A4410-25; A5306-15; A5593-5600; A5707-09; A6559-65; A6820-27.) Myriad pointed to the various steps in the method claims that transform the tissue or blood sample into a different state or thing, rendering the method claims patent-eligible. (A3473-78; A4425-32.)

The district court delivered a 151-page opinion on March 29, 2010 (amended four days later), holding the challenged claims patent-ineligible because the isolated BRCA DNA molecules are the "physical embodiment of information" and thus not "markedly different" from native DNA. (A89-247; A214-28.) The district court also held that the claimed methods for detecting *BRCA* genes and diagnosing predisposition to cancer are not patent-eligible because they involve

nothing more than comparing genes and mental thought. (A228-42.) The court invoked constitutional avoidance to dismiss the constitutional claims. (A242-44.)

SUMMARY OF ARGUMENT

I. The district court erred by entertaining plaintiffs' declaratory-judgment complaint. None of the assembly of recruited plaintiffs had any controversy "of sufficient immediacy and reality to warrant the issuance of a declaratory judgment" under *MedImmune.* To the contrary, the only affirmative acts taken by Myriad with respect to any of the patents-in-suit and any of the plaintiffs occurred over ten years ago. The district court improperly truncated the *MedImmune* inquiry and found jurisdiction based on a standardless "all the circumstances" test instead of inquiring, as *MedImmune* commands, whether "all the circumstances . . . show that there is a substantial controversy, *between parties having adverse legal interests, of sufficient immediacy and reality*." Under the proper standard, there is no adversity here—just a complaint manufactured to serve the ends of two public-advocacy groups. This is precisely the type of "abstract" dispute that the constitutional case-or-controversy requirement excludes from federal jurisdiction.

II. If the Court reaches the merits, it should reverse. As to the composition-of-matter claims, each of which is drawn to isolated BRCA DNA molecules, those claims satisfy § 101. The isolated molecules fall within the literal

language of that section, because they are undisputedly compositions of matter. They do not fall within any of the three narrowly cabined non-textual exceptions to § 101 ("laws of nature, physical phenomena, and abstract ideas"). To the contrary, these molecules are patent-eligible because such a holding is consistent with § 101's command that "any" composition of matter that is "new and useful" is patent-eligible, and compelled by a long and consistent line of precedent and agency practice holding that molecules and substances isolated from naturally occurring products are "new" and thus patent-eligible compositions of matter. Moreover, they are not unpatentable because of any categorical restriction on patenting "products of nature." Even were there a prohibition upon patenting "products of nature" that are not "markedly different" from the naturally occurring substances, Myriad was still entitled to summary judgment. Alternatively, the court erred by resolving fact questions against Myriad on summary judgment.

III. The method claims are likewise patent-eligible under § 101. They would be patent-eligible under even the narrow "machine-or-transformation" test that governed before the Supreme Court's decision in *Bilski*; they are certainly patent-eligible under the more generous approach endorsed by that decision. The district court's contrary decision was wrong because it erroneously construed the term "sequence . . . from a human sample" (which appears in all of the disputed method claims) as mere information, not an actual, physical molecule. Allowing

patent protection for these transformative and extraordinarily useful method claims is consistent with § 101 because they are new and useful methods. Moreover, patent protection for these methods furthers the larger object of the patent laws—incentivizing valuable inventions without transgressing the public domain.

IV. Because it is clear that Myriad's patent claims cover patent-eligible subject matter as a matter of law, the judgment should be reversed, and summary judgment ordered in favor of Myriad.

STANDARDS OF REVIEW

Jurisdictional issues are reviewed *de novo*. *Prasco, LLC v. Medicis Pharm. Corp.*, 537 F.3d 1329, 1335 (Fed. Cir. 2008). Orders granting or denying summary judgment are also reviewed *de novo*, and should be affirmed only when "there is no genuine issue as to any material fact and . . . the moving party is entitled to a judgment as a matter of law." *Crown Operations Int'l v. Solutia Inc.*, 289 F.3d 1367, 1375 (Fed. Cir. 2002).

ARGUMENT

I. THE DISTRICT COURT LACKED DECLARATORY-JUDGMENT JURISDICTION

A justiciable controversy under the Declaratory Judgment Act requires that, "under all the circumstances," there must be a "substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *MedImmune, Inc. v. Genentech,*

Inc., 549 U.S. 118, 127 (2007). Plaintiffs bear the burden of establishing declaratory-judgment jurisdiction. *See Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 95 (1993).

The district court noted that "there is now an ease of achieving declaratory judgment jurisdiction" after *MedImmune* (A54), but this Court has confirmed that "a lowered bar *does not mean no bar at all.*" *Hewlett-Packard Co. v. Acceleron, LLC*, 587 F.3d 1358, 1361-62 (Fed. Cir. 2009). The court's application of the "all the circumstances" test eliminated any meaningful threshold for declaratory-judgment jurisdiction by allowing any plaintiff with "the ability and desire" to infringe (A64) the right to challenge the patent's validity based solely on subjective fears of suit. The district court reached this erroneous result by divorcing *MedImmune*'s "all the circumstances" language from the probative elements of the inquiry—namely, "all the circumstances" must demonstrate a controversy that: (1) exists "between [] parties having adverse legal interests"; and (2) is "of sufficient immediacy and reality." *MedImmune*, 549 U.S. at 127. Plaintiffs fail on both grounds.

A. Plaintiffs And Myriad Do Not Have "Adverse Legal Interests"

Declaratory-judgment jurisdiction requires an immediate controversy "*touching the legal relations of parties having adverse legal interests*." *MedImmune*, 549 U.S. at 127. Here, the record lacks any allegation that, at any

recent time, (1) Myriad had any affirmative contact with plaintiffs concerning the patents-in-suit, or (2) plaintiffs informed Myriad about their "ability and desire" to infringe the patents-in-suit. (A64.) Thus, the parties have no adverse legal interests because "not only ha[s] [Myriad] not taken a concrete position adverse to [plaintiffs], but [Myriad] also ha[s] taken no affirmative actions at all related to [plaintiffs'] current product[s]." *Prasco*, 537 F.3d at 1340. Indeed, plaintiffs have no "current products" or methods.

1. Plaintiffs Fail To Allege Any "Affirmative Act" By Myriad

"[D]eclaratory judgment jurisdiction generally will not arise merely on the basis that a party learns of the existence of a patent owned by another or even perceives such a patent to pose a risk of infringement, *without some affirmative act by the patentee*." *SanDisk Corp. v. STMicroelectronics, N.V.*, 480 F.3d 1372, 1380-81 (Fed. Cir. 2007).

Here, neither plaintiffs' complaint nor the district court's opinion identifies any "affirmative act" by Myriad within the past ten years putting plaintiffs at risk of an infringement suit. There is no allegation, much less evidence, that Myriad ever identified the patents-in-suit (or any claim thereof) to any plaintiff, or identified any plaintiff's product or conduct as infringing. In fact, there is no allegation that Myriad was even aware of any plaintiff's "ability and desire" to infringe (A1034-64), let alone that Myriad evaluated any product or conduct to

determine infringement. Accordingly, plaintiffs have no basis for declaratory-judgment jurisdiction because "the totality of the circumstances analysis in the instant case is that which has *not* occurred." *Prasco*, 537 F.3d at 1339 (original emphasis).

The district court incorrectly dismissed the absence of any affirmative act by Myriad toward plaintiffs by observing that "[a] requirement that there must be a specific, affirmative act directed towards the plaintiff to establish standing to seek a declaratory judgment of patent invalidity would be inconsistent" with the "all the circumstances" test. (A59.) This was incorrect. This Court in *SanDisk* explicitly held otherwise, and *MedImmune* itself confirms that the touchstone of an "adverse legal interest" is defendant's "*threatened enforcement action*" that creates a "legal disagreement" with plaintiff. 549 U.S. at 129-34 (explaining that declaratory-judgment jurisdiction existed when defendant's threatening actions ("actively contested legal rights") would coerce plaintiff to "destroy a large building, bet the farm, or [ ] risk treble damages and the loss of 80 percent of its business"). Plaintiffs here have nothing at stake other than an inchoate desire to do something in the future *if* these patents are invalidated.

The district court's reasoning is also refuted by this Court's instruction that "a *communication from a patent owner to another party*, merely identifying its patent and the other party's product line, *without more, cannot establish adverse*

legal interests between the parties, let alone the existence of a 'definite and concrete' dispute." *Hewlett-Packard*, 587 F.3d at 1362. The record here does not even rise to that insufficient level because there is no allegation or evidence of recent communications from Myriad to any plaintiff regarding the patents-in-suit.

Moreover, the court's supposition regarding "the widespread knowledge of Myriad's BRCA1/2 patents and the breadth of the relevant claims" is insufficient to establish jurisdiction. (A64 n.16.) This Court rejected a similar argument in *Prasco*, where the plaintiff sought a declaratory-judgment based on a patentee's marking of its products. *See* 537 F.3d at 1340-41. This Court explained that patent marking "provides little, if any, evidence that [a patentee] will ever enforce its patents" and "is not a circumstance which supports finding an imminent threat of harm sufficient to create an actual controversy." *Id.* Thus, a patentee providing "notice to the public that [its] goods are patented" cannot "overcome the complete lack of evidence of a defined, *preexisting dispute between the parties* concerning [plaintiff's product]." *Id.* at 1340.

2. Plaintiffs' Subjective Perceptions Cannot Establish Jurisdiction

Unable to identify any defined, preexisting dispute between Myriad and any plaintiff, the district court exercised jurisdiction based on its questionable perception (in light of the extensive research actually performed) that "it is widely understood within the research community that Myriad has taken the position that

any BRCA1/2 related activity infringes its patents and that Myriad will assert its patent rights against parties engaged in such activity." (A35-36) Neither rumor and innuendo, nor others' subjective "underst[andings]," absent some type of threatening action by the patentee, support declaratory-judgment jurisdiction: "The mere existence of a potentially adverse patent does not cause an injury nor create an imminent risk of an injury." *Prasco*, 537 F.3d at 1338.

Even after *MedImmune*, the law does "not hold that a patent can always be challenged whenever it appears to pose a risk of infringement." *Innovative Therapies, Inc. v. Kinetic Concepts, Inc.*, 599 F.3d 1377, 1382 (Fed. Cir. 2010). The possibility that plaintiffs subjectively "perceive[] [Myriad's] patent to pose a risk of infringement" is insufficient. *SanDisk*, 480 F.3d at 1381. Rather, a "controversy must be based on a real and immediate injury or threat of future injury *that is caused by the defendants—an objective standard that cannot be met by a purely subjective or speculative fear of future harm*." *Prasco*, 537 F.3d at 1339 (emphasis shifted); *see also Indium Corp. of Am. v. Semi-Alloys, Inc.*, 781 F.2d 879, 883 (Fed. Cir. 1985) ("purely subjective apprehension" insufficient to show an actual controversy).

The court's observation that "researchers are chilled from engaging in research on BRCA" (A40) is not only contrary to the extensive research that *has* occurred, but also is legally insufficient. "Allegations of a subjective 'chill' are not

an adequate substitute for a claim of specific present objective harm or a threat of specific future harm." *Laird v. Tatum*, 408 U.S. 1, 13-14 (1972); *see also City of Los Angeles v. Lyons*, 461 U.S. 95, 107 n.8 (1983) ("It is the *reality* of the threat of [ ] injury that is relevant to the standing inquiry, not the plaintiff's subjective apprehensions.") (original emphasis).

B. Plaintiffs Fail To Demonstrate A Controversy Of "Sufficient Immediacy And Reality"

"[T]here can be no controversy without a showing that this threat [of suit] was *real, imminent, and traceable* to defendants." *Prasco*, 537 F.3d at 1339. Here, Myriad took no action towards plaintiffs threatening imminent suit.

1. Stale Communications Do Not Establish A "Real," "Immediate" Controversy

The only allegations or findings of "specific affirmative acts" relating to any named plaintiffs are letters and communications between Myriad and Drs. Kazazian, Ganguly, and Ostrer from May 1998 to June 1999, and an alleged exchange of phone calls between some Myriad employee and Dr. Matloff in 2005. (A11-12; A31-33; A1038-40.) Given the extensive passage of time, none of these communications remotely demonstrates a controversy of "sufficient immediacy and reality." *MedImmune*, 549 U.S. at 127.

The court discounted the staleness of these communications by noting that the extended-passage-of-time consideration related to the "now-defunct

'apprehension of suit' test." (A60.) This was wrong in law and fact. "While the Supreme Court rejected the reasonable apprehension of suit test as the sole test for jurisdiction, it did not completely do away with the relevance of a reasonable apprehension of suit." *Prasco*, 537 F.3d at 1336. That remains an important consideration. *Id.* at 1339; *see Innovative Therapies*, 599 F.3d at 1382. Indeed, because "all the circumstances" must show a controversy having "immediacy and reality," the fact that the only direct communications were so aged is powerful evidence that any "controversy" here was imagined and manufactured.

Given the long passage of time between these communications and the filing of the complaint, those communications fail to evince, under any measure, that Myriad has an imminent plan to assert its patents against these doctors (or anyone else). *See Sierra Applied Scis., Inc. v. Advanced Energy Indus., Inc.*, 363 F.3d 1361, 1374 (Fed. Cir. 2004) (after four-year lapse in communication, plaintiff "could no longer have reasonably apprehended an infringement suit"); *Cygnus Therapeutics Sys. v. ALZA Corp.*, 92 F.3d 1153, 1159 (Fed. Cir. 1996) (five-year lapse in communication eliminated apprehension of suit); *see generally Lujan v. Defenders of Wildlife*, 504 U.S. 555, 564 (1992) (old and stale conduct "do[es] not support a finding of the 'actual or imminent' injury that our cases require").

The absence of a real, immediate controversy is cemented by this Court's instruction that "at the root of most justiciable declaratory judgment controversies

in the patent context is a 'restraint on the free exploitation of non-infringing goods,' or an imminent threat of such restraint." *Prasco*, 537 F.3d at 1339. Here, since 1999, Myriad has not threatened suit against, demanded any royalty from, or suggested a license to, any plaintiff. Nor has Myriad taken any action to interfere with any plaintiff's conduct. Just as the law recognizes that a patentee's six-year delay in filing suit creates a presumption of laches "aris[ing] out of considerations of *fairness*, *public policy, and probability*," *A.C. Aukerman Co. v. R.L. Chaides Constr. Co.*, 960 F.2d 1020, 1034-35 (Fed. Cir. 1992) (en banc), by the same token, a patentee's ten-year silence presumptively extinguishes any reasonably objective fear of suit.

Finally, the court referred to a purported 2005 telephone call initiated by plaintiff Matloff to an unnamed Myriad employee, regarding "whether it was permissible for [Yale Laboratory] to perform genetic screening of BRCA genes." (A34.) The district court did not rely upon this alleged exchange of phone calls in its legal analysis, however. (A56-64.) Such a vague and uncorroborated allegation does not constitute the "*affirmative act by the patentee*" required for jurisdiction. *SanDisk*, 480 F.3d at 1381. In *Innovative Therapies*, this Court declined declaratory-judgment jurisdiction based on plaintiff-initiated phone calls. 599 F.3d at 1380-81. If anything, *Innovative Therapies* presented more compelling facts: The record contained detailed allegations regarding plaintiff's repeated calls to the

patentee's employees, during which plaintiff provided a specific description of its product and was informed that the odds were "100% no doubt about it" that the patentee would sue. Yet the district court there, affirmed by this Court, refused to allow such "a '*sub rosa*' effort to create jurisdiction 'by initiating telephone conversations to employees of the patentee who were not in decision-making positions and who were not informed of the real purpose behind the conversations.'" *Id.* at 1381. Were the law otherwise, anyone could manufacture jurisdiction by initiating phone calls or letters to a patentee; the patentee would be left with an untenable choice—grant permission to infringe or face a declaratory-judgment suit. *MedImmune* does not go so far.

2. Ten-Year-Old Litigation And Licensing Activities Cannot Establish Jurisdiction

The court also cited Myriad's prior litigation and licensing activities as support for the finding that Myriad engaged in a "continuing course of conduct over a period of several years." (A61-62.) Its opinion, however, fails to explain how such aged conduct created a "substantially immediate" controversy *with plaintiffs*. For example, the court referenced two patent cases, one of which was not initiated by Myriad, from over a decade earlier, neither of which named any of the 20 plaintiffs here. (A35-36.) This Court has explained: "[W]hile prior litigation is a circumstance to be considered in assessing the totality of circumstances, the fact that [patentee] had filed infringement suits against other

parties for other products does not, in the absence of any act directed toward [plaintiff], meet the minimum standard discussed in *MedImmune*." *Innovative Therapies*, 599 F.3d at 1382.

Likewise, Myriad's old licensing efforts—referenced only in a single 1998 letter sent to nonparty Dr. Nayfield—occurred nearly a decade before plaintiffs filed their complaint. (A33-34.) The present circumstances thus stand in sharp contrast to cases in which this Court has found declaratory-judgment jurisdiction based on patentees' continued and systematic contacts with an alleged infringer. *See, e.g., Hewlett-Packard*, 587 F.3d at 1364 (patentee "took the affirmative step of twice contacting [plaintiff] directly [and] making an implied assertion of its rights under [the disputed] patent against" plaintiff's products); *Sony Elecs., Inc. v. Guardian Media Techs., Ltd.*, 497 F.3d 1271, 1285 (Fed. Cir. 2007) (patentee "explicitly identified the patents it believes that [plaintiff] infringes, the relevant claims of those patents, and the relevant [] products that it alleges infringe those patents"); *SanDisk*, 480 F.3d at 1382-83, 1384 (patentee "show[ed] a preparedness and willingness to enforce its patent rights" by making "a studied and considered determination of [plaintiff's] infringement," "communicat[ing] that determination to [plaintiff]," and seeking "a right to royalty under its patents based on specific, identified activity").

C. The District Court Improperly Expanded The "All The Circumstances" Test Beyond Article III's Proper Scope

Contrary to the district court's suggestion, the "all the circumstances" test does not confer jurisdiction because a particular case presents a unique "scope and significance of the issues" or "consequences of the remedy sought." (A5.) As this Court has explained, while "we understand [plantiff's] desire to have a definitive answer on whether its products infringe [patentees'] patents, were the district court to reach the merits of this case it would merely be providing an advisory opinion. This is impermissible under Article III." *Prasco*, 537 F.3d at 1341-42. Yet that is exactly what the district court did.

The court's conclusion that "Plaintiffs [are] in precisely the situation that the Declaratory Judgment Act was designed to address" (A64) is refuted by proper application of *MedImmune*'s "all the circumstances" test. The Act was intended to put potential defendants on an even playing field when a patentee sought to "engag[e] in 'extra-judicial patent enforcement' tactics" without suing. *Sony*, 497 F.3d at 1285. Here, Myriad engaged in nothing of the sort: Myriad made no suggestion of infringement *by anyone* for over a decade, and may never sue the plaintiffs at all. Plaintiffs' attempt to invoke Article III jurisdiction frustrates the Declaratory Judgment Act's purpose of providing a party with "an equal start in the race to the court house, *not a headstart*." *Kerotest Mfg. Co. v. C-O-Two Fire*

Equip. Co., 342 U.S. 180, 185 (1952). This reasoning applies with special force here, since there is no objective indication that any "race" will ever be run.

In sum, this is a manufactured controversy with recruited plaintiffs having no dispute with Myriad beyond a desire to assist two public-advocacy groups' effort to use the courts to dictate public policy on DNA patents. That sort of "abstract" dispute is not enough for declaratory-judgment jurisdiction. *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240 (1937).

II. THE COMPOSITION CLAIMS ARE DRAWN TO PATENT-ELIGIBLE SUBJECT MATTER

If the Court reaches the merits, it should reverse and hold that Myriad's challenged composition claims, as well as its method claims (Section III, below), are patent-eligible under 35 U.S.C. § 101.

A. Isolated DNA Molecules Are "Compositions Of Matter" Under § 101

Section 101 of the Patent Act 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 therefor, subject to the conditions and requirements of this title.

"In choosing such expansive terms . . . modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope." *Diamond v. Chakrabarty*, 447 U.S. 303, 308 (1980). This breadth "ensure[s] that 'ingenuity should receive a liberal encouragement.'" *Bilski v. Kappos*, 130 S. Ct.

3218, 3225 (2010) (quoting, through *Chakrabarty*, 5 Writings of Thomas Jefferson 75-76 (H. Washington ed. 1871)).

The term "composition of matter" is to be understood "consistent with common usage." *Bilski*, 130 S. Ct. at 3226 (citing *Chakrabarty*, 447 U.S. at 308, and *Shell Development Co. v. Watson*, 149 F. Supp. 279, 280 (D.D.C. 1957)). In *Shell Development*, cited by the Supreme Court in *Bilski* and quoted with approval in *Chakrabarty*, 447 U.S. at 308, the court held that the term "covers all compositions of two or more substances and includes all composite articles, whether they be results of chemical union, or of mechanical mixture, or whether they be gases, fluids, powders or solids." 149 F. Supp. at 280 (citing Walker on Patents, vol. 1, p. 55, ¶ 14).

Under this definition, the claimed isolated DNA molecules are unquestionably "compositions of matter," or at the very least a "new and useful improvement" upon native DNA. As set forth at p. 6, above, DNA is a composition of "two or more substances": nucleotides linked to each other by a phosphodiester backbone. *See also In re Bergy*, 596 F.2d 952, 987 (C.C.P.A. 1979) ("the biologically pure culture of Bergy . . . clearly fit[s] into the plain terms 'manufacture' and 'composition of matter'"). Indeed, plaintiffs' district-court briefing repeatedly referred to Myriad's "patented composition" (A6911), so there

should be no dispute that isolated DNA molecules fall within the plain language of Section 101.

This is supported by the PTO's 2001 *Utility Examination Guidelines*, issued after an extensive notice-and-comment process: Because Congress "specifically authorized issuing a patent to a person who 'invents or discovers' a new and useful composition of matter, . . . an inventor's discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it. . . . A purified DNA *molecule* isolated from its natural environment . . . is a chemical compound and is patentable if all the statutory requirements are met." 66 Fed. Reg. 1092, 1093, 1094 (emphasis in original).

Other provisions of the Patent Act—notably § 103(b), which presumes that patents are available for "nucleotide sequences"—confirm that Congress thought DNA molecules were patent-eligible. That subsection, added in 1995, requires that patents to "a biotechnological process" must also contain claims to the "composition of matter" that is "used in or made by" that process," either in the same application or in another application with the same effective filing date. 35 U.S.C. § 103(b)(1). In § 103(b)(3)(A)(i), Congress explicitly anticipated that "nucleotide sequences" would be one category of those patentable starting compositions. In *Bilski*, the Supreme Court concluded that § 273(a)(3) and its

definition of "method" as including "a method of doing or conducting business" demonstrated that Congress did not view business methods as categorically ineligible for patenting. 130 S. Ct. at 3228-29. Section 103(b) similarly confirms that Congress viewed "nucleotide sequences" as appropriate subjects for patents; at minimum, it shows that Congress knows how to legislate in this area. *Accord* 141 Cong. Rec. S15220, S15222 (Oct. 17, 1995) (statement of Sen. Hatch) ("[t]he U.S. patent on the starting materials—typically *a new DNA molecule*, a genetically altered host cell, or a vector—can prevent others from using them in the United States in any way").

In short, an isolated BRCA DNA molecule is a "composition of matter" by any understanding, and satisfies § 101.

B. Isolated DNA Molecules Do Not Fall Within The Three Judge-Made Exceptions To § 101

"The [Supreme] Court's precedents provide three specific exceptions to § 101's broad patent-eligibility principles: 'laws of nature, physical phenomena, and abstract ideas.'" *Bilski*, 130 S. Ct. at 3225 (quoting *Chakrabarty*, 447 U.S. at 309). "[T]hese exceptions are not required by the statutory text," but "they are consistent with the notion that a patentable process must be 'new and useful.' . . . The concepts covered by these exceptions are 'part of the storehouse of knowledge of all men . . . free to all men and reserved exclusively to none.'" *Id.* (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)). As *Bilski*

demonstrates, the touchstones of the three non-textual exceptions to patent eligibility are novelty and utility.

Isolated BRCA DNA molecules fall within none of these three judicially created exceptions. They are not "laws of nature" like gravity or $E=mc^2$, nor are they "physical phenomena" like electricity, nor are they abstract ideas like Bilski's method of hedging in a commodity market. Rather, these isolated molecules are new chemical compositions, which were unavailable to the public until these inventors discovered and isolated them. They did not cease to be patent-eligible compositions of matter simply because one characteristic of an isolated DNA molecule is (in the words of the district court) a "physical embodiment of genetic information." (A95.)

C. "Products Of Nature" Are Not Categorically Ineligible For Patenting

The district court believed that "products of nature" are categorically excluded from "patentable subject matter under § 101," and bottomed its rejection of Myriad's isolated DNA molecules upon its application of that supposed exception. (A191-228.) This ruling reflected an erroneous understanding of Supreme Court precedent.

1. "Products Of Nature" Is Not One Of The "Three Specific Exceptions" To § 101

Most simply, "products of nature" are not one of the narrowly cabined "three specific exceptions to § 101's broad patent-eligibility principles" set forth by the Supreme Court. *Bilski*, 130 S. Ct. at 3225. "[T]he Judiciary [does not have] *carte blanche* to impose other limitations that are inconsistent with the text and the statute's purpose and design." *Bilski*, 130 S. Ct. at 3226.

2. A Sweeping "Products Of Nature" Exception Would Not Protect Valuable, New, And Useful Inventions

A sweeping exception to patent eligibility for "products of nature" would improperly exclude from patent protection truly "new" and truly "useful" discoveries, like pharmaceuticals derived from natural sources. Before the inventors performed the work resulting in the isolated BRCA1 and BRCA2 DNA molecules, those molecules did not exist. They were not naturally isolated by the body (A3445; A3486-70; A3494-96; A3707-10; A4291, A4320-22; A4324; A4325; A4410-12; A4414; A4416; A4540; A5301; A5303-04; A5307-08; A5314-15; A5594-95; A6561-65; A6769; A6772-74; A6947; A7286; A7290-93; A7332-35; A7369-71), and were unavailable (until the patented invention) to doctors and scientists for use as primers, probes, and for sequencing, in the detection and treatment of breast and other cancers. (A3473; A3713; A4779-80; A4801-03; A5197-98; A6774; A6827-28; A7370.) As the district court put it, "it is

undisputed that the claimed compositions and methods possess utility." (A195.) Those useful molecules are true inventions, and until their invention they were not available to the public.

The decisions of this Court's predecessor, which remain controlling precedent, compel the same conclusion. *In re Bergy*, 596 F.2d at 976 ("a biologically pure culture produced by great labor in a laboratory and so claimed" is patent-eligible under § 101); *In re Kratz*, 592 F.2d 1169, 1174 (C.C.P.A. 1979) (claim to a "substantially purified" chemical composition naturally occurring in strawberries, 2-methyl-2-pentenoic acid, was patent-eligible "[s]ince the claims do not encompass natural compositions, in that 'substantially pure' 2M2PA does not apparently occur in nature"); *In re Bergstrom*, 427 F.2d 1394, 1401 (C.C.P.A. 1970) ("[W]hat appellants claim—pure PGE_2 and PGE_3 [prostaglandins]—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."). Indeed, the claimed molecules here are not only purified; they are chemically extracted (breaking their covalent bonds) and isolated from the native DNA as well, resulting in a new composition that is structurally and functionally different from native DNA. (A288:19:6-15; A3468-70; A4322; A7370.)

3. Categorical Exclusion Of DNA Molecules From § 101 Would Disrespect Longstanding PTO Practice, A Long And Consistent Line Of Precedent, And Congress's Proper Role In Making Patent Law

The court's ruling that isolated BRCA DNA molecules are patent-ineligible "products of nature" gave insufficient respect to the PTO's contrary determination, as well as to a long line of authority from this Court, its predecessor, and other respected jurists, holding that molecules that are newly isolated from natural products and useful are eligible for patents. Changes to such a longstanding practice should come from Congress, not the courts. This was exactly the modest judicial approach taken in *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred International, Inc.*, 534 U.S. 124 (2001), and echoed most recently in *Bilski.* In *J.E.M. Ag Supply*, the Supreme Court noted that § 101 has "broad scope and applicability," and held that where a particular view of the statute's applicability reflects a longstanding approach of the PTO and the courts, that view should be followed 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. *Accord Bilski*, 130 S. Ct. at 3226, 3228-29.

The district court gave this argument short shrift, misinterpreting Myriad's position as one for "not engag[ing] the substance of Plaintiffs' claims, but . . . instead dismiss[ing] them out of hand." (A196.) Yet it was the district court that refused to "engage the substance" of the PTO's carefully considered *Utility*

Examination Guidelines. These guidelines reflect not only an accurate summary of prior decisional law, but the PTO's consistent practice of allowing patents, under § 101, on isolated DNA molecules: "A patent on a gene covers the isolated and purified gene but does not cover the gene as it occurs in nature." 66 Fed. Reg. at 1093. In *J.E.M. Ag Supply*, the Supreme Court rejected the argument that plants were not within the scope of § 101 by noting "that the PTO has assigned utility patents for plants for at least 16 years and there has been no indication from either Congress or agencies with expertise that such coverage is inconsistent with [federal law]." 534 U.S. at 144-45. The Court further noted that the courts' and the PTO's practices had "led to the issuance of some 1,800 utility patents for plants," and that "the PTO, which administers § 101 as well as the [Plant Patent Act], recognizes and regularly issues utility patents for plants." *Id.* at 145.

The same salient facts are present here, and have engendered even greater public reliance. The PTO has granted utility patents for isolated DNA molecules for over 25 years. (A3467; A3710.) *See, e.g.*, *In re Kubin*, 561 F.3d 1351, 1352 (Fed. Cir. 2009) (the patent claim at issue there, ultimately held obvious under § 103, claimed "a classic biotechnology invention—the isolation and sequencing of a human gene that encodes a particular domain of a protein"); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1329 (Fed. Cir. 2003) (claim drawn to "non-naturally occurring" erythropoietin "avoids claiming specific subject

matter that would be unpatentable under § 101."); *In re Deuel*, 51 F.3d 1552, 1560 (Fed. Cir. 1995) (reversing rejection of claims directed to a "purified and isolated DNA sequence"); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991) (upholding, against validity challenges, composition claims of U.S. Patent 4,703,008, issued on October 27, 1987, and directed to "a purified and isolated DNA sequence"); *see generally Intervet Inc. v. Merial Ltd.*, — F.3d —, —, 2010 WL 3064311, at *10 (Fed. Cir. 2010) (Dyk, J., dissenting in part) ("we have upheld the validity of several gene patents").

Indeed, the *Utility Examination Guidelines* themselves have been in force for almost 10 years, and the longstanding agency practice reflected there has resulted in the issuance of more than 2,645 patents with claims to "isolated DNA," and over 50,000 patents containing claims to a nucleic acid sequence. (*See* n.1, above.) In the face of that consistent agency and court practice, "there has been no indication from either congress or agencies with expertise that such coverage is inconsistent with" the patent statute. To the contrary, as set forth at pp. 32-33, above, § 103(b), which presumes that patents are available for "nucleotide sequences," demonstrates that Congress thought that isolated DNA molecules *are* patent-eligible.

However, by refusing to give any consideration to this historical practice, and the significant industries built up in reliance thereon, the district court

disregarded almost 100 years of precedent, dating back at least to Judge Learned Hand's opinion in *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95 (S.D.N.Y. 1911), *aff'd*, 196 F. 496 (2d Cir. 1912). In the face of this consistent and long-followed view of § 101's scope, plaintiffs' arguments are better addressed to Congress, not to the courts. The Supreme Court has long held that courts "should not read into the patent laws limitations and conditions which the legislature has not expressed." *United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199 (1933).

The district court erroneously dismissed all of this long-standing precedent on the ground that the cases involved questions of "novelty (a modern-day § 102 question), not of patentable subject matter (the § 101 question before this Court)." (A208; *see also* A210-14.)[2] But *Bilski*—decided after the district court's opinion—confirms that the questions of novelty and patent-eligible subject matter are inextricably intertwined, not "distinc[t]," as the district court thought. (A209-12.) As *Bilski* emphasized, the non-textual exceptions to § 101's broad applicability are "consistent with the notion that a patentable process must be 'new and useful.'" 130 S. Ct. at 3225. That principle explains the *Funk Brothers* dictum on which the district court relied—matters covered by the three non-textual

[2] In distinguishing *Parke-Davis*, the district judge also added the remarkable personal anecdote that Judge Learned Hand "once turned his back on the author of this opinion arguing before him on behalf of the Government." (A207 n.46.)

exceptions are not "new," but "'part of the storehouse of knowledge of all men . . . free to all men and reserved exclusively to none.'" *Id.* at 3225 (quoting *Funk Bros.*, 333 U.S. at 130).

4. The District Court Misread Supreme Court Precedent As Supporting A Broad Exclusion Of "Products Of Nature" From § 101

The district court misread *Chakrabarty* and *Funk Brothers* as supporting a broad exclusion of "products of nature" from patent eligibility. The district court erroneously divined from *Chakrabarty* a legal standard requiring a claimed invention to be "markedly different" from a naturally occurring product in order to be patent-eligible (A202-03), and applied that new standard in a sweeping, subjective manner that ignored the numerous, significant differences between isolated BRCA1 and BRCA2 DNA molecules and native DNA.

Chakrabarty did not pronounce or apply a *legal* standard that an invention must be "markedly different" from a naturally occurring substance in order to be patent-eligible. Rather, the Court used "markedly different characteristics" to describe the *factual* "contrast" between the particular bacterium in that case and the mixture of bacteria in *Funk Brothers*: "Here, by contrast, the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility." 447 U.S. at 310. The proper *legal* standard under § 101 appears earlier in the opinion: "a nonnaturally

occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character and use.'" *Id.* at 309-10 (citation omitted). *Accord In re Kratz*, 592 F.2d at 1174 ("the natural composition must inherently contain the [claimed] naturally occurring compound" *and* the claim must be so broad that it "encompass[es] both the known natural composition and the [claimed] naturally occurring compound" before it will be rejected). Under that standard, as shown above at pp. 35-36, and below at pp. 47-48, the isolated DNA molecule is plainly patent-eligible.

The "markedly different characteristics" identified by the Court confirmed that the organism was indeed "new," but the opinion contains no statement or implication that the adverbial phrase "markedly different characteristics" was meant to create a new test for patent eligibility. For one, the phrase appears nowhere else in Supreme Court precedent or elsewhere in *Chakrabarty* itself. For another, it was unnecessary to resolving the case. But most tellingly, the term "markedly" was wholly unexplained in the opinion. Such a loose phrase, especially without further definition, invites litigants and judges to make their own subjective decisions about how different is "markedly" different. "Markedly different" is a fine term for judges to use when describing the particular facts of a particular case, as in *Chakrabarty*, but it surely was not meant as a legal standard to govern all future cases decided under the statute. As shown at pp. 50-52, below,

the district court here freely applied that dubious standard by dismissing all the factual showings about the substantial *differences* between isolated BRCA DNA molecules and native DNA, instead concluding as a matter of law that the isolated molecules were not "markedly different."

The court misread *Funk Brothers* as standing for the same proposition. (A202-03.) The patent there claimed a product—"[a]n inoculant for leguminous plants" made up of "a plurality of selected . . . strains of different species of bacteria of the genus Rhizobium." 333 U.S. at 128 n.1 (quoting claim 4). The *Funk Brothers* district court thought that "invention was not achieved" by mixing preexisting, commercially available strains of bacteria, and thereby invalidated the claims "because they did not involve invention or discovery of any new or useful art." *Kalo Inoculant Co. v. Funk Bros. Seed Co.*, 161 F.2d 981, 984 (7th Cir. 1947) (summarizing district-court holding). This holding of lack of "invention" did not address patent-eligibility under present § 101; rather, "invention," under the pre-1952 Patent Act, was the equivalent of "nonobviousness" under current § 103. *See, e.g.*, *Dann v. Johnston*, 425 U.S. 219, 225-26 (1976) ("As a judicial test, 'invention,' *i.e.*, an exercise of the inventive faculty, has long been regarded as an absolute prerequisite to patentability. However, it was only in 1952 that Congress, in the interest of 'uniformity and definiteness,' articulated the requirement in a statute, framing it as a requirement of 'nonobviousness.'").

The Seventh Circuit reversed the *Funk Brothers* district court, finding that the claims possessed "inventive conception." 161 F.2d at 988. The Supreme Court then reversed the Seventh Circuit. In an opinion by Justice Douglas, the Court agreed with the district court's conclusion and held that "the product claims do not disclose an invention or discovery within the meaning of the patent statutes." 333 U.S. at 132 (citing *Cuno Eng'g Corp. v. Automatic Devices Corp.*, 314 U.S. 84, 90, 91 (1941), another pre-1952 Act "invention" (obviousness) case). There was no dispute in *Funk Brothers* that the combination of bacteria was a patent-eligible "composition of matter"; instead, the claims were struck down for what is now obviousness under § 103.[3]

The *Funk Brothers* opinion did refer to principles of patent eligibility, but only to explain the reasoning behind its obviousness determination. As Justice Douglas repeatedly explained, the only way the Court could view the inventor's work as passing from the realm of ordinary skill to that of "invention" would have been to view the inhibitive or non-inhibitive properties of the selected bacteria as a patentable invention, since claim 4 was not limited to mixtures of any particular

[3] *See also General Elec. Co. v. De Forest Radio Co.*, 28 F.2d 641, 644 (3d Cir. 1928) (stipulating that the claimed "tungsten wire" was both "new" and "useful," but nonetheless "obvious"); *In re Marden*, 47 F.2d 957, 958 (C.C.P.A. 1931) (ductile uranium and uranium wire were obvious advances over old, known, naturally occurring uranium); *In re Marden*, 47 F.2d 958, 959-60 (C.C.P.A. 1931) (ductile vanadium was an obvious advance over old, known, naturally occurring vanadium).

strains—rather, it claimed broadly all mixtures that had the desired properties: "[T]here is no invention here unless the discovery that certain strains of the several species of these bacteria are non-inhibitive and may thus be safely mixed is invention." 333 U.S. at 132; *see also id*. at 130; *id.* at 133-34 (Frankfurter, J., concurring) (noting that the claims were so broad as to cover any composite culture possessing that natural effect, not just mixtures of the particular strains the inventor had discovered). The combination was thus ruled obvious.

The analogy chosen by Judge Dyk in his separate opinion in *Intervet* illustrates the important differences between *Funk Brothers* and this case. There, Judge Dyk suggested that "[i]t would be difficult to argue, for instance, that one could patent the leaves of a plant merely because the leaves do not occur in nature in their isolated form." — F.3d at —, 2010 WL 3064311, at *11 (Dyk, J., dissenting in part). Those leaves, however, would likely fail under §§ 102 or 103, because the mere plucking of leaves would not invent a new product or constitute a nonobvious "invention." Or it might fail under the logic of *Funk Brothers*, because the plucked leaf would have exactly the same properties as the unplucked leaf—unlike here, where isolated DNA molecules possess significantly different structural and functional characteristics from native DNA. In the words of *Chakrabarty*, the picked leaves would not be "a product of human ingenuity,"

because one of ordinary skill would be able to pluck the leaf off of the previously known plant. *See also Ex parte Latimer*, 1889 Dec. Comm'r Pat. 123, 127 (1889).

Isolated DNA molecules are "products of human ingenuity" and thus fall comfortably within any definition of "invention." (Again, it bears noting that plaintiffs only challenge Myriad's patent claims under § 101, not §§ 102 or 103, and their utility is undisputed.) These inventors' work yielded a new composition of matter with substantial societal benefit, which added to the body of human knowledge. That is enough to demonstrate that these compositions of matter are patent-eligible under § 101.

5. A Categorical "Products Of Nature" Exception Would Be Inconsistent With The Statute And Unworkable

A sweeping exception for "products of nature" would be at odds with cases such as *Chakrabarty* and *J.E.M. Ag Supply*, which upheld patents on living organisms and seeds, respectively. Further, such an exception would be impossible to administer from a judicial perspective—at some level, every composition of matter is a composition of natural materials, and a sweeping "products of nature" exception could potentially make patent-ineligible a wide range of truly new and useful inventions, from the purified extract of a naturally occurring plant (*e.g.*, the cancer-fighting drug Taxol, an extract from the Pacific Yew tree) to the new and useful combination of two or more naturally occurring substances, to the potentially life-saving isolated DNA molecules at issue here. As

the Supreme Court recognized in *Diamond v. Diehr*, "[t]o accept th[is] analysis . . . would, if carried to its extreme, make all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious." 450 U.S. 175, 189 n.12 (1981). *See also Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156, 161-62 (4th Cir. 1958) ("All of the tangible things with which man deals and for which patent protection is granted are products of nature in the sense that nature provides the basic source materials.").

These principles explain the dictum from *Chakrabarty* on which plaintiffs and the district court have relied in claiming a "products of nature" exception to § 101. There, the Court upheld as patent-eligible the applicant's claim to a microorganism, noting that his claim was drawn "to a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character and use.'" 447 U.S. at 309-10 (quoting *Hartranft v. Wiegmann*, 121 U.S. 609, 615 (1887)). Here, the isolated DNA claimed in the Myriad patents is "a nonnaturally occurring manufacture or composition of matter"—*in the form claimed in the patents*, the isolated BRCA1 and BRCA2 molecules are "nonnaturally occurring" (A3445; A3468-70; A3494-96; A3707-10; A4320-22; A4324, A4325, A4410-12; A4416; A4540; A4723; A5301; A5304-05; A5314-15; A5594-95; A6561-65; A6769, A6772-74; A6848; A6947; A7286;

A7369-71), and exist only because of "human ingenuity" in discovering and isolating them. (A3445; A4291; A4320-22; A4414; A5307-08; A6769; A6772-74; A7290-93; A7332-35; A7369-71.) These isolated molecules also have a "distinctive name," and their "character and use" are unlike any found in nature: Their distinctive character allows them to be used in distinctive ways—*e.g.*, as probes and primers, and in the diagnosis and treatment of cancers. (A507-08; A513-20; A712-14; A718-24; A897-98; A899-904; A905-09; A3446-47; A3469-74; A3497-3501; A3708; A4322-24; A4335-43; A4728-29; A4840; A5596; A6561; A6564; A6769-70; A7298; A7373-76.) *See also Dolbear v. Am. Bell Tel. Co.*, 126 U.S. 1, 532 (1888) (While "electricity, one of the forces of nature, is employed" in the telephone, "electricity, left to itself, will not do what is wanted. The art consists in so controlling the force as to make it accomplish the purpose."). These compositions are human inventions that, by their patenting, have added significantly to human knowledge, and "promote[d] the Progress of Science and useful Arts."

These principles also distinguish the other decisions on which the district court relied. In *American Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874), the Court rejected a manufacture claim drawn to cellulose extracted from vegetable substances, because "[p]aper-pulp obtained from various vegetable substances was in common use before the original patent was granted to Watt &

Burgess, and whatever may be said of their process for obtaining it, the product *was in no sense new*." *Id.* at 596. However, "had [it] not been introduced to the public, the Watt & Burgess product *might have been patented as a new manufacture*." *Id.*[4] In *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884), the Court rejected a product patent where the "artificial" alizarine dye, though produced by a different process, was the same substance that had long been isolated from madder root by dyers: "It was an old article. . . . Calling it artificial alizarine *did not make it a new composition of matter*, and patentable as such." *Id.* at 311. In *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1 (1931), the Court concluded that the addition of a small amount of borax to the rind of a fresh orange did not meet the definition of a "manufacture," because the dictionary definition of that term required the creation of "an article for use which possesses *a new or distinctive form*, quality, or property." *Id.* at 11. The orange at issue was not a "manufacture," in the Court's view, because "[t]here is no change in the name, appearance, or general character of the fruit. It remains a fresh orange, fit only for the same beneficial uses as theretofore." *Id.* at 12.

[4] Immediately following *American Wood-Paper*, the circuit courts began upholding the patenting of claims drawn to isolated or purified substances that were not previously known. *See, e.g.*, *Blumenthal v. Burrell*, 53 F. 105, 107 (2d Cir. 1892) (upholding patent for pure chymosin, which is used to curdle milk in cheese manufacturing: "His patent for a product is not for chymosin, but for chymosin separated from pepsin, and uncombined with foreign substances. Such an article was new, and, if actually produced in the condition of purity which the patent describes, was patentable.") (citing *American Wood-Paper*).

As *Bilski* underscored, the patent laws are appropriately concerned that the exclusive rights granted in a U.S. patent are not used to monopolize old, preexisting matter. 130 S. Ct. at 3231. But, an ersatz "products-of-nature" exception to patent eligibility is too blunt a tool for sorting true, patent-eligible invention from old natural phenomena. Other portions of the Patent Act—§ 101's utility requirement, § 102 (anticipation), § 103 (obviousness), and § 112 (written description)—provide finer, more appropriate filters for separating truly inventive additions to human knowledge from unpatentable matter. *Id.* at 3225; *In re Bergy*, 596 F.2d at 960-64; *see generally* Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 Va. L. Rev. 1575, 1644-54 (2003).

In sum: The BRCA1 and BRCA2 molecules were not old matter when they were isolated from native DNA. The work of the inventors in this case constituted invention of a new composition of matter, or certainly an "improvement thereon," which added greatly to human knowledge. Under § 101, these new compositions are patent-eligible.

D. Even If The Proper Legal Standard Required "Markedly Different Characteristics," The District Court Still Erred By Granting Summary Judgment To Plaintiffs

If *Chakrabarty*'s reference to "markedly different characteristics" were meant to provide a legal standard rather than a description of the facts of that case, then the court was still wrong to grant summary judgment to plaintiffs and deny

Myriad's motion. For the same reasons that the claimed isolated DNA molecules are new, useful, and therefore patent-eligible, they also possess "markedly different characteristics" from native genes and are patent-eligible even under this standard. Native DNA is useless for the diagnostic and detection applications for which the isolated molecules may be utilized.

In applying its "markedly different" standard, the district court, citing *Diehr*, 450 U.S. at 188, correctly stated that the claims must be "considered as a whole" (A219), but violated that rule by focusing on only one aspect of isolated DNA—its informational content—while ignoring the manifold differences between isolated and native DNA. *See* pp. 35-36, 47-48, above. In *Diehr*, the Supreme Court *upheld* Diehr's claim to a method for treating rubber, where one of the method steps recited a mathematical formula, because the claim "as a whole" was not directed at the formula itself, but to "a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect." 450 U.S. at 192. Here, similarly, the claims "as a whole" are directed to isolated DNA molecules for identifying and diagnosing predisposition to cancer. The patent laws were surely designed to protect such important functions, which could not be performed by DNA molecules in their native state. *See also Funk Bros.*, 333 U.S. at 130 ("If there is to be invention from such a discovery [of a

previously unknown phenomenon of nature], it must come from the application of the law of nature to a new and useful end.").

Alternatively, if "markedly different characteristics" is understood as a required factual showing, summary judgment should not have been granted to plaintiffs because fact questions would remain regarding whether the characteristics of isolated DNA are "markedly" different from those of native DNA. Myriad provided copious record evidence demonstrating that the isolated BRCA1 and BRCA2 DNA molecules indeed possess "markedly different characteristics" from native DNA. (A3468-70; A3496-3500; A3707-10; A4320-43; A4410-25; A4428; A4723-29; A4840; A6766-71.) Because the meaning of "markedly different" has never been developed in case law, the court improperly viewed itself as free to draw the "legal" conclusion that "none of the structural and functional differences . . . between native BRCA DNA and the isolated BRCA DNA claimed in the patents-in-suit render the claimed DNA 'markedly different.'" (A217-18.) However, ascertaining "differences between the prior art and the claims at issue" is a "basic factual inquir[y]." *Graham v. John Deere & Co.*, 383 U.S. 1, 17 (1966).

III. MYRIAD'S METHOD CLAIMS COVER PATENT-ELIGIBLE SUBJECT MATTER UNDER 35 U.S.C. § 101

Likewise, the method claims are patent-eligible.

A. Methods That Include "Transformations" Of A Human Sample Are Patent-Eligible Subject Matter

In *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) (en banc), this Court held: "A claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." *Id.* at 954. On review, the Supreme Court held that while "the machine-or-transformation test is a useful and important clue . . . for determining whether some claimed inventions are processes under § 101," that test "is not the sole test for deciding whether an invention is a patent-eligible 'process.'" *Bilski*, 130 S. Ct. at 3227. In so holding, the Court expressed concerns that the machine-or-transformation test "may well provide a sufficient basis for evaluating processes similar to those in the Industrial Age," but that, in an "Information Age," limiting the inquiry to the machine-or-transformation test may, particularly in the case of "emerging technologies, . . . pose questions of such intricacy and refinement that they risk obscuring the larger object of securing patents for valuable inventions without transgressing the public domain." *Id.*

The Court specifically mentioned "advanced diagnostic medical techniques" as one of those "emerging technologies." *Id.* at 3227. In *Prometheus Laboratories*

v. Mayo Collaborative Services, 581 F.3d 1336 (Fed. Cir. 2009), *certiorari granted, judgment vacated, and remanded*, 130 S. Ct. 3543 (2010), this Court applied the now non-exclusive "machine-or-transformation" test to medical diagnostic method claims and held that diagnostic methods involving the transformations of human tissue and blood samples are patent-eligible under § 101. There, the Court addressed methods for calibrating the dosage of thiopurine drugs by measuring metabolites in patients with gastrointestinal disorders. 581 F.3d 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 based on those levels. *Id.* at 1339-40.

This Court held those methods patent-eligible 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 also transformative and central to the claimed methods." *Id.* at 1347. The Court held that determining levels of the metabolite in the subject "necessarily involves a transformation, for those levels cannot be determined by mere inspection." *Id.* Quoting Prometheus's expert with approval, this Court said: "[A]t the end of the process, the human blood sample is no longer human blood; the human tissue is no

longer human tissue." *Id.* Importantly, *Prometheus* held that "determining" step transformative, even when derivation from "a sample" was not explicitly recited in the claims.

B. Myriad's Claimed Methods Are Patent-Eligible Because They Require Extracting, Processing, And Analyzing A Human Tissue Or Blood Sample Using "Nucleotide Sequences," Which Are Molecules

The claims involving "analyzing" and "comparing" DNA sequences require extraction and processing of human tissue or blood samples. They are therefore transformative just as the claims involving "determining" were held patent-eligible in the now-vacated *Prometheus* opinion. The district court ruled otherwise, holding that the claims requiring "analyzing" or "comparing" BRCA1 or BRCA2 gene sequences (claim 1 of the '999 patent, claim 1 of the '001, '441, and '857 patents, and claim 2 of the '857 patent) were not patent-eligible because they were "directed only to the abstract mental processes of 'comparing' or 'analyzing' gene sequences." (A234.)

In so ruling, the court erroneously read out critical elements of the claims, elements which show that the methods are "transformative" and thus patent-eligible even under the narrower machine-or-transformation test. Patent-eligibility is not determined based on individual parts of the claims; 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." *Diehr*, 450 U.S. at 188; *see also Parker v. Flook*,

437 U.S. 584, 594 (1978). The district court erred by failing to give weight to the entirety of those method claims.

The district court thought that transformations either were not required by the claims, or constituted "data-gathering steps" not "central to the purpose of the claims." (A238.) To the contrary, Myriad's diagnostic-method claims satisfy § 101 because they involve precisely the same sort of transformation that rendered the *Prometheus* claims patent-eligible.[5] Each requires the physical manipulation—transformation—of tissue or blood "from a human sample" in order to isolate the patient's DNA. That transformation, which is what allows scientists to detect a cancer-indicating mutation, is "central to the purpose of the claims." 581 F.3d at 1347.

Under a proper claim construction, the claims require the transformation of a human sample, and the transformation of the specific BRCA molecules in that sample. Using claim 1 of the '999 patent as an example: First, in order to analyze the *BRCA1* gene, RNA or a BRCA1 cDNA made from mRNA of the human sample, the sample must be transformed. (A388-91; A396-97; A401-02; A407-17; A4291; A4302-04; A4322; A4324; A4340-43.) The *BRCA1* gene and mRNA are within the patient's body and must be isolated from a patient's tissue sample in

[5] Indeed, the facts here show an even stronger claim to patent-eligibility: 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* 581 F.3d at 1339.

order to be sequenced. (A4342.) To this end, the cells of the tissue sample must be broken open, and a sample of the DNA or RNA extracted. (A4342.) Sequencing is accomplished using a diagnostic probe or primer to hybridize to the target DNA or RNA extracted from the sample to inititate a sequencing reaction. (A4324; A4340-42.) 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; a new "hybrid" DNA/DNA or DNA/RNA compound is formed, allowing its sequence to be analyzed. (A388-91; A396-97; A401-02; A407-17; A4304-05; A4322-24; A4340-42.) As a result, the original human sample is no longer the same human sample, and the DNA and mRNA obtained from that sample are no longer the same DNA and mRNA from the original sample. (A413-14; A4305; A4342.)

This is transformation under Supreme Court precedent. *See Gottschalk v. Benson*, 409 U.S. 63, 70 (1972); *Diehr*, 450 U.S. at 192; *Parker*, 437 U.S. at 588 n.9. And this transformation is central to the purpose of the claim—detecting "germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer." (A384:4:36-39.)

The other method claims at issue, properly construed, likewise have transformations at their core. None claims merely a mental process. Each involves a method for detecting, screening, or identifying mutations and alterations

in the *BRCA1/2* genes (*e.g.*, claim 1 of the '001 patent, claim 1 of the '441 patent, and claim 1 of the '857 patent), or for diagnosing a predisposition for breast cancer (*e.g.*, claim 2 of the '857 patent). Simply put, the patents themselves undermine the court's conclusion that the claims are at most limited to using the DNA molecule for "data-gathering steps." (A239.) The transformations are core to the claimed methods.

The court's contrary conclusion (A234) relied upon an erroneous claim construction—it construed the term "sequence" in the method claims as mere information (*i.e.*, letters from the alphabet), rather than as a physical molecule. Specifically, the court construed "analyzing the sequence of a BRCA1 gene or BRCA1 RNA from a human sample" and "analyzing a sequence of a BRCA1 cDNA made from mRNA from a human sample" as merely requiring one to look at a series of letters on a page to see if it contains one of the identified alterations: "Although Myriad asserts that the challenged method claims are directed to comparing DNA molecules rather than DNA sequences, the language of the claims belies such an interpretation." (A234.) In so ruling, the district court erroneously focused on "the language of the claims" (particularly the meaning of "sequence") in a vacuum, divorced from the specification. That was error. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc).

In "the context of the entire patent[s]," including the specification and prosecution history, *id.*, a "sequence" is a molecule, not just information. For one, the claim language specifically calls for "analyzing a sequence . . . from a human sample"—*i.e.*, a substance, not mere "information." Claim 1 of the '999 patent, which is exemplary, 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*." That is a clear reference to the molecule, not just information.

For another, the descriptions of the methods in the specifications make clear that the term "sequence" in the claimed methods refers to the BRCA1 and BRCA2 DNA molecules themselves, not simply a sequence of letters. The '999 patent is exemplary: "the target nucleic acid sequence is amplified with polymerases" (A396:28:44-45); "if the sequence is double-stranded, the sequence will probably need to be denatured." (A396:28:64-65.) Letters of the alphabet cannot be "amplified" or "denatured," but a nucleic acid—an actual, physical molecule—can.

One of ordinary skill would further understand that analyzing a sequence "from a human sample" would require not just a mental process, but at least two transformations—isolating the DNA molecule, and then further transforming those molecules by analysing them. (A3455-56; A3473-79; A4291; A4302-05; A4322-24; A4340-43.) This is confirmed by the prosecution histories. For example, in

allowing claim 1 of the '999 patent, the examiner stated: "The claims are drawn to methods . . . by detecting alterations in the BRCA1 nucleic acids." (A7379-80; A7413-16.) Nucleic acids, of course, are chemical compositions, not letter sequences or mere information. (A4317-18.)

The court's separate holding that claim 20 of the '282 patent is patent-ineligible (A240-42) is even farther afield. The court acknowledged that the claim "arguably recites certain transformative steps, such as the administration of the test compound" (A241), yet concluded that "the essence of the claim, when considered in its entirety, is the act of comparing cell growth rates and concluding that 'a slower growth of said host cell in the presence of said compound is indicative of a cancer therapeutic.'" (A241, quoting A665:156:25-27.) This "essence of the claim" approach was improper, as it gave the court license to entirely ignore the "arguably" transformative steps, which involve administering a substance to a cell in the expectation that the substance will slow its growth. If that is not transformative, nothing ever could be.

While the method claims are transformative, and thus patent-eligible, it bears noting that *Bilski* removed any suggestion that the rigid "machine-or-transformation" test provides the exclusive test for patent-eligibility, particularly as applied to "Information Age" technologies like the advanced diagnostic techniques claimed in the Myriad patents. Thus, even apart from the machine-or-

transformation test, these method claims satisfy § 101: Under the plain statutory language, these methods are "new and useful process[es]" (again, their utility is stipulated), and these extraordinarily useful (indeed, lifesaving) methods are not mere "concepts," or "unpatentable abstract idea[s]," as was the method of hedging ruled ineligible in *Bilski*, 130 S. Ct. at 3231. They are very real ways of diagnosing and treating cancers. They are patent-eligible because patent protection is in accord with the "larger object of securing patents for valuable inventions without transgressing the public domain." *Id.* at 3227. Patents representative of this "Information Age," *id.*, should not be invalidated because they involve the use of information.

IV. THE DISTRICT COURT SHOULD HAVE GRANTED MYRIAD'S SUMMARY-JUDGMENT MOTION

Particularly in view of the unwillingness of the Supreme Court to "impose limitations on the Patent Act that are inconsistent with the Act's text," *Bilski*, 130 S. Ct. at 3231, the challenged patent claims plainly satisfy § 101's "expansive terms" and "wide scope." *Id.* at 3225 (quoting *Chakrabarty*, 447 U.S. at 308). Thus, the district court should have granted Myriad's summary-judgment motion and held that these claims satisfy § 101.

The alternative, constitutional arguments dismissed by the district court are baseless and do not stand in the way of outright reversal. Plaintiffs' claim that the issuance of these patents violated Article I, Section 8, Clause 8 is contrary to that

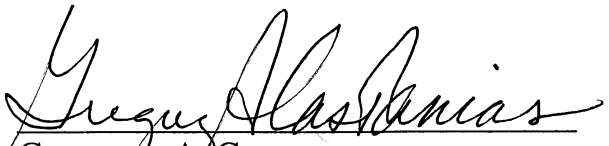
provision, which has no bearing on the patent-eligibility *vel non* of a particular patent claim; rather, it is only a grant of congressional authority to make patent laws. Likewise, the First Amendment claim is frivolous, because these patent claims do not impede speech or thought; they are, as shown above, new and useful compositions and methods critical to the ongoing fight against one of the most insidious diseases known to man.

CONCLUSION

The judgment of the district court should be reversed.

Dated: October 22, 2010

Respectfully submitted,



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ADDENDUM

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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,

Plaintiffs,

09 Civ. 4515

-against-

OPINION

UNITED STATES PATENT AND TRADEMARK OFFICE, ET AL.,

Defendants.

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Sweet, D.J.

In this action the Plaintiffs challenge certain patent claims granted to defendants Myriad Genetics and the Directors[1] of the University of Utah Research Foundation ("UURF") (collectively, "Myriad") by defendant United States Patent and Trademark Office ("USPTO") (collectively, the "Defendants"). The identified patent claims (the "patents-in-suit" or the "claims-in-suit") cover two human genes known as *BRCA1* and *BRCA2* (collectively, "*BRCA1/2*" or the "*BRCA* genes"). Compl. ¶¶ 37, 55-80. The claims-in-suit also cover certain mutations in those genes, the mental act of comparing different forms of the *BRCA* genes, and the correlations between certain genetic mutations and an increased risk of breast and/or ovarian cancer. Id.

The Plaintiffs allege that these patents are unlawful under each of (1) the Patent Act, 35 U.S.C. § 101 (1952), (2) Article I, Section 8, Clause 8 of the United States Constitution, and (3) the First and Fourteenth Amendments because they cover products of nature, laws of

[1] Defendants Lorris Betz, Roger Boyer, Jack Brittan, Arnold B. Combe, Raymond Gesteland, James U. Jenson, John Kendall Morris, Thomas Parks, David W. Pershing, and Michael K. Young. For purposes of this opinion, they will be referred to as the "Directors" or the "UURF Directors."

nature and/or natural phenomena, and abstract ideas or basic human knowledge or thought. Compl. ¶ 102.

The Defendants now move, pursuant to Rules 12(b)(1), (b)(2), and (b)(6), Fed. R. Civ. P., to dismiss Plaintiffs' complaint (the "Complaint") for lack of subject matter jurisdiction, lack of personal jurisdiction, and failure to state a claim.

This action is unique in the identity of the parties, the scope and significance of the issues presented, and the consequences of the remedy sought. The Plaintiffs in this action comprise a broad range of parties, including researchers, genetic counselors, medical and/or advocacy organizations, and women facing the threat of breast cancer or who are in the midst of their struggle with the illness. The challenges to the patents-in-suit raise questions of difficult legal dimensions concerning constitutional protections over the information that serves as our genetic identities and the need to adopt policies that promote scientific innovation in biomedical research. The widespread use of gene sequence information as the foundation for biomedical research means that resolution of these issues will have far-reaching implications, not only

for gene-based health care and the health of millions of women facing the specter of breast cancer, but also for the future course of biomedical research.

Based on the conclusions set forth below, the motions to dismiss are denied.

I. PRIOR PROCEEDINGS

The Complaint in this action was filed on May 12, 2009.

The Plaintiffs moved for summary judgment pursuant to Rule 56, Fed. R. Civ. P., on August 26, 2009.

Defendants' motion to dismiss and Plaintiffs' motion for jurisdictional discovery[2] were heard and marked fully submitted on September 30, 2009, and Plaintiffs'

[2] Defendants' motion to dismiss incorporates, by reference, challenges to the exercise of personal jurisdiction over the Directors raised in Defendants' opposition to Plaintiffs' motion for jurisdictional discovery. Consequently, the arguments concerning personal jurisdiction set forth by the parties in connection with Plaintiffs' motion for jurisdictional discovery will be considered here.

motion for summary judgment was stayed pending resolution of Defendants' motion to dismiss.

II. THE COMPLAINT AND THE AFFIDAVITS

The following allegations, taken from the Complaint and the affidavits submitted by the parties in connection with Defendants' motion to dismiss, are accepted as true for the purpose of resolving the motions to dismiss.

A. The Plaintiffs

Plaintiff the Association for Molecular Pathology ("AMP") is a not-for profit scientific society dedicated to the advancement, practice, and science of clinical molecular laboratory medicine and translational research based on the applications of genomics and proteomics. AMP members participate in basic and translational research aimed at broadening the understanding of gene/protein structure and function, disease processes, and molecular diagnostics, and provide clinical medical services for

patients, including diagnosis of breast cancer. Compl. ¶ 7.

Plaintiff the American College of Medical Genetics ("ACMG") is a non-profit organization of clinical and laboratory geneticists seeking to improve health through the practice of medical genetics. AMCG strives to 1) promote excellence in medical genetics practice and the integration of translational research into practice; 2) promote and provide medical genetics education; 3) increase access to medical genetics services and integrate genetics into patient care; and 4) advocate for and represent providers of medical genetics services and their patients. Compl. ¶ 8.

Plaintiff the American Society for Clinical Pathology ("ASCP") is the largest and oldest organization representing pathologists and laboratory professionals. ASCP members design and interpret the tests that detect disease, predict outcome, and determine the appropriate therapy for the patient. Compl. ¶ 9.

Plaintiff the College of American Pathologists ("CAP") is a national medical society representing board-

certified pathologists and pathologists in training who practice anatomic pathology and laboratory medicine worldwide. The CAP is an advocate of high-quality and cost-effective medical care. Compl. ¶ 10.

The affidavits submitted by the Plaintiffs state that members of AMP, ACMG, ASCP, and CAP are ready, willing, and able to engage in research and clinical practice involving the *BRCA1/2* genes if the patents-in-suit were to be invalidated. For example, Madhuri Hegde, Ph.D. ("Dr. Hegde"), is a member of AMP and ACMG and serves as an Associate Professor in the Department of Human Genetics at Emory University School of Medicine, Adjunct Assistant Professor at the University of Texas M.D. Anderson Cancer Center, and Senior Laboratory Director at the Emory Genetics Laboratory. He currently conducts research on human genes in addition to supervising one of the largest and most technologically advanced clinical laboratories in the country. The laboratory sequences and analyzes approximately sixty genes every day for sequence variants and their clinical significance. Dr. Hegde has personally sequenced the *BRCA1*/2 genes while at the Auckland Hospital in New Zealand, and his lab would begin sequencing an analyzing *BRCA1/2* genes for clinically significant variants

within weeks if the patents-in-suit were invalidated. Hegde Decl. ¶¶ 3-12.[3]

Roger Hubbard, Ph.D. ("Dr. Hubbard"), a member of ASCP, is the President and Chief Executive Officer, Molecular Pathology Laboratory Network, Inc. ("MPLN"), and an Adjunct Associate Professor at the University of Tennessee Medical Center/Knoxville, Department of Pathology. MPLN offers molecular diagnostics and cytogenetic testing services that target hematological malignancies, oncology, and medical diseases. MPLN currently sequences genes and has the personnel, experience and equipment to analyze the *BRCA* genes. They currently receive inquiries every few weeks from a hospital or laboratory asking them to analyze the BRCA genes, but they do not do so as solely because of the patents-in-suit. If the patents-in-suit were to be invalidated, Dr. Hubbard and MPLN would immediately consider doing *BRCA1/2* testing in their laboratory. Hubbard ¶¶ 1-4, 6, 8-9.

Jeffrey Kant, M.D., Ph.D. ("Dr. Kant"), a member of AMP and CAP, is the Director of the Division of

[3] For purposes of this opinion, references to the parties' declarations will be in the format [Declarant name] ¶ [paragraph number].

Molecular Diagnostics in the Department of Pathology at the University of Pittsburgh Medical Center and a Professor Pathology and Human Genetics at the University of Pittsburgh. As part of his responsibilities, he supervises a clinical laboratory that analyzes human genes and is experienced in sequencing and analyzing genes for inherited diseases. His laboratory currently tests nine genes, including five related to hereditary predisposition for cancer. His laboratory was asked in the late 1990s to engage in the sequencing and analysis of *BRCA1/2*, but declined to do so because of the patents-in-suit. If the patents-in-suit were to be invalidated, Dr. Kant would immediately consider doing full gene testing for the *BRCA* genes. Kant ¶¶ 1-2, 4-6.

Plaintiff Haig Kazazian, Jr., M.D. ("Dr. Kazazian"), is the Seymour Gray Professor of Molecular Medicine in Genetics in the Department of Genetics at the University of Pennsylvania School of Medicine. He is the previous chair of the Department. Kazazian ¶ 1, 2. Plaintiff Arupa Ganguly, Ph.D. ("Dr. Ganguly"), is an Associate Professor in the Department of Genetics at the Hospital of the University of Pennsylvania. Ganguly ¶ 1. Drs. Kazazian and Ganguly have served as co-Directors of

the University of Pennsylvania Genetic Diagnostic Laboratory ("GDL") since 1995. Kazazian ¶ 3; Ganguly ¶ 2. The GDL provides state-of-the-art DNA-based diagnostic testing for a variety of genetic conditions and diseases, as well as prenatal and predictive testing and genetic counseling services. Kazazian ¶ 3. Starting in 1996, the GDL was providing *BRCA1* genetic testing services to approximately 500 women per year. Id. ¶ 4. By late 1996, the GDL had designed and provided a similar test for the *BRCA2* gene. Id. Following Dr. Kazazian's and the University of Pennsylvania's receipt of a series of cease-and-desist letters from Myriad in 1998 and 1999, described infra, the GDL ceased its *BRCA1/2* genetic testing services. Id. ¶¶ 5-7; Ganguly ¶¶ 4-10. If the patents-in-suit were to be invalidated, the GDL possesses the technological capability necessary to begin performing *BRCA1/2* testing again within a matter of weeks, and Drs. Ganguly and Kazazian have the desire to consider doing so. Kazazian ¶ 11; Ganguly ¶ 14.

Plaintiff Wendy Chung, M.D., Ph.D. ("Dr. Chung"), is the Herbert Irving Professor of Pediatrics and Medicine in the Division of Molecular Genetics at Columbia University and is the Director of Clinical Genetics and

Director of Clinical Oncogenetics. She is also a member of ACMG. Dr. Chung is a human geneticist whose current research includes research on the *BRCA* genes, for which she has received grants of over $1 million. Dr. Chung is a co-investigator of the Breast Cancer Family Registry, funded by the National Cancer Institute of the National Institute of Health. The goal of the Registry is to collect and study families with multiple cases of breast and/or ovarian cancer and to study genetic and environmental factors influencing cancer susceptibility and clinical outcomes. As part of her research, Dr. Chung's lab sequences human genes, including the *BRCA1/2* genes of research subjects to determine whether there exist alterations in the gene sequences and investigate their clinical significance. Because of the patents-in-suit, Dr. Chung does not tell the research subjects in her studies the results of the analysis of their *BRCA* genes. Dr. Chung's clinical diagnostic laboratory at Columbia University sends samples to Myriad for any analysis of *BRCA1/2* in order to tell the subjects the results and use the results clinically. It does not do *BRCA* testing on its own because of the patents-in-suit. If the patents-in-suit were to be invalidated, Dr. Chung would begin clinical testing of *BRCA1/2* immediately. Her clinical laboratory has the personnel,

expertise to do various forms of *BRCA1/2* sequencing and would be able to offer genetic testing that is more comprehensive than the testing currently offered by Myriad. Chung Decl. ¶ 1, 4, 8-9, 11-14, 16-18.

Plaintiff Harry Ostrer, M.D. ("Dr. Ostrer"), is a Professor of Pediatrics, Pathology and Medicine, Director of the Human Genetics Program in the Department of Pediatrics at the New York University ("NYU") Langone Medical Center, and a member of ACMG. As Director of the Human Genetics Program, Dr. Ostrer helped establish the Molecular Genetics Laboratory ("MGL") at the NYU Langone Medical Center, one of the largest academic genetic testing laboratories in the United States. Dr. Ostrer's work through the MGL has focused on understanding the genetic basis of development and disease, including genetic susceptibility to breast cancer. Dr. Ostrer is actively engaged in identifying genes that convey the risk of breast cancer and may mitigate the effects of mutations in *BRCA1/2*. His laboratory has the ability to evaluate *BRCA1/2* gene sequences, including in custom-designed tests that may be more cost-effective than Myriad's current offerings. However, because of Myriad's assertions of the patents-in-suit, Dr. Ostrer sends all of his patient

samples to Myriad for *BRCA1/2* analysis. If the patents-in-suit were to be invalidated, Dr. Ostrer would immediately begin clinical sequencing of the *BRCA1/2* genes. His laboratory possesses all of the personnel, expertise, and facilities necessary to do various types of sequencing of the *BRCA1/2* genes, including full sequencing, detection of deletions and rearrangements, and searches for large rearrangements that Myriad currently does not offer as a service. If the patents-in-suit were to be invalidated, Dr. Ostrer would also tell patients involved in his current research program the results of their *BRCA1/2*-related genetic screening. Ostrer Decl. ¶¶ 1-5; 8-10.

Plaintiff David Ledbetter, Ph.D. ("Dr. Ledbetter"), is the Robert W. Woodruff Professor of Human Genetics and Director of the Division of Medical Genetics at the Emory University School of Medicine. He is also a diplomat of the American Board of Medical Genetics (Clinical Cytogenetics) and a Founding Fellow of the ACMG. He has previously served as the Director of the Kleberg Cytogenetics Laboratory at Baylor College of Medicine and in the Senior Executive Service of the federal government as Branch Chief of the Diagnostic Development Branch at the National Center for Human Genome Research (now the National

Human Genome Research Institute). He was also the founding Chair of the Department of Human Genetics at the University of Chicago where he held the Marjorie I. and Bernard A. Mitchell Professor of Human Genetics. As Director of the Division of Medical Genetics, Dr. Ledbetter is responsible for very large genetic testing laboratories at the Emory University School of Medicine which provide clinical testing services for patients and families with genetic diseases, including biochemical, cytogenetics, and molecular genetics testing. The genetic testing laboratory utilizes state-of-the-art technology and has the personnel, experience, expertise, and facilities necessary to conduct comprehensive mutation analysis (including full gene sequencing and high-resolution deletion/duplication analysis) of any human gene, including the *BRCA* genes. If the patents-in-suit were to be invalidated, Dr. Ledbetter would begin offering comprehensive *BRCA1/2* testing and would likely have an operational program within one month's time. Ledbetter Decl. ¶¶ 1, 3-4, 8-10, 18.

Plaintiff Stephen T. Warren, Ph.D. ("Dr. Warren"), is the William Patterson Timmie Professor of Human Genetics and Professor of Biochemistry and Professor of Pediatrics at Emory University as well as a past

President of the American Society of Human Genetics. He personally supervises genetic research at Emory University and is also responsible for the Emory Genetics Laboratory. Dr. Warren is ready, willing, and able to being *BRCA1/2* genetic testing if the patents-in-suit were to be invalidated. Compl. ¶ 17.

Plaintiff Ellen Matloff, M.S. ("Ms. Matloff"), is Director of the Yale Cancer Genetic Counseling Program and a Research Scientist in the Department of Genetics at the Yale University School of Medicine. Ms. Matloff advises women on the desirability of obtaining an analysis of their genes to determine if the women have the genetic mutations that correlate with an increased risk of breast and/or ovarian cancer. Ms. Matloff also arranges for such genetic analysis and advises women on the significance of the results. As a result of the patents-in-suit, Ms. Matloff is currently required to utilize Myriad's testing services for analysis of *BRCA1/2*. If the patents-in-suit were to be invalidated, Ms. Matloff would immediately begin sending samples from women who are appropriate candidates for *BRCA* gene analysis to laboratories other than Myriad, such as the laboratories of Drs. Chung, Ledbetter, and Ostrer, for

gene sequencing as well as large rearrangement testing. Matloff Decl. ¶¶ 1, 4, 10-15.

Plaintiff Elsa W. Reich, M.S. ("Ms. Reich"), is a Professor of Pediatrics in the Human Genetics Program at the NYU School of Medicine Department of Pediatrics, where she has served as a genetic counselor since 1974. Ms. Reich provides risk assessment and information to women and men about their risk of having a heritable form of cancer and advises them on the potential utility of obtaining an analysis of their genes to determine if they have genetic mutations that correlate with an increased risk of developing breast cancer, ovarian cancer, or other malignancies. The genes of most interest to be analyzed are the *BRCA1/2* genes. If a patient requests this testing, Ms. Reich sends samples to Myriad and explains the results to the patient. If the patents-in-suit were to be invalidated, Ms. Reich would immediately begin sending samples, including ones previously tested by Myriad, to other laboratories, such as those of Drs. Chung, Ostrer, and Ledbetter for *BRCA1/2* testing. Reich Decl. ¶¶ 1-3, 7-9, 14-15.

Plaintiff Breast Cancer Action ("BCA") is a national organization of approximately 30,000 members based in San Francisco, California that works with researchers to encourage innovative approaches to unresolved issues in breast cancer. Members of Breast Cancer Action have had their *BRCA* genes analyzed or sought analysis to determine if they have genetic mutations that correlate with an increased risk of breast and/or ovarian cancer. In some instances, members have been unable to obtain testing at a laboratory of their choice or choose to be tested at a laboratory that would share data with researchers. In other instances, members have been unable to obtain *BRCA1/2* genetic testing because of the high cost of the test. Members have also received ambiguous genetic test results from Myriad that show they have a genetic variant of uncertain significance, but have been unable to obtaining testing from a second laboratory. BCA staff and volunteers also provide information to members of the public about genetic analysis but have been unable to refer patients to labs other than Myriad. If the patents-in-suit were to be invalidated, BCA and its members would immediately begin utilizing other alternatives to Myriad's *BRCA1/2* testing services in addition to publicizing the existence of such

alternatives, such as the laboratories of Drs. Chung and Ostrer. Compl. ¶ 19; Brenner Decl. ¶¶ 2-3, 7, 9.

Plaintiff Boston Women's Health Book Collective ("BWHBC"), doing business as Our Bodies Ourselves ("OBOS"), is a women's health education, advocacy, and consulting organization that seeks to educate women about health, sexuality, and reproduction. OBOS staff provides information to members of the public about genetic analysis, but does not, as a result of the patents-in-suit, refer their readers to or publicize genetic testing services at, laboratories other than Myriad. BWHC also does not advocate for researchers and clinicians to perform *BRCA* testing as a result of the patents-in-suit. If the patents-in-suit were to be invalidated, BWHBC and OBOS are ready, willing, and able to provide information about testing options offered by labs other than Myriad and would directly benefit from any increased research on *BRCA1/2*. Compl. ¶ 20; Norsigian Decl. ¶¶ 2-3.

Plaintiff Lisbeth Ceriani ("Ms. Ceriani") is a 43-year-old single mother who was diagnosed with cancer in both breasts in May 2008. Ms. Ceriani's oncologist and genetic counselor recommended that she obtain *BRCA1/2*

genetic testing to determine whether she should consider further surgery in order to reduce her risk of ovarian cancer. Because Myriad refused to accept Ms. Ceriani's insurance, however, her blood samples would not be processed unless she paid for the service out-of-pocket. Ms. Ceriani is unable to pay the full cost out-of-pocket and, to date, has not been tested and cannot determine her best medical course of action. Were Ms. Ceriani able to obtain genetic testing from Myriad, she would also want verification of the results of the *BRCA1/2* test before deciding whether to undergo removal of her ovaries. If the patents-in-suit were to be invalidated, Ms. Ceriani would pursue *BRCA1/2* genetic testing through laboratories other than Myriad, such as those of Drs. Chung and Ostrer. She would also seek verification of her *BRCA1/2* test results at a second lab. Ceriani Decl. ¶¶ 2-5, 7-11.

Plaintiff Runi Limary ("Ms. Limary") is a 32-year-old Asian-American woman who was diagnosed with aggressive breast cancer in November 2005. Following her diagnosis, she sought *BRCA1/2* genetic testing on the advice of her doctor. However, she was unable to be tested by Myriad until two years later, when she obtained insurance that provided coverage for the test. Her test results

informed her that she possessed a "genetic variant of uncertain significance" in her *BRCA1* gene frequently identified in women of Asian descent and other racial minorities but whose significance as an indicator of predisposition to cancer was unclear. However, her test did not examine all known types of mutations in her *BRCA* genes, including known large rearrangements. Ms. Limary seeks additional resources for testing and research that could reveal the significance of her genetic variant, including whether it is correlated with an increased risk of breast or ovarian cancer, and could allow her to make an informed decision about her future medical treatment. If the patents-in-suit were to be invalidated, Ms. Limary would immediately pursue additional *BRCA1/2* genetic testing through other laboratories, such as those of Drs. Chung and Ostrer. Such testing would include additional analysis to determine the significance of her *BRCA1* variant of unknown significance. Limary Decl. ¶¶ 2-6, 8-9.

Plaintiff Genae Girard ("Ms. Girard") is a 39-year-old woman who was diagnosed with breast cancer in 2006. Shortly after her diagnosis, she obtained *BRCA1/2* genetic testing from Myriad and tested positive for a deleterious mutation on the *BRCA2* gene. She sought, but

was unable to obtain a second opinion confirming the test result before making any decisions concerning prophylactic bilateral breast surgery and ovarian surgery. IF the patents-in-suit were to be invalidated, Ms. Girard would immediately pursue *BRCA1/2* genetic testing through other laboratories, such as those of Drs. Chung and Ostrer. Girard Decl. ¶¶ 2-5, 10.

Plaintiff Patrice Fortune ("Ms. Fortune") is a 48-year-old woman who was diagnosed with breast cancer in February 2009. Because Ms. Fortune has a family history of breast cancer, her genetic counselor and oncologist advised her to seek *BRCA1/2* genetic testing. However, as a result of incomplete coverage for Myriad's test by Ms. Fortune's health insurance, Ms. Fortune would be required by Myriad to pay the full out-of-pocket cost for her genetic testing. Because Ms. Fortune currently works in unpaid positions while receiving treatment for her cancer, she cannot afford the cost of Myriad's genetic testing. If the patents-in-suit were to be invalidated, Ms. Fortune would immediately seek testing through other laboratories, such as those of Drs. Chung and Ostrer, in addition to seeking a second opinion by another lab before making any major decisions about her treatment. Fortune Decl. ¶¶ 2-5, 8.

Plaintiff Vicky Thomason ("Ms. Thomason") is a 52-year-old woman who was diagnosed with ovarian cancer in 2006. She obtained *BRCA1/2* genetic testing from Myriad in 2007 at the advice of her doctor and genetic counselor and was found to be negative for mutations covered by that test. However, in light of her family history of cancer, her genetic counselor advised her that she was an appropriate candidate for the additional *BRCA1/2* genetic testing offered by Myriad that looks for large genetic rearrangements that are not detected by Myriad's standard genetic test. However, Ms. Thomason's insurance will not cover the entire cost of Myriad's additional test, and Ms. Thomason is unable to afford the extra cost. If the patents-in-suit were to be invalidated, Ms. Thomason would immediately seek *BRCA1/2* testing, including the large rearrangement testing that she currently cannot afford, through other laboratories, such as those of Drs. Chung and Ostrer. Thomason Decl. ¶¶ 2-6, 8, 10.

Plaintiff Kathleen Raker ("Ms. Raker") is a 42-year-old woman whose mother and maternal grandmother died from breast cancer. She obtained *BRCA1/2* genetic testing from Myriad in 2007 and was found to be negative for

mutations covered by that test. However, her genetic counselor advised her that she could still face hereditary risks for breast cancer due to a mutation in her *BRCA* genes that could not be detected by Myriad's standard test, but might be detected by Myriad's test for large rearrangements. Ms. Raker is unable to afford the cost of Myriad's additional testing and, to date, has not received this testing. Without those results, she cannot determine the risk of cancer she or her children face. If the patents-in-suit were to be invalidated, Ms. Raker would immediately pursue *BRCA1/2* testing through other laboratories, such as those of Drs. Chung and Ostrer. Raker Decl. ¶¶ 2-3, 5-7, 8-9, 11-12.

B. The Defendants

The USPTO is an agency of the Commerce Department of the United States. Compl. ¶ 27. The Plaintiffs assert only their claims for constitutional violations against the USPTO.

Myriad is a for-profit corporation located in Salt Lake City, Utah, doing business throughout the United

States. Myriad Genetics is a co-owner of one of the patents-in-suit and holds the exclusive licenses for the remaining ones. It is currently the sole clinical provider of full sequencing of the *BRCA* genes in the United States. Compl. ¶ 28.

The Directors are directors of the UURF, a not-for-profit corporation located in Salt Lake City, Utah, that the Plaintiffs allege is operated, supervised, and/or controlled by the University of Utah. The UURF is an owner or part-owner of all of the patents-in-suit.[4] Compl. ¶ 29.

C. ***BRCA1* and *BRCA2***

The human body is composed of cells. Contained in the nucleus of each cell are the genes that serve as the blueprints used by the body to create the proteins and gene products required for its function. Human genes are

[4] The United States of America, represented by the Secretary of Health and Human Services, is an additional owner of the '001, '441, '897, and '282 patents. Endo Recherche, Inc., of Quebec, Canada, HSC Research and Development Limited Partnership of Toronto, Canada, and the Trustees of the University of Pennsylvania are additional owners of the '492 and '857 patents. Compl. ¶ 30.

composed of unique combinations of four DNA[5] nucleotides (i.e., bases) referred to by the letters A, T, C, and G. The sequence of each gene reflects the string of hundreds or thousands of A, T, C, and G nucleotides that make up the gene. Each gene has a normal, or "wild-type" sequence of nucleotides. Compl. ¶¶ 33, 35, 36.

The sequence of any given human gene varies in nature from one person to another and frequently varies from the "wild-type" sequence. Some of the variations, referred to as "mutations" or "variants," can impact the body's ability to create proteins necessary for sound health. These mutations can include individual nucleotide substitutions (e.g., a T where G would normally appear in a gene), individual nucleotide deletions (e.g. a G being deleted altogether from a particular location in a gene), or much larger variations (e.g. a section of a gene containing numerous nucleotides is deleted or displaced). Mutations can be inherited from an individual's parents as well as be acquired during an individual's lifetime. Id.

[5] DNA, which stands for deoxyribonucleic acid, is a chemical compound made by the body. Compl. ¶ 34.

To find out if the nucleotide sequence of a person's gene differs from the normal, or "wild-type" nucleotide sequence for the gene, a genetic researcher or clinician can sequence the person's gene to determine its nucleotide sequence. Once the sequence of the gene has been obtained, the researcher or clinician can examine the entire sequence to see if the A, T, C, and Gs encode a healthy sequence, a sequence with mutations known to be associated with cancer, or a sequence with one or more variants of uncertain significance. Alternatively, the researcher or clinician can sequence and examine a small section of the gene where a particular mutation or variant is known to occur. The methods by which researchers or clinicians identify the sequence of either the whole gene or any part thereof are not patented in the claims at issue here and are well known in the field. Compl. ¶ 36.

In the 1990s, a number of genetic researchers around the world began looking for a human gene that correlated with an increased risk of breast and/or ovarian cancer. Many of those researchers, including the researchers who ultimately formed Myriad, were funded, at least in part, by the federal government. Researchers, using techniques widely available in the profession,

determined in 1990 that one gene that correlated with an increased risk of breast and/or ovarian cancer was located in the body on chromosome 17. Another research team that was eventually associated with Myriad, using techniques widely available in the profession, sequenced the precise gene, which was named *BRCA1* because of its correlation with breast cancer susceptibility. These researchers subsequently formed Myriad. Myriad sought, and ultimately obtained, several patents on this human *BRCA1* gene. Researchers also began looking for other genes similar to *BRCA1*, and Myriad, using techniques widely available in the profession, subsequently identified *BRCA2* and obtained a series of patents over the human *BRCA2* gene. As a result, Myriad holds, either through ownership or exclusive license, numerous patents relating to the human *BRCA1* and *BRCA2* genes. Compl. ¶¶ 41-45.

The patents for *BRCA1/2* were granted by the USPTO pursuant to a formal written policy that provides that naturally occurring genes can be patented if they are "isolated from their natural state and purified." Compl. ¶ 50. According to USPTO policy, an "isolated and purified" gene includes one that is simply removed from the body and separated from the other contents of the cell. Compl. ¶

51. However, the information dictated by the gene is identical whether it is inside or outside of the body, and an "isolated and purified" human gene performs the same function as the human gene in a person's body. Id. USPTO policy also permits patenting of comparisons or correlations created by nature, but identified by a patent holder. Compl. ¶ 53.

Everyone carries the *BRCA1* and *BRCA2* genes, but the sequence of each person's *BRCA* genes can differ. Compl. ¶ 37. Certain mutations in the genes are correlated with an increased risk of breast and/or ovarian cancer and may also be associated with other cancers, such as prostate and pancreatic cancers. Id. Women with these mutations have an approximately 40-85% lifetime risk of developing breast cancer. Compl. ¶ 39. Approximately 5-10% of women who develop breast cancer are likely to have a mutation in their *BRCA1* or *BRCA2* genes predisposing them to breast cancer and which they inherited from their parents. Compl. ¶ 38.

A *BRCA1/2* genetic test result that is positive for one of these mutations can have a substantial impact on a woman's medical decisions and health. Many women will

obtain earlier and more vigilant screening for breast and/or ovarian cancers, and some women may choose to have prophylactic surgery to remove their breasts and/or ovaries in order to reduce the risk of future cancers. Compl. ¶ 40.

D. Enforcement of the Patents-in-Suit

In the late 1990s, the GDL at the University of Pennsylvania was engaged in providing *BRCA1* genetic testing services to women. Kazazian Decl. ¶ 4. Around this time, Dr. Kazazian, one of the co-Directors of the GDL, met with Dr. Mark Skolnick ("Dr. Skolnick"), the Chief Science Officer at Myriad. During the meeting, Dr. Skolnick informed Dr. Kazazian that Myriad planned to stop the *BRCA1* and *BRCA2* testing being done by the GDL. Kazazian Decl. ¶ 6. Shortly thereafter, on or about May 29, 1998, Dr. Kazazian received a letter from William A. Hockett, Director of Corporate Communications for Myriad which asserted that Myriad is "the patent holder for the BRCA1 gene" covering, among other things "composition of matter covering the BRCA1 gene [and] any fragments of the BRCA1 gene." Ganguly Decl. ¶ 5. The letter further offered the

University a collaboration license of very limited scope. Id.

On or about August 26, 1998, Dr. Kazazian received a cease-and-desist letter from George A. Riley of O'Melveny & Myers, LLP, asserting that the Dr. Kazazian's commercial testing activities infringed the patents-in-suit and demanding that he cease "all infringing testing activity." Ganguly Decl. ¶ 6.

On or about June 10, 1999, the University of Pennsylvania general counsel, Robert Terrell, received a letter from Christopher Wright, Myriad's General Counsel, asserting that Dr. Kazazian's *BRCA* testing activities infringed the patents-in-suit and demanding that the university cease all such commercial genetic testing services. Ganguly Decl. ¶ 7. In a subsequent letter to the University dated September 22, 1999, Myriad reiterated its belief that the genetic testing activities being performed at the GDL infringed the patents-in-suit and repeated its demand that such activities cease. Ganguly Decl. ¶ 9.

As a result of these letters, the University of Pennsylvania advised Drs. Kazazian and Ganguly to discontinue their *BRCA1/2* testing, which they did. Kazazian Decl. ¶ 7; Ganguly Decl. ¶ 10.

During this same period, Dr. Harry Ostrer was sending patient samples to Dr. Kazazian for *BRCA1/2* related genetic screening. Ostrer Decl. ¶ 5. On May 21,1998, Dr. Ostrer also received a letter from William Hocket similar to that sent to Dr. Kazazian. The letter notified Dr. Ostrer of Myriad's patents and offered him a license for *BRCA*1/2-related genetic testing. Ostrer Decl. ¶ 7. Because of the narrow scope of the proposed license, Dr. Ostrer did not enter into a licensing agreement with Myriad. Id.

On or about September 15, 1998, Gregory Critchfield, the President of Myriad, sent a letter to Dr. Susan Nayfield of the National Cancer Institute ("NCI"). Ganguly Decl. Ex. 7. The letter assured Dr. Nayfield that Myriad would not interfere with research activities supported by the NCI in any way, but noted that Myriad had, over the past several months, sent several laboratories engaged in the "commercial testing" of the *BRCA1* gene draft

license agreements defining the conditions under which those laboratories would be allowed to conduct commercial genetic testing. Id.

On or about September 2, 1999, a Myriad representative sent a letter to a Georgetown laboratory demanding that it no longer sent genetic samples to the GDL for testing because such testing infringed the patents-in-suit. Ganguly Decl. ¶ 13. As a result of the letter, Georgetown stopped sending samples to the GDL for *BRCA1/2* screening. Id.

In December 2000, the director of the Yale DNA Diagnostics Laboratory (the "YDL") received a letter from Myriad directing that the YDL cease the *BRCA1/2* genetic testing that was being conducted in the laboratory because the testing allegedly infringed the patents-in-suit. Matloff Decl. ¶ 7. Following receipt of the letter, the laboratory ceased offering such genetic testing. Id.

In 2005, Ms. Matloff telephoned Myriad to inquire whether it was permissible for the YDL to perform genetic screening of the *BRCA* genes that looked for large rearrangement mutations. Matloff Decl. ¶ 8. Several

scientific studies had demonstrated that Myriad's full sequencing test missed large rearrangements that are also correlated with cancer risk. Myriad informed Ms. Matloff that this large rearrangement testing could not be done by the Yale laboratory because it would infringe the patents-in-suit. Id.

Myriad has also engaged in litigation to assert its rights under the patents-in-suit. In 1997 and 1998, Myriad filed suit against Oncormed, a company offering competing *BRCA1/2* genetic testing. See Myriad Genetics v. Oncormed, 2:97-cv-922 (D. Utah); Myriad Genetics v. Oncormed, 2:98-cv-35 (D. Utah). In November 1998, Myriad sued the University of Pennsylvania for infringing its *BRCA* patents. See Myriad Genetics v. Univ. of Pennsylvania, 2:98-cv-829 (D. Utah). Although the lawsuit was dismissed after the University agreed to cease its BRCA testing, the dismissal was "without prejudice." See 2:98-cv-829 (D. Utah) (docket entry 3).

As a result of these efforts, it is widely understood within the research community that Myriad has taken the position that any *BRCA1/2* related activity infringes its patents and that Myriad will assert its

patent rights against parties engaged in such activity. See, Ostrer Decl. ¶¶ 5-6; Chung Decl. ¶ 15; Hubbard Decl. ¶ 7; Kant Decl. ¶ 4; Matloff Decl. ¶¶ 7-9; Reich Decl. ¶ 5; see also Mildred K. Cho, et al., Effects of Patents and License on the Provision of Genetic Testing Services, 5 J. Molecular Diagnostics 3 (2003) (reporting that nine clinical genetic testing laboratories ceased *BRCA1/2* testing as a result of Myriad's patents).

III. THE PARTIES' CONTENTIONS

The Plaintiffs challenge the validity of claims 1, 2, 5, 6, 7, and 20 of patent 5,747,282 (the "'282 patent"); claims 1, 6, and 7 of patent 5,837,492 (the "'492 patent"); claim 1 of patent 5,693,473 (the "'473 patent"); claim 1 of patent 5,709,999 (the "'999 patent"); claim 1 of patent 5,710,001 (the "'001 patent"); claim 1 of patent 5,753,441 (the "'441 patent"); and claims 1 and 2 of patent 6,033,857 (the "'857 patent").

The Plaintiffs divide the claims-in-suit into four categories. The first category of claims, which include claims 1, 2, 5, and 6 of the '282 patent and claim 1 of the '492 patent, cover isolated, non-mutated forms of

BRCA1 and *BRCA2* as well as fragments of *BRCA1* of 15 nucleotides or more. The second category of claims, which includes claim 1 of the '473 patent, claim 7 of the '282 patent and claims 6 and 7 of the '492 patent, cover isolated forms of *BRCA1* and *BRCA2* that contain mutations that may or may not have any correlation with an increased risk of breast and ovarian cancer. The third category of claims, comprised of claim 1 of the '999 patent, covers any method of analyzing an individual's *BRCA1* gene to determine whether the individual's gene contains an inherited mutation. The fourth category of claims, which includes claim 1 of the '001 patent, claim 1 of the '441 patent, and claims 1 and 2 of the '857 patent, covers comparison of a patients' *BRCA1* and *BRCA2* gene sequences with the normal *BRCA1* and *BRCA2* gene sequences to determine whether there are differences that would indicate a genetic predisposition to breast cancer. Claim 20 of the '282 patent, which the Plaintiffs include in this fourth category of claims, covers a method of examining the growth of cells containing a mutated form of *BRCA1* following their treatment with a potential therapeutic compound. None of the claims in the fourth category of claims are limited to "isolated" DNA.

The Plaintiffs allege that because human genes are products of nature, laws of nature, and/or natural phenomena, and abstract ideas or basic human knowledge or thought, the claims-in-suit are invalid for violating Article 1, section 8, clause 8 of the United States Constitution, the First and Fourteenth Amendments to the Constitution, and 35 U.S.C. § 101 of the patent statute. Compl. ¶ 52, 54.

According to the Plaintiffs, these genes exist as naturally occurring products of nature, and Myriad did not invent, create, or in any way construct or engineer the genes. Rather, Myriad located them in nature and described their informational content as it exists and functions in nature. According to the Plaintiffs, Myriad did not invent, create, or in any way construct the differences that may be found when a patient's *BRCA1/2* gene sequences are compared to the normal *BRCA1/2* gene sequences or the correlations between certain mutations in *BRCA1/2* and an increased risk of breast and/or ovarian cancer. Compl. ¶¶ 46, 48.

Myriad currently offers two types of tests: the Comprehensive BRACAnalysis Test and the BRACAnalysis

Rearrangement Test ("BART"). The Comprehensive BRACAnalysis Test costs over $3000; BART costs approximately $600, although Myriad will offer BART testing for free to some women who meet certain criteria. Compl. ¶ 92, 94. Although Myriad's tests examine many mutations known to correlate with a predisposition to breast and/or ovarian cancer, they do not look for all mutations known to correlate with breast and/or ovarian cancer. Ledbetter Decl. ¶ 16. The Plaintiffs allege that Myriad's patents on *BRCA1/2* have allowed it to bar any other entity from conducting genetic testing on the *BRCA* genes despite the ability of other clinical laboratories, such as the laboratories of Drs. Chung, Ostrer, and Ledbetter, to do so and the desire of patients, such as Ms. Limary and Ms. Girard, to seek such alternative testing. Compl. ¶ 84. As a result, any person seeking testing of their *BRCA1/2* genes is required to utilize Myriad's tests. Compl. ¶ 90.

According to the Plaintiffs, Myriad also has the ability to prevent researchers from conducing any research examining the *BRCA* genes. Compl. ¶ 96. Myriad has permitted some scientists to conduct pure research on *BRCA1/2*, but the Plaintiffs allege that Myriad has no official policy permitting such research and has not

publicized its willingness to allow such research. Compl. ¶ 97. The Plaintiffs allege that the patents on the *BRCA* gene sequences deny researchers access to genomic information which, unlike other patented inventions, cannot be "invented around" or built upon to foster scientific progress. Commpl. ¶ 88. As a result, researchers are chilled from engaging in research on *BRCA1/2* as well as research on other genes that may interact with *BRCA1/2*. Compl. ¶ 98. Included in such activities would be the development of new tests for breast and/or ovarian cancer that might be linked to *BRCA1/2*. The Plaintiffs assert that this infringes on quality medical practice and compromises quality assurance and improvement of testing. Compl. ¶ 101; Ledbetter Decl. ¶ 23.

The Defendants have moved to dismiss the claims against them pursuant to Fed. R. Civ. P. 12(b)(1) on the grounds that the Court lacks subject matter jurisdiction over Plaintiffs' claims against the USPTO and that the Plaintiffs lack standing to bring this declaratory judgment action. The Defendants have also moved to dismiss the claims against the UURF Directors pursuant to Fed. R. Civ. P. 12(b)(2) on the grounds that the Court lacks personal jurisdiction over the Directors. Finally, the Defendants

move to dismiss the constitutional claims pursuant to Fed. R. Civ. P. 12(b)(6) for failure to sufficiently plead a claim.

IV. THERE IS SUBJECT MATTER JURISDICTION OVER THE CLAIMS AGAINST THE USPTO

The USPTO has moved to dismiss the Complaint, pursuant to Rule 12(b)(1), on the grounds that the Court lacks subject matter jurisdiction over the Plaintiffs' claims. A claim is "properly dismissed for lack of subject matter jurisdiction under Rule 12(b)(1) when the district court lacks the statutory or constitutional power to adjudicate it." Makarova v. United States, 201 F.3d 110, 113 (2d Cir. 2000). "When jurisdiction is challenged, the plaintiff 'bears the burden of showing by a preponderance of the evidence that subject matter jurisdiction exists.'" Arar v. Ashcroft, 532 F.3d 157, 168 (2d Cir. 2008) (quoting APWU v. Potter, 343 F.3d 619, 623 (2d Cir. 2003)). "[J]urisdiction must be shown affirmatively, and that showing is not made by drawing from the pleadings inferences favorable to the party asserting it." Shipping Fin. Servs. Corp. v. Drakos, 140 F.3d 129, 131 (2d Cir. 1998) (citation omitted). As such, the Court may rely on

evidence outside the pleadings, including declarations submitted in support of the motion and the records attached to these declarations. See Makarova, 201 F.3d at 113 ("In resolving a motion to dismiss . . . under Rule 12(b)(1), a district court . . . may refer to evidence outside the pleadings.").

The Plaintiffs premise their assertion of subject matter jurisdiction on 28 U.S.C. §§ 1331 & 1338(a).[6] 28 U.S.C. § 1331 vests the district courts with subject matter jurisdiction for "all civil actions arising under the Constitution." The USPTO, however, asserts that the Court lacks subject matter jurisdiction over Plaintiffs' claims against them in light of the "comprehensive scheme Congress established to govern patent grants."[7] Hitachi Metals, Ltd. v. Quigg, 776 F. Supp. 3, 7 (D.D.C. 1991). According to the USPTO, the existence of this comprehensive statutory

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[6] Although Plaintiffs also cite 28 U.S.C. § 2201 as a basis for jurisdiction, "[i]t is settled law that the Declaratory Judgment Act, 28 U.S.C. § 2201 (1994), does not enlarge the jurisdiction of the federal courts . . . and that a declaratory judgment action must therefore have an independent basis for subject matter jurisdiction." Concerned Citizens of Cohocton Valley, Inc. v. N.Y. State Dep't of Envtl. Conservation, 127 F.3d 201, 206 (2d Cir. 1997) (citing Skelly Oil Co. v. Phillips Petroleum Co., 339 U.S. 667, 671 (1950)).

[7] The USPTO also argues that sovereign immunity serves to bar this action. Courts, however, routinely entertain actions against federal agencies alleging violations of the Constitution. See, e.g., Reno v. ACLU, 521 U.S. 844 (1997). As Plaintiffs note in their Complaint, the only claims raised against the USPTO are of a constitutional nature. Compl. ¶ 27.

scheme reflects Congress' intention to preclude judicial challenges of the type brought by the Plaintiffs.

The cases cited by the USPTO, however, involved claims alleging statutory violations for which the Patent Act provided a remedy. The issue before the courts, then, was whether the existence of a comprehensive statutory scheme that addressed the alleged statutory violation precluded the right to also seek judicial review of the alleged violations. See Syntex (U.S.A.), Inc. v. U.S. Patent & Trademark Office, 883 F.2d 1570, 1572-74 (Fed. Cir. 1989) (concluding remedy provided by patent statute for alleged statutory violations precluded private judicial remedy for those claims);[8] Hallmark Cards, Inc. v. Lehman, 959 F. Supp. 539, 543 (D.D.C. 1997) (concluding Congress' statutory framework providing means to challenge issuance of Certificates of Correction "implicitly preclude[d]" a right to judicial relief); Hitachi Metals, 776 F. Supp. at 7-8 (finding statutory scheme for administrative and judicial review of patent reissue decisions precluded third-party judicial challenges to reissue process).

[8] The Syntex opinion noted in passing that the plaintiff had pled a violation of the 5th Amendment, but included no discussion concerning the claim in its analysis of subject matter jurisdiction.

In Bush v. Lucas, 462 U.S. 367 (1983), cited by the USPTO, the Supreme Court considered whether an employee subjected to adverse employment action as a result of his criticism of the federal agency employing him could maintain a suit against the agency for violation of his First Amendment rights. Id. at 369-72. Noting that "the ultimate question on the merits . . . may appropriately be characterized as one of 'federal personnel policy,'" id. at 380-81, the Court went on to describe Congress' "repeated consideration of the conflicting interests involved in providing job security, protecting the right to speak freely, and maintaining discipline and efficiency in the federal workforce." Id. at 385. The result, the Court concluded, was an "elaborate, comprehensive scheme" within which "Constitutional challenges to agency action, such as First Amendment claims raised by petitioner, are fully cognizable." Id. As a result, the Court was presented with a question "quite different from the typical remedial issue confronted by a common-law court" since the issue was not whether a judicial remedy should be created where none existed, but rather whether a judicial remedy should be created where a plaintiff was merely dissatisfied by the statutory remedy Congress provided for his alleged wrong. Id. at 388.

While the USPTO notes the existence of a comprehensive scheme to redress violations of the Patent Act, it cites to no comparable statutory scheme providing a remedy for persons who complain about the constitutionality of patents issued by the USPTO and/or the policies and practices of the USPTO. See Block v. Cmty. Nutrition Inst., 467 U.S. 340, 349 (1984) ("[W]hen a statute provides a detailed mechanism for judicial consideration of particular issues at the behest of particular persons, judicial review of those issues at the behest of other persons may be found to be impliedly precluded." (emphasis added)); see generally Marbury v. Madison, 5 U.S. 137 (1803). In such circumstances, the Supreme Court has held that Congress did not intend to preclude enforcement of federal rights through private actions. See Wright v. Roanoke, 479 U.S. 418, 427-28 (1987) (citing absence of statutorily defined private judicial remedy for alleged violation of federal housing law as evidence that Congress did not intend to foreclose private right of action). Indeed, even when Congress has created a statutory remedy, if that remedy is not coextensive with the remedy provided by the Constitution, plaintiffs may still bring a separate action to enforce the Constitution. See Fitzgerald v.

Barnstable Sch. Comm., __ U.S. __ , 129 S. Ct. 788, 796-97 (2009).

The novel circumstances presented by this action against the USPTO, the absence of any remedy provided in the Patent Act, and the important constitutional rights the Plaintiffs seek to vindicate establish subject matter jurisdiction over the Plaintiffs' claim against the USPTO.[9] See, e.g., Reno v. ACLU, 521 U.S. 844 (1997); Mace v. Skinner, 34 F.3d 854, 859-60 (9th Cir. 1994).

V. THERE IS STANDING

A. The Plaintiffs Have Standing to Sue the USPTO for Constitutional Violations

The "judicial power . . defined by Art. III is not an unconditioned authority to determine the constitutionality of legislative or executive acts" but, rather, is limited to the resolution of "cases" and

[9] Although the USPTO suggests that finding subject matter jurisdiction over Plaintiffs' constitutional claims would open the gates to a flood of challenges to patents based on alleged constitutional violations, it is difficult to see how a colorable claim for constitutional violations could arise out of patents for more commonly patented inventions, such as computer chips or carburetors.

"controversies." Valley Forge Christian Coll. v. Ams. United for Separation of Church & State, Inc., 454 U.S. 464, 471 (1982); Lujan v. Defenders of Wildlife, 504 U.S. 555, 559-60 (1992). An "essential and unchanging part" of that limitation is the doctrine of standing. Lujan, 504 U.S. at 560. Indeed, "[t]he Art. III doctrine that requires a litigant to have 'standing' to invoke the power of a federal court is perhaps the most important of these doctrines." Allen v. Wright, 468 U.S. 737, 750 (1984). "At an irreducible minimum, Art. III requires the party who invokes the court's authority to show (1) that he personally has suffered some actual or threatened injury as a result of the putatively illegal conduct of the defendant, that (2) the injury fairly can be traced to the challenged action, and (3) is likely to be redressed by a favorable decision." Valley Forge, 454 U.S. at 472 (internal citations omitted).[10]

Beyond these constitutional requirements, a plaintiff must also satisfy certain prudential standing

[10] The USPTO's challenge to Plaintiffs' standing is intertwined with its challenge to Plaintiffs' subject matter jurisdiction. See Syntex, 882 F.2d at 1573 ("The standing and reviewability inquiries tend to merge. A plaintiff cannot claim standing based on violation of an asserted personal statutorily-created procedural right when Congress intended to grant that plaintiff no such right." (quoting Banzhaf v. Smith, 737 F.2d 1167, 1170 n.* (D.C. Cir. 1984))).

requirements, based on the principle that the judiciary should "avoid deciding questions of broad social import where no individual rights would be vindicated." Phillips Petroleum Co. v. Shutts, 472 U.S. 797, 804 (1985). Prudential standing requires, inter alia, that a party "assert his own legal interests rather than those of third parties," id. at 804, and that a claim must not be a "generalized grievance" shared in by all or a large class of citizens, Warth v. Seldin, 422 U.S. 490, 499 (1975). Prudential standing also addresses whether "the constitutional or statutory provision on which [a plaintiff's] claim rests properly can be understood as granting persons in the plaintiff's position a right to judicial relief." See id. at 499-500. Thus, the litigant's complaint must fall within the "zone of interests to be protected or regulated by the statute or constitutional guarantee in question." Valley Forge, 454 U.S. at 475.

The Defendants allege that it is well established that third parties do not have standing to challenge the USPTO's issuance of a patent. The authorities cited by the USPTO, however, address a party's standing to bring claims for statutory violations and establish only that the

existence of a comprehensive framework within the Patent Act designed to address certain statutory violations may demonstrate Congressional intent to foreclose a judicial remedy for those violations. See Syntex, 882 F.2d at 1572-74; Hitachi Metals, 776 F. Supp. at 7-8; Godtfredsen v. Banner, 503 F. Supp. 642, 644-45 (D.D.C. 1980) (finding statutory remedies for claims of examiner error during interference proceedings precluded judicial review of the proceedings prior to the exhaustion of administrative remedies).[11] As discussed supra in Section IV, these cases do not, as the USPTO suggests, establish that the remedial scheme provided by the Patent Act for statutory violations divests the Plaintiffs of standing to assert constitutional claims for which the Patent Act provides no remedy.

The USPTO also argues that the Plaintiffs do not have standing because the injuries alleged are not "fairly

[11] Animal Legal Defense Fund, 932 F.2d 920 (Fed. Cir. 1991), cited by the USPTO, did not involve allegations of constitutional violations. Moreover, the court's analysis of standing turned on the specific APA provisions involved and was, in substance, a finding that no legally cognizable right was violated. See id. at 929-30. The court's holding also turned on the fact that no patents on animals had been granted and therefore any harm that might occur in the future from such patents was speculative. Id. at 933. The same cannot be said here, where patents over *BRCA1/2* have already been granted and have been used to prevent Plaintiffs from engaging in clinical analysis of the *BRCA1/2* genes, from informing women about testing options other than by Myriad, and from obtaining genetic testing or second opinions. Plaintiffs alleged harms are therefore not the type of speculative harms at issue in Animal Legal Defense Fund.

traceable" to the USPTO's allegedly improper conduct. The "fairly traceable" requirement "examines the causal connection between the assertedly unlawful conduct and the alleged injury." Allen, 468 U.S. at 753 n.19. While the USPTO is correct that Myriad's refusal to license its patent broadly contributes to Plaintiffs' alleged injuries, the patents were issued by the USPTO, in accordance with its policies and practices. It is those policies and practices that the Plaintiffs allege are unconstitutional. The injury alleged is therefore "fairly traceable" to the USPTO.

Finally, the USPTO argues that Plaintiffs' claim against it fails to meet the redressibility requirement, which "examines the causal connection between the alleged injury and the judicial relief requested." Allen, 468 U.S. at 753 n.9. The Plaintiffs ask the Court to enjoin the Defendants from taking any actions to enforce the challenged claims in Myriad's patents. Fairly included in this prayer for relief is a request that the Court declare unconstitutional the USPTO's policies and practices with respect to the challenged claims and similar classes of claims. Granting Plaintiffs' request for relief would serve to render the claims-at-issue definitionally invalid.

As a result, the Plaintiffs would be allowed to engage in conduct currently prohibited by Myriad's patents, and the alleged injuries would be redressed.

B. The Plaintiffs Have Established Standing to Sue Myriad and the Directors

Article III limits federal jurisdiction to disputes involving an actual "case or controversy," and not merely "a difference or dispute of a hypothetical or abstract character." Aetna Life Ins. Co. v. Haworth, 300 U.S. 227, 240 (1937). As the Supreme Court has recently observed, there exists no bright-line rule for determining whether an action satisfies the case or controversy requirement. MedImmune, Inc. v. Genentech, Inc., 549 U.S. 118, 127 (2007). Rather, "[t]he difference between an abstract question and a 'controversy' contemplated by the Declaratory Judgment Act is necessarily one of degree, and it would be difficult, if it would be possible, to fashion a precise test for determining in every case whether there is such a controversy." Md. Cas. Co. v. Pac. Coal & Oil Co., 312 U.S. 270, 273 (1941). Consequently, "the analysis must be calibrated to the particular facts of each case."

Cat Tech LLC v. TubMasters, Inc., 528 F.3d 871, 879 (Fed. Cir. 2008).

"Whether an actual case or controversy exists so that a district court may entertain an action for a declaratory judgment of non-infringement and/or invalidity is governed by Federal Circuit law." MedImmune, Inc. v. Centocor, Inc., 409 F.3d 1376, 1378 (Fed. Cir. 2005) (citations omitted), rev'd on other grounds, 549 U.S. 118 (2007). "The purpose of the Declaratory Judgment Act . . . in patent cases is to provide the allegedly infringing party relief from uncertainty and delay regarding its legal rights." Goodyear Tire & Rubber Co. v. Releasomers, Inc., 824 F.2d 953, 956 (Fed. Cir. 1987). As the Federal Circuit has explained:

> [A] patent owner . . . attempts extra-judicial enforcement with scare-the-customer-and-run tactics that infect the competitive environment of the business community with uncertainty and insecurity . . . . Before the Act, competitors . . . were rendered helpless and immobile so long as the patent owner refused to grasp the nettle and sue. After the Act, those competitors were no longer restricted to an in terrorem choice between the incurrence of a growing potential liability for patent infringement and abandonment of their enterprises; they could clear the air by suing for a judgment that would settle the conflict of interests.

Elecs. for Imaging, Inc. v. Coyle, 394 F.3d 1341, 1346 (Fed. Cir. 2005) (quoting Arrowhead Indus. Water, Inc. v. Ecolochem, Inc., 846 F.2d 731, 735 (Fed. Cir. 1988), overruled on other grounds by MedImmune, 549 U.S. 118).

The Federal Circuit's jurisprudence governing a party's standing to seek a declaratory judgment of patent invalidity was recently revised by the Supreme Court in MedImmune, 549 U.S. 118. There, the Supreme Court considered whether the licensee of a patent had standing to seek a judgment declaring the underlying patent invalid, unenforceable, or not infringed without first breaching or terminating the license agreement. Id. at 137. In concluding that subject matter jurisdiction existed over the plaintiff's declaratory judgment claim, the Supreme Court rejected the Federal Circuit's "reasonable apprehension of suit" test as conflicting with the Court's precedent. Id. at 132 n.11; see also Revolution Eyewear, Inc. v. Aspex Eyewear, Inc., 556 F.3d 1294, 1297 (Fed Cir. 2009) (observing that "the Federal Circuit's requirements, specific to patent cases, that there be both a threat or other action by the patentee sufficient to create a reasonable apprehension of infringement suit, and present activity that could constitute infringement or concrete

steps taken with the intent to conduct such activity, were more rigorous than warranted by the principle and purpose of declaratory actions.").[12] Instead, the Court held that the jurisdictional analysis was properly based on an examination of "all the circumstances." MedImmune, 549 U.S. at 127.

Under the "all the circumstances" test, "the question in each case is whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between the parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." Id. at 127 (quoting Md. Cas. Co., 312 U.S. at 273). This "more lenient legal standard facilitates or enhances the availability of declaratory judgment jurisdiction in patent cases," and, accordingly, there is now an "ease of achieving declaratory judgment jurisdiction." Micron Tech. v. Mosaid Techs. Inc., 518 F.3d 897, 902 (Fed. Cir. 2008). Courts in this district have likewise recognized that since

[12] Under the "reasonable apprehension of suit" test, determining whether a party seeking a declaratory judgment of invalidity possessed the necessary standing required examining (1) "whether the declaratory judgment plaintiff actually produced or was prepared to produce an infringing product;" and (2) "whether conduct by the patentee had created on the part of the declaratory judgment plaintiff a reasonable apprehension that the patentee would file suit if the allegedly infringing activity continued." Sony Elecs. Inc v. Guardian Media Techs., Ltd., 497 F.3d 1271, 1283 (Fed. Cir. 2007).

MedImmune, "the trend is to find an actual controversy, at least where the declaratory judgment plaintiff's product arguably practices a patent and the patentee has given some indication it will enforce its rights." Diamonds.net LLC v. IDEX Online, Ltd., 590 F. Supp. 2d 593, 597-98 (S.D.N.Y. 2008).

Although MedImmune did not define the precise contours of the "all the circumstances" test, guidance is provided by other courts' standing analysis. First, there must be some affirmative act by the defendant relating to enforcement of its patent rights. See, e.g., Prasco, LLC v. Medicis Pharm. Corp., 537 F.3d 1329, 1338-39 (Fed. Cir. 2008); SanDisk Corp. v. STMicroelectronics, Inc., 480 F.3d 1372, 1380-81 (Fed. Cir. 2007) ("[J]urisdiction generally will not arise merely on the basis that a party learns of the existence of a patent owned by another or even perceives such a patent to pose a risk of infringement, without some affirmative act by the patentee."). Second, the declaratory judgment plaintiff must have undertaken "meaningful preparation to conduct potentially infringing activity." Cat Tech LLC, 528 F.3d at 880. This inquiry ensures that a party does not seek a declaratory judgment "merely because it would like an advisory opinion on

whether it would be liable for patent infringement if it were to initiate some merely contemplated activity." Arrowhead, 846 F.2d at 736 (citations omitted). Whether there exists "sufficient 'preparation' is a question of degree to be resolved on a case-by-case basis." Id. (citing Md. Cas. Co., 312 U.S. at 273).

1. Affirmative Acts by the Defendants

The Defendants assert that in order to satisfy the "affirmative act" requirement for declaratory judgment standing, there must be some act by the Defendants directed towards the Plaintiffs. As an initial matter, the Defendants have, in fact, taken specific affirmative acts toward Drs. Kazazian and Ganguly.[13] Moreover, other courts have recognized that "an overt, specific act toward the declaratory judgment plaintiff is not required to demonstrate the existence of an actual controversy." Edmunds Holding Co. v. Autobytel, Inc., 598 F. Supp. 2d 606, 610 (D. Del. 2009).

[13] The Defendants argue that the cease-and-desist letters addressed to the University of Pennsylvania cannot be viewed as affirmative acts directed towards Dr. Ganguly. However, the letters were designed to stop the *BRCA1/2* testing being conducted by the lab jointly overseen by Drs. Kazazian and Ganguly, and Defendants seek to draw an overly formalistic distinction.

The cases cited by the Defendants unquestionably considered the absence of "affirmative acts" directed towards the plaintiff in finding a lack of standing to bring the declaratory judgment action. None of the cases, however, establish a requirement that only acts directed towards the plaintiff could be considered for purposes of the standing analysis or even that there must exist acts specifically directed towards the plaintiffs in order to establish standing. Instead, in most of the cases, the dismissal was based on a lack of any legally cognizable acts by the defendant upon which a declaratory judgment could be established. See, e.g., Prasco, 537 F.3d at 1334, 1340 (observing that the plaintiff's only basis for standing was the plaintiff's allegation that its product did not infringe the defendants' patents); Indigodental GMBH & Co. KG v. Ivoclar Vivadent, Inc., No. 08 Civ. 7657 (RJS), 2008 WL 5262694, at *2 (S.D.N.Y. Dec. 10, 2008) (concluding that "Plaintiff had done little more than become aware of Defendant's patent"); Document Sec. Sys., Inc. v. Adler Techs., Inc., No. 03-CV-6044, 2008 WL 596879, at *10-*11 (W.D.N.Y. Feb. 29. 2008) (finding single page of deposition testimony and an unrelated patent litigation insufficient basis for standing); Broadcom Corp. v. Qualcomm Inc., No. 08cv1829 WQH (LSP), 2009 WL 684835, at

*6 (S.D. Cal. Mar. 12, 2009) (citing, as the basis for its holding, plaintiff's failure "to specify any affirmative act by the defendants" that would support jurisdiction); Impax Labs., Inc v. Medicis Pharm. Corp., No. C-08-0253 MMC, 2008 WL 1767044, at *2 (N.D. Cal. Apr. 16, 2008) (finding plaintiff's filing of an Abbreviated New Drug Application coupled with defendant's public statements of intent to enforce patents insufficient to create an "actual controversy"); The Wooster Brush Co. v. Bercom Int'l, LLC, No. 5:06CV474, 2008 WL 1744782, at *4-*5 (N.D. Ohio Apr. 11, 2008) (finding defendant had never engaged in any activity that would suggest the plaintiffs infringed its patent); Baker Hughes Oilfield Operations, Inc. v. Reedhycalog UK, Ltd., No. 2:05-CV-931, 2008 WL 345849, at *2-*3 (D. Utah Feb. 6, 2008) (dismissing case where letters from defendant did not indicate that it thought plaintiffs were infringing its patents).[14]

[14] In Geospan Corp. v. Pictometry Int'l Corp., 598 F. Supp. 2d 968 (D. Minn. 2008), the court observed that the only instances post-MedImmune in which declaratory judgment jurisdiction had been found to exist were those in which the defendants had engaged in some form of activity against the plaintiff. Id. at 970. It did not, however, state a general rule that actions directed towards the plaintiff were required to establish subject matter jurisdiction over a declaratory judgment action, nor how such a requirement would be consistent with the "all the circumstances" test. To the extent that Geospan may be read to set forth such a requirement concerning a defendant's relevant "affirmative acts," the Court declines to adopt a similar holding.

A requirement that there be a specific, affirmative act directed towards the plaintiff to establish standing to seek a declaratory judgment of patent invalidity would be inconsistent with the Supreme Court's mandate that the Court examine "the facts alleged, under all the circumstances," in assessing the existence of a case or controversy. See MedImmune, 549 U.S. at 127 (quoting Md. Cas. Co., 312 U.S. at 273). As the Federal Circuit has previously stated:

> Article III jurisdiction may be met where the patentee takes a position that puts the declaratory judgment plaintiff in the position of either pursuing arguably illegal behavior or abandoning that which he claims a right to do. We need not define the outer boundaries of declaratory judgment jurisdiction, which will depend on the application of the principle of declaratory judgment jurisdiction to the facts and circumstances of each case.

SanDisk, 480 F.3d at 1381. In light of these principles, an examination of the totality of Myriad's conduct relating to the patents-in-suit is appropriate.

The Defendants raise several challenges to the legal significance of the acts relied on by the Plaintiffs to establish standing. First, the Defendants argue that Myriad's 1998 letter to Dr. Kazazian is too old to serve as

the basis for a case or controversy. The Federal Circuit cases cited by the Defendants in support of their argument, however, pre-date MedImmune and examined the timeliness of letters in the context of the now-defunct "apprehension of suit" test. See Sierra Applied Scis., Inc. v. Advanced Energy Indus., Inc., 363 F.3d 1361, 1374 (Fed. Cir. 2004); Cygnus Therapeutics Sys. v. ALZA Corp., 92 F.3d 1153, 1159 (Fed. Cir. 1996). Given the recent changes to the standing analysis for declaratory judgment claims, those cases no longer serve as controlling authorities. See Benitec Austl., Ltd. v. Nucleonics, Inc., 495 F.3d 1340, 1346 (Fed. Cir. 2007) (questioning holdings in prior cases applying the "reasonable apprehension of suit" test for declaratory judgment jurisdiction in light of MedImmune). Furthermore, the Defendants cite no authority that would preclude the Court from considering the letter as part of "all the circumstances."

While the district court cases cited by the Defendants correctly applied the "all the circumstances" test in dismissing the declaratory judgment actions, they are also distinguishable from the present situation. In Avante, the affirmative act cited by the plaintiff consisted of a single, brief infringement suit lasting a

few weeks. See Avante Int'l Tech., Inc. v. Hart Intercivic, Inc., No 08-832-GPM, 2009 WL 2431993, at *3 (S.D. Ill. July 31, 2009). In Edmunds Holding, the court's dismissal turned on the a finding that "[n]one of the facts adduced by [the plaintiff] established that [the defendant] believe[d] [the plaintiff] to be infringing the '517 patent." Edmunds Holding, 598 F. Supp. 2d at 610. While the Court agrees that an 11-year old letter may not, alone, be sufficient to establish declaratory judgment jurisdiction, those are not the circumstances presented here. Myriad's assertions of its patent rights consist not only of the letter to Dr. Kazazian, but a continuing course of conduct over a period of several years. In addition, Defendants' prior efforts to prevent the Plaintiffs and other similarly situated parties from engaging in *BRCA1/2* testing establish that Plaintiffs' planned activities would be considered infringing by the Defendants. The totality of the circumstances, as alleged by the Plaintiffs, cannot be said to be comparable to the circumstances presented by Avante and Edmunds.

The Defendants also dispute the relevance of prior litigation to the standing analysis. The Defendants argue at the outset that only litigation brought against

the Plaintiffs may be considered by the Court in its jurisdictional analysis; none of the cited cases, however, supports such a rule,[15] and, as discussed supra, this approach is inconsistent with the premise of the "all the circumstances" test. Further, although the lawsuits brought by Myriad against Oncormed and the University of Pennsylvania were dismissed, both serve as evidence of Myriad's willingness to assert its rights granted by the patents-in-suit against others. See Prasco, 537 F.3d at 1341 ("Prior litigious conduct is one circumstance to be considered in assessing whether the totality of the circumstances creates an actual controversy."). Finally, the suit against the University of Pennsylvania was dismissed without prejudice and therefore would not bar a new infringement action by Myriad against the University of Pennsylvania or Drs. Kazazian and Ganguly. Consequently, Myriad's prior litigations involving the patents-in-suit are fairly included in the Court's standing analysis.

[15] Prasco held only that the particular prior lawsuit in question did not establish the existence of a case or controversy between the parties in light of the absence of any other evidence that the defendants had taken a position adverse to the plaintiff's position. See Prasco, 537 F.3d at 1340, 1341 n.9. It did not set forth a general rule concerning the consideration of prior litigation. The court in Edmunds similarly did not prohibit consideration of prior litigation directed to third parties. See Edmunds, 598 F. Supp. 2d at 610 (distinguishing cases cited by the plaintiff in support of its assertion of the existence of case or controversy).

The Plaintiffs cite counsel's August 11, 2009 letter to Defendants' counsel requesting a waiver of claims against intended *BRCA*-related activities and Defendants' subsequent refusal to grant such a waiver as evidence in support of the existence of subject matter jurisdiction. See Ravicher Decl. Ex. 1. However, the presence or absence of jurisdiction must be determined on the facts existing at the time the complaint under consideration was filed. GAF Bldg Materials Corp. v. Elk Corp. of Dallas, 90 F.3d 479, 483 (Fed. Cir. 1996) (citing Arrowhead, 846 F.2d at 734 n.2). Because the filing of the Complaint pre-dated the August 11, 2009 letter, the letter does not factor into the standing analysis.

Taken together, Plaintiffs' allegations establish the existence of sufficient "affirmative acts" by the Defendants for purposes of declaratory judgment jurisdiction. The Defendants have asserted their right to preclude others from engaging in *BRCA1/2* genetic testing through personal communications, cease-and-desist letters, licensing offers, and litigation. The result, as alleged by the Plaintiffs and supported by affidavits, is the widespread understanding that one may engage in *BRCA1/2* testing at the risk of being sued for infringement

liability by Myriad. This places the Plaintiffs in precisely the situation that the Declaratory Judgment Act was designed to address: the Plaintiffs have the ability and desire to engage in *BRCA1/2* testing as well as the belief that such testing is within their rights, but cannot do so without risking infringement liability.[16]

In light of "all the circumstances," there exists a sufficiently "real and immediate injury or threat of future injury that is caused by the defendants" to satisfy the "affirmative act" requirement for a declaratory judgment action. Prasco, 537 F.3d at 1339; see also Adenta GmbH v. OrthoArm, Inc., 501 F.3d 1364, 1370 (Fed. Cir. 2007); Micron Tech., 518 F.3d at 899 (patentee "pursues a systematic licensing and litigation strategy").

2. Meaningful Preparations for Infringing Action

The Defendants also assert that the Plaintiffs have failed to demonstrate the existence of "meaningful preparation" to engage in infringing activity.

[16] Indeed, in light of the widespread knowledge of Myriad's *BRCA1/2* patents and the breadth of the relevant claims, a finding of patent infringement would likely be considered willful and result in treble damages. See 35 U.S.C. § 284.

With respect to the researcher Plaintiffs, the Defendants argue that the Plaintiffs allege only that they are "ready, willing, and able" to infringe and that such expressions of desire and ability are insufficient to establish "meaningful preparations" without reference to specific preparatory activities. However, the "meaningful preparation" inquiry properly focuses on whether the Plaintiffs are meaningfully prepared to engage in the infringing act such that the court's decision would serve as more than an "advisory opinion." See Cat Tech LLC, 528 F.3d at 879; SanDisk, 480 F.3d at 1381 ("[A] party need not risk a suit for infringement by engaging in the identified activity before seeking a declaration of its legal rights."). Where plaintiffs' normal course of business renders them meaningfully prepared to engage in the infringing activity at issue, the lack of some identifiable preparatory effort separate and apart from their normal activities cannot, without more, serve as the basis for finding that there has been no "meaningful preparation" for purposes of declaratory judgment jurisdiction. To hold otherwise would render those most prepared to engage in infringing activity, i.e., those for whom essentially no additional preparation is required to perform the infringing activity, the parties least likely to satisfy

the standing requirements for a declaratory judgment action.

The Defendants also cite Benitec, 495 F.3d 1340, and Mega Lift Sys., LLC v. MGM Well Services, Inc., No. 6:08 CV 420, 2009 WL 1851919 (E.D. Tex. June 29, 2009), in support of their assertion that the researcher Plaintiffs' preparation is insufficient as a matter of law to establish standing. In Benitec, the Federal Circuit found the plaintiff's plans to adapt its human gene silencing technology for use in the animal husbandry and veterinary markets insufficiently immediate for standing purposes. Benitec, 495 F.3d at 1349. The court based its holding on the fact that (1) the plaintiff had merely stated that it "expect[ed]" to begin work "shortly" on adapting its existing gene silencing technology to livestock; (2) the plaintiff had provided insufficient information for the court to assess whether the plaintiff's planned activities would be infringing; and (3) the parties agreed that the plaintiff's planned activities would fall within the safe harbor provision to infringement under 35 U.S.C. § 271(e)(1). See Benitec, 495 F.3d at 1349. In Mega Lift, the district court relied on the fact that the plaintiff had failed to include in its complaint any "allegation

about its readiness to manufacture and sell" the future product that was the subject of the declaratory judgment action. Mega Lift, 2009 WL 1851919, at *4.

The factual circumstances, as set forth in the Plaintiffs' affidavits, render Benitec and Mega Lift distinguishable on their facts and demonstrate sufficient preparation by the researcher Plaintiffs to establish standing. The Plaintiffs have demonstrated that the researcher Plaintiffs are poised to begin *BRCA1/2* testing and that the patents-in-suit present the only obstruction to doing so.[17] See, e.g., Chung Decl. ¶¶ 13, 15-18; Ledbetter Decl. ¶¶ 8-9. All are established human geneticists whose laboratories are routinely engaged in genetic testing and therefore possess the necessary equipment and expertise to immediately begin performing *BRCA1/2* genetic testing. Compl. ¶¶ 11-16; Kazazian Decl. ¶¶ 3-5, 8-11; Ganguly Decl. ¶¶ 3, 14; Chung Decl. ¶¶ 17-18, 21; Ostrer Decl. ¶¶ 8-10, 13; Ledbetter Decl. ¶¶ 18-19 (speaking for himself and Dr. Warren). Moreover, Drs. Kazazian, Ganguly, and Ostrer had previously engaged in

[17] The affidavits also establish that the proposed *BRCA* testing would infringe the claims-in-suit and provide sufficient information to satisfy the Federal Circuit's requirement that "the existence of a case or controversy [] be evaluated on a claim-by-claim basis." Jervis B. Webb Co. v. Southern Sys., Inc., 742 F.2d 1388, 1399 (Fed. Cir. 1984).

BRCA1/2 testing prior to Myriad's assertion of its patent rights against them.[18] Kazazian Decl. ¶¶ 4-10; Ganguly Decl. ¶¶ 3-10. Consequently, the researcher Plaintiffs are meaningfully prepared to begin "BRCA testing to advance research and/or to offer . . . an important service to the public" and "could do so within a matter of weeks." Ganguly Decl. ¶ 14; see also Ledbetter Decl. ¶ 18.[19]

Plaintiffs' affidavits similarly establish that members of the various medical organizations, represented by the organizations under the "doctrine of associational standing," are, like the researcher Plaintiffs, also meaningfully prepared and possess the desire to engage in *BRCA1/2* testing were the patents-in-suit invalidated. See, e.g., Hegde Decl. ¶ 6-12; Hubbard Decl. ¶ 3–9; Kant Decl. ¶ 4-6.

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[18] Defendants argue that Drs. Kazazian and Ganguly state only that they would "consider" engaging in infringing Myriad's patents, and that such speculative intent cannot satisfy the "meaningful preparation" prong. However, the proper focus of this inquiry is whether the plaintiffs are meaningfully prepared, not whether they have made a final, conclusive decision to engage in the infringing activity. See Cat Tech LLC, 528 F.3d at 879 (describing inquiry as requiring "a showing of 'meaningful preparation' for making or using that product").

[19] According to Plaintiffs' counsel, all that would be required to begin genetic testing would be to order the necessary oligonucleotides specific to the *BRCA1/2* genes, a delay of less than a month. Although Defendants raise the possibility that state certification may, in some instances, be required in order for Plaintiffs to engage in clinical *BRCA* testing, they have offered no evidence suggesting that this would constitute a delay of sufficient length to render the dispute of insufficient immediacy to warrant judicial intervention.

The remaining non-researcher Plaintiffs have also established the existence of sufficient "meaningful preparations" to satisfy this prong of the standing inquiry. As an initial matter, the non-researcher Plaintiffs cannot be found to have failed to satisfy the meaningful preparation requirement on the grounds that the researcher Plaintiffs have not yet chosen to engage in infringing *BRCA* testing. Potential contributory infringers, such as the non-researcher Plaintiffs, may very well understand the precise nature of, and be prepared to take advantage of, the services of a potential infringer were the latter not prevented from offering those services by a third party's assertion of its patent rights. Here, it is alleged that the researcher Plaintiffs would offer infringing *BRCA1/2* genetic testing services of the type the non-researcher Plaintiffs would solicit or encourage others to solicit. The Defendants cite no authorities establishing that only potential direct, and not potential contributory infringers can have standing in a declaratory judgment action.[20]

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[20] Animal Legal Defense Fund, cited by Defendants, addressed the standing of a third party to challenge the findings of a PTO Examiner during examination of a patent and has no bearing on standing in the context of a declaratory judgment action. See Animal Legal Defense Fund, 932 F.2d, 920, 930 (Fed. Cir. 1991) ("A third party has no right to intervene in the prosecution of a particular patent application to prevent issuance of an allegedly invalid patent.").

The Plaintiffs have set forth sufficient factual allegations to establish that the non-researcher Plaintiffs are meaningfully prepared to engage in contributory infringement so as to render the controversy between them and the Defendants of "sufficient immediacy and reality." MedImmune, 549 U.S. at 126 (citation omitted); see, e.g., Matloff Decl. ¶¶ 4, 10-15; Reich Decl. ¶¶ 3, 7-11, 14-15; Brenner Decl. ¶¶ 2-3, 9; Ceriani Decl. ¶ 11; Limary Decl. ¶ 9; Girard Decl. ¶ 10; Fortune Decl. ¶ 8; Thomason Decl. ¶ 10. Indeed, for these Plaintiffs, whose infringing activity would constitute nothing more than taking advantage of alternatives to Myriad's *BRCA1/2* testing or encouraging others to do the same, it is difficult to conceive what more "meaningful preparation" would be required.[21]

The contentions of the Defendants in urging the Plaintiffs' lack of standing to bring a declaratory judgment action present a stark alternative: the deliberate violation of the patents-in-suit in order to challenge their constitutionality and validity. The risks, expense,

[21] Similarly, it is difficult to envision what preparatory activity would be required to infringe the claims-in-suit covering the comparison of *BRCA1/2* gene sequences.

and uncertainty of that protracted litigation process to compel the Defendants to defend the patents-in-suit are well known and recognized. Under the unique circumstances of this action and the pendency of the Plaintiffs' motion for summary judgment, the declaratory judgment procedure is preferable. It offers a far speedier and potentially less risky and protracted route to a resolution of the direct and fundamental issues. See Elecs. for Imaging, 394 F.3d at 1346.

For the foregoing reasons, the Plaintiffs possess the necessary standing to bring their claims against the Defendants.

VI. JURISDICTION EXISTS OVER THE DIRECTORS

The Defendants have moved to dismiss the Directors as defendants, pursuant to Fed. R. Civ. P. 12(b)(2), for lack of personal jurisdiction. In considering this challenge to personal jurisdiction, Federal Circuit law applies because the jurisdictional issue is "intimately involved with the substance of the patent laws." Autogenomics, Inc. v. Oxford Gene Tech. Ltd., 566 F.3d 1012, 1016 (Fed. Cir. 2009) (quoting Avocent

Huntsville Corp. v. Aten Int'l Co., 552 F.3d 1324, 1328 (Fed. Cir. 2008).

"In the procedural posture of a motion to dismiss, a district court must accept the uncontroverted allegations in the plaintiff's complaint as true and resolve any factual conflicts in the affidavits in the plaintiff's favor." Elecs. for Imaging, 340 F.3d at 1349 (internal citations omitted). Furthermore, because discovery has not yet been conducted, the Plaintiffs need only make a prima facie showing that the Directors are subject to personal jurisdiction. Avocent, 552 F.3d at 1329; Elecs. for Imaging, 340 F.3d at 1349.

"Determining whether personal jurisdiction exists over an out-of-state defendant involves two inquiries: whether a forum state's long-arm statute permits service of process, and whether the assertion of personal jurisdiction would violate due process." Avocent, 552 F.3d at 1329 (quoting Inamed Corp. v. Kuzmak, 249 F.3d 1356, 1359 (Fed. Cir. 2001)). "[D]ue process requires only that in order to subject a defendant to a judgment in personam, if he be not present within the territory of the forum, he have certain minimum contacts with it such that the maintenance of the

suit does not offend traditional notions of fair play and substantial justice." Int'l Shoe Co. v. Washington, 326 U.S. 310, 316 (1945) (internal quotations omitted).

The Supreme Court has distinguished between "general" and "specific" forms of personal jurisdiction. General jurisdiction requires that a defendant have "continuous and systematic" contacts with the forum state. Helicopteros Nacionales de Columbia, S.A. v. Hall, 466 U.S. 408, 415-16 (1984). Minimum contacts establishing specific jurisdiction exist where "the defendant has purposefully directed his activities at residents of the forum and the litigation results from alleged injuries that arise out of or relate to those activities." Burger King Corp. v. Rudzewicz, 471 U.S. 462, 472-73 (1985) (internal quotes and citations omitted). "Once it has been decided that a defendant purposefully established minimum contacts within the forum State, these contacts may be considered in light of other factors to determine whether the assertion of personal jurisdiction would comport with 'fair play and substantial justice.'" Id. (quoting Int'l Shoe, 326 U.S. at 320). Relevant factors include "'the burden on the defendant,' 'the forum State's interest in adjudicating the dispute,' 'the plaintiff's interest in obtaining convenient

and effective relief,' 'the interstate judicial system's interest in obtaining the most efficient resolution of controversies,' and the 'shared interest of the several States in furthering fundamental substantive social policies.'" Id. at 477 (quoting World-Wide Volkswagen Corp. v. Woodson, 444 U.S. 286, 292 (1980)).

In an action seeking a declaratory judgment of patent invalidity, the Federal Circuit has held that specific jurisdiction exists if "(1) the defendant purposefully directed its activities at residents of the forum, (2) the claim arises out of or relates to those activities, and (3) the assertion of personal jurisdiction is reasonable and fair." Breckenridge Pharm., Inc. v. Metabolite Labs, Inc., 444 F.3d 1356, 1363 (Fed. Cir. 2006). "The first two factors correspond with the 'minimum contacts' prong of the International Shoe analysis, and the third factor corresponds with the 'fair play and substantial justice' prong of the analysis." Inamed, 249 F.3d at 1360. With respect to the last prong, the burden of proof is on the defendant, which must "present a compelling case that the presence of some other considerations would render jurisdiction unreasonable." Burger King, 471 U.S. at 476-77.

The Plaintiffs assert claims against the Directors not in their individual capacities, but in their capacity as state officials, pursuant to Ex parte Young, 209 U.S. 123 (1908). The threshold question is whether, for purposes of the personal jurisdiction analysis, the contacts of the Directors as individuals or as state officials should be examined.

Under Ex parte Young, state officials are treated as state actors for all but Eleventh Amendment sovereign immunity issues, regardless of whether the conduct in question is authorized by state law. See Florida Dep't of State v. Treasure Salvos, Inc., 458 U.S. 670, 697 (1982) (suit for relief against a state officer is not barred by the Eleventh Amendment); Home Tel. & Tel. v. Los Angeles, 227 U.S. 278, 282-85 (1913) (officer sued in his official capacity treated as state actor for 14th Amendment purposes). As a result, an official capacity action is, in all but name, a suit against the governmental entity. Kentucky v. Graham, 473 U.S. 159, 165-66 (1985) ("Official capacity suits . . . 'generally represent only another way of pleading an action against an entity of which an officer is an agent.'" (quoting Monell v. N.Y. City Dep't of Social

Servs., 436 U.S. 658, 690 n.55 (1978))); see also Will v. Mich. Dep't of State Police, 491 U.S. 58, 71 (1989) ("[A] suit against a state official in his or her official capacity is not a suit against the official but rather is a suit against the official's office. As such, it is no different from a suit against the State itself." (internal citations omitted)). Consistent with these principles, official capacity defendants may assert only those defenses available to the governmental entity, rather than those available to the defendant as an individual. Graham, 473 U.S. at 165-66; see also Will, 491 U.S. at 71.[22]

When confronted with the issue of specific personal jurisdiction[23] over a non-forum state official, courts routinely examine the contacts of the state officials in their capacity as representatives of the state, rather than their contacts with the forum in their individual capacity. See, e.g., Stroman Realty, Inc. v. Wercinski, 513 F.3d 476, 484 (5th Cir. 2008) (examining

[22] The treatment of state officials sued in their official capacities by the Federal Rules of Civil Procedure reflects this conception of official capacity suits. Those officials need not be identified by name; they are automatically replaced as parties by their successors; and any relief granted is automatically binding not just on the named individual but on his or her successor. See Fed. R. Civ. P. 17(d), 25(d); Hafer v. Melo, 502 U.S. 21, 25 (1991).

[23] Because specific personal jurisdiction exists over the Directors, Plaintiffs' general personal jurisdiction arguments are not addressed here.

extent of defendant's contact with forum as a representative of the state of Arizona);[24] Grand River Enters. Six Nations, Ltd. v. Pryor, 425 F.3d 158, 166 & n.2 (2d Cir. 2005) (analyzing contacts of state attorneys general with New York as representatives of their states).

The Defendants rely on Great Western United Corp. v. Kidwell, 577 F.2d 1256 (5th Cir. 1978), rev'd on other grounds by Leroy v. Great Western United Corp., 443 U.S. 173 (1979), for their assertion that the jurisdictional analysis properly focuses on the contacts of the Directors as individuals with New York. In Great Western, the Court of Appeals considered whether a court in the Northern District of Texas could assert personal jurisdiction over Idaho officials enforcing an Idaho law that had "substantial consequences" in the forum. Great Western, 557 F.2d at 1265, 1267. The Defendants argue that the Fifth Circuit's opinion established that because a state

[24] Defendants cite language in Stroman which they assert refutes Plaintiffs' position. See Defs.' Mem. of Law in Opp. to Pls.' Mot. to Conduct Jurisdictional Disc. at 4 (citing Stroman, 513 F.3d at 485 ("Even if the State of Arizona itself - as a sovereign state, subject to Eleventh Amendment protections - derived a benefit from any 'effects' in Texas generated by the action of the Commissioner, the benefit does not run to those officials in their individual capacity, stripped of their sovereign immunity cloak.")). The cited language, however, in addition to being dicta, is taken from the discussion of whether a "commercial benefit" accrued to the state. It does not establish that the contacts of the official's department are not imputed to her as an official defendant for purposes of personal jurisdiction.

cannot authorize unconstitutional action, a suit for injunctive relief against a state official in his official capacity cannot be viewed as a suit against the state. Instead, it must be viewed as a suit against the official as a private individual, and the contacts to be examined for purposes of personal jurisdiction must be the contacts of the defendant as an individual, rather than as an extension of the state.

The discussion in Great Western cited by the Defendants, however, did not address the question of personal jurisdiction. Instead, the Fifth Circuit considered only the narrow issue of whether the Idaho official was immune from suit outside of Idaho. See id. at 1265 ("Initially McEldowney contends that his status as a state official means that even though he may be sued under Ex Parte Young . . . he may not be sued outside Idaho without his consent." (citation omitted)).[25] In contrast, when the court turned to the issue of "whether due process permits a court in Texas to exercise jurisdiction over the Idaho official who has enforced the Idaho takeover law

[25] To the extent the Fifth Circuit's discussion may be viewed more broadly as establishing that a state official sued in his official capacity should be treated as an individual defendant, such a holding is at odds with subsequent Supreme Court caselaw. See Hafer, 502 U.S. at 26; Will, 491 U.S. at 71; Graham, 473 U.S. at 165-66.

[against a Texas corporation]," id. at 1266, the Fifth Circuit examined the actions of the defendants as representatives of the state, not as individual defendants. See, e.g., id. at 1267 (evaluating defendants' contacts with the forum by examining activities relating to the enforcement of the Idaho takeover statute). On the basis of those contacts, the court concluded that exercising personal jurisdiction over the Idaho officials pursuant to the Texas long arm statute did not violate considerations of due process. Id. at 1266.

The Defendants also rely on Pennington Seed, Inc. v. Produce Exch. No. 299, 457 F.3d 1334 (Fed. Cir. 2006). There, the Federal Circuit's opinion contained no discussion about the proper analysis for considering a state official's contacts with a forum for personal jurisdiction purposes, instead finding that there were no allegations that the university officials had the necessary contacts with the forum. Id. at 1344. The court's observation concerning the location of the officials' residences was made only in passing to note that even that fact failed to establish purposeful activity directed to the forum. Id.

In light of the foregoing, the question of jurisdiction over the Directors should be resolved based upon the Directors' contacts, as representatives of the state, with New York.

Under New York C.P.L.R. § 302(a)(1), specific jurisdiction exists where a defendant "transacts any business within the state or contracts anywhere to supply goods or services in the state." A party "transacts business" when it "purposefully avails [itself] of the privilege of conducting activities within [New York], thus invoking the benefits and protections of its laws." McKee Elec. Co. v. Rauland-Borg Corp., 20 N.Y.2d 377, 382 (1967) (citation omitted). Here, the Directors have entered into an exclusive license agreement that permits Myriad to market the UURF's products and services in New York and creates continuing obligations for UURF.[26] As a result, the Directors have purposefully availed themselves of the privilege of conducting business in New York. Because the claims in this case are directly related to that license agreement and to Defendants' patent enforcement activities that have occurred in New York, the requisite "articulable nexus" between the cause of action and the business

[26] See infra.

activity is present. See, e.g., Credit Lyonais Sec. (U.S.A.), Inc. v. Alcantara, 183 F.3d 151, 153 (2d Cir. 1999). Consequently, specific personal jurisdiction over the Directors exists under New York's long arm statute. See N.Y. C.P.L.R. § 302(a)(1) (2008).

The exercise of specific personal jurisdiction over the Directors also comports with considerations of due process. The Federal Circuit has established that in the context of an action seeking a declaration of patent invalidity, due process considerations are satisfied when the defendants have (1) engaged in cease-and-desist efforts directed to parties in the forum state or attempted to license the patents at issue in the forum state;[27] and (2) entered into an exclusive license agreement with an entity that markets and sells its products and services in the forum state. See Breckenridge, 444 F.3d at 1366; see also Avocent, 552 F.3d at 1333-35; Akro Corp. v. Luker, 45 F.3d 1541, 1546 (Fed Cir. 1995); Genetic Implant Sys. v. Core-Vent Corp., 123 F.3d 1455, 1458-59 (Fed. Cir. 1997). The

[27] Although Defendants appear to assert that only cease-and-desist letters sent to a party in the forum may be relied upon to establish subject matter jurisdiction, the Federal Circuit has stated that offers to license may also serve as the requisite first point of contact with the forum. See Breckenridge, 444 F.3d at 1366 ("Thus, the crux of the due process inquiry should focus first on whether the defendant has had contacts with parties in the forum state beyond the sending of cease and desist letters or mere attempts to license the patent at issue there.").

critical requirement for purposes of establishing due process is that the license agreement impose continuing obligations on the patentee, such as the right to enforce or defend the patents, so that the patentee maintains an ongoing relationship with the licensee operating within the forum that goes beyond the mere receipt of royalty income. See Breckenridge, 444 F.3d at 1366. The personal jurisdiction analysis of the Directors' contacts with the forum state thus turns on "the defendant's relationship with its exclusive licensee." Id. at 1365; see also Akro, 45 F.3d at 1546-47.

Here, the Defendants have attempted to license the patents-in-suit to Dr. Ostrer, a resident of New York.[28] See Ostrer Decl. ¶ 7 & Ex. 2. They have also caused or participated in direct in-person cease-and-desist efforts that occurred in New York. Kazazian Decl. ¶ 6. In addition, the agreement between Myriad and UURF creates ongoing obligations on the part of the UURF beyond the mere receipt of royalty payments. As set forth in the standard licensing term sheet, UURF's policy is to retain the right to enforce licensed patents and to initiate proceedings

[28] While the offer to license made to Dr. Ostrer was sent on Myriad Genetics' letterhead, Plaintiffs assert that Myriad and UURF acted together in asserting the rights granted by the patents-in-suit. See, e.g., Compl. ¶¶ 29, 49.

regarding them. Ravicher Aff. Ex. 7. Myriad, of course, has a similar ability to take action enforcing the patents as demonstrated by its actions to enforce the patents-in-suit.[29] See supra. Both UURF and Myriad appear to have obligations relating to the enforcement and maintenance of the patents at issue in this lawsuit which establishes that the Directors have purposefully directed their activities at New York as a matter of law.[30] See, e.g., Avocent, 55 F.3d at 1336 ("[W]hen the patentee enters into an exclusive license or other obligation relating to the exploitation of the patent by such licensee or contracting party in the forum . . . the patentee may be said to purposefully avail itself of the forum and to engage in activity that relates to the validity and enforceability of the patent."); Breckenridge, 444 F.3d at 1366; Akro, 45 F.3d at 1546.

In addition, the claims in this suit directly relate to the license agreement between the Defendants and their efforts to enforce the patents. See, e.g., Akro, 45 F.3d at 1548-49 ("[The patentee's] exclusive license agreement with [the plaintiff's] local competitor Pretty

[29] Neither party contests that Myriad purposefully engages in business in New York, where it both solicits and sells a significant volume of its testing services.

[30] In addition, both the Directors and Myriad are represented jointly by counsel, further suggesting the existence of an ongoing relationship between the two entities. See Breckenridge, 444 F.3d at 1367.

Products undoubtedly relates to [the plaintiff's] challenge to the validity and enforceability of the '602 patent."). Finally, the Defendants have not presented other considerations that would render it unfair or unjust for the Court to exercise jurisdiction over them.

Consequently, the Court's exercise of personal jurisdiction over the Directors satisfies the requirements of due process.

VII. THE ALLEGATIONS OF CONSTITUTIONAL VIOLATIONS ARE ADEQUATE

In ruling on a motion to dismiss made pursuant to Rule 12(b)(6), the Court must accept all well-pleaded factual allegations in the complaint as true. Erickson v. Pardus, 551 U.S. 89, 94 (2007) (citing Bell Atl. Corp. v. Twombly, 550 U.S. 544, 555 (2007)). In addition, the Court must "construe[] the complaint liberally" and "draw[] all reasonable inferences in the plaintiff's favor." Chambers v. Time Warner, Inc., 282 F.3d 147, 152 (2d Cir. 2002) (citing Gregory v. Daly, 243 F.3d 687, 691 (2d Cir. 2001)). The question before the court "is not whether a plaintiff will ultimately prevail but whether the claimant is

entitled to offer evidence to support the claims." Villager Pond, Inc. v. Town of Darien, 56 F.3d 375, 378 (2d Cir. 1995) (quoting Scheuer v. Rhodes, 416 U.S. 232, 235-36 (1974)). Consequently, the complaint should not be dismissed on a motion for judgment on the pleadings unless it appears beyond doubt that the plaintiff can prove no set of facts in support of its claims that would entitle it to the relief it seeks. Faconti v. Potter, 242 Fed. App'x 775, 777 (2d Cir. 2007).

The USPTO challenges the sufficiency of Plaintiffs' complaint in light of the Supreme Court's recent holding in Ashcroft v. Iqbal, 129 S.Ct. 1937 (2009). Iqbal set forth "[t]wo working principles" to guide a court's analysis of a complaint's sufficiency. Id. at 1949. "First, the tenet that a court must accept as true all of the allegations contained in a complaint is inapplicable to legal conclusions." Id. "Second, only a complaint that states a plausible claim for relief survives a motion to dismiss." Id. at 1950.

In this case, the Plaintiffs have pled sufficient factual allegations to satisfy the standard set forth in Iqbal. The Complaint alleges the existence of a specific,

written policy for the patenting of genes and the parameters of the policy. Compl. ¶ 50. The policy, contained in the Federal Register, Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001), is alleged by the Plaintiffs to be applied to a series of specific patents and patent claims. Compl. passim. The Plaintiffs describe each application of the policy in considerable detail. See, e.g., Compl. ¶¶ 55-80. Similar allegations and specificity apply to the Plaintiffs' allegations of the USPTO's practices. See, e.g., Compl. ¶¶ 53-54.

The Complaint further alleges that the information encoded in the *BRCA1/2* genetic sequences, rather than being the result of an inventive process, exists in nature. See Compl. ¶¶ 34, 46, 51, 55-60. The Complaint also alleges that the existence of certain mutations in *BRCA1/2* and their correlation with an increased risk of breast and/or ovarian cancer constitutes nothing more than a naturally occurring phenomenon. See Compl. ¶¶ 61-80. Based on these factual allegations, the Plaintiffs assert that the patents-in-suit grant Myriad ownership rights over products of nature, laws of nature, natural phenomena, abstract ideas, and basic human knowledge and thought in violation of the First Amendment's

protections over freedom of thought. Compl. ¶¶ 52, 54. In addition, the Plaintiffs assert that Myriad's ownership of correlations between certain *BRCA1/2* mutations and an increased risk of breast and/or ovarian cancer has inhibited further research on *BRCA1/2* as well as genes that interact with *BRCA1/2*. See, e.g., Compl. ¶¶ 96-98, 101. As a result, the patents-in-suit are alleged to violate Article I, section 8, clause 8 of the Constitution which directs Congress to "promote the Progress of Science and useful Arts . . . ." Compl. ¶¶ 52, 54.

The facts alleged in the Complaint are plausible, specific, and form a sufficient basis for Plaintiff's legal arguments. Consequently, the pleading requirements as set forth in Iqbal are satisfied.

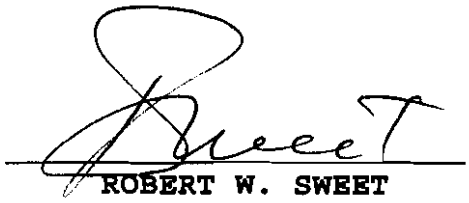
VIII. CONCLUSION

For the reasons stated above, Defendants' motion to dismiss the Complaint is denied.

Defendants' opposition to Plaintiffs' motion for summary judgment will be due December 2, 2009. Plaintiffs' reply will be due on December 9, 2009, and argument will be heard on December 11, 2009, at ten o'clock in the forenoon in Courtroom 18C, unless good cause is shown to alter the date of the submissions.

It is so ordered.

New York, N.Y.
November 1, 2009



ROBERT W. SWEET
U.S.D.J.

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,

Plaintiffs,

09 Civ. 4515

-against-

AMENDED OPINION

UNITED STATES PATENT AND TRADEMARK OFFICE, ET AL.,

Defendants.

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Sweet, D.J.

Plaintiffs Association for Molecular Pathology, et al. (collectively "Plaintiffs") have moved for summary judgment pursuant to Rule 56, Fed. R. Civ. P., to declare invalid fifteen claims (the "claims-in-suit") contained in seven patents (the "patents-in-suit") relating to the human *BRCA1* and *BRCA2* genes (Breast Cancer Susceptibility Genes 1 and 2) (collectively, "*BRCA1/2*") under each of (1) the Patent Act, 35 U.S.C. § 101 (1952), (2) Article I, Section 8, Clause 8 of the United States Constitution, and (3) the First and Fourteenth Amendments of the Constitution because the patent claims cover products of nature, laws of nature and/or natural phenomena, and abstract ideas or basic human knowledge or thought. The defendant United States Patent and Trademark Office ("USPTO") issued the patents-in-suit which are held by defendants Myriad Genetics and the University of Utah Research Foundation ("UURF") (collectively "Myriad" or the "Myriad Defendants"). Myriad has cross-moved under Rule 56, Fed. R. Civ. P., for summary judgment dismissing Plaintiffs' complaint, and the USPTO has cross-moved under Rule 12(c), Fed. R. Civ. P., for judgment on the pleadings. Based upon the findings and conclusions set forth below, the motion of Plaintiffs to

declare the claims-in-suit invalid is granted, the cross-motion of Myriad is denied, and the motion of the USPTO is granted.

As discussed infra in greater detail, the challenged patent claims are directed to (1) isolated DNA containing all or portions of the *BRCA1* and *BRCA2* gene sequence and (2) methods for "comparing" or "analyzing" *BRCA1* and *BRCA2* gene sequences to identify the presence of mutations correlating with a predisposition to breast or ovarian cancer. Plaintiffs' challenge to the validity of these claims, and the arguments presented by the parties and amici, have presented a unique and challenging question:

> Are isolated human genes and the comparison of their sequences patentable?

Two complicated areas of science and law are involved: molecular biology and patent law. The task is to seek the governing principles in each and to determine the essential elements of the claimed biological compositions and processes and their relationship to the laws of nature. The resolution of the issues presented to this Court deeply

concerns breast cancer patients, medical professionals, researchers, caregivers, advocacy groups, existing gene patent holders and their investors, and those seeking to advance public health.

The claims-in-suit directed to "isolated DNA" containing human *BRCA1/2* gene sequences reflect the USPTO's practice of granting patents on DNA sequences so long as those sequences are claimed in the form of "isolated DNA." This practice is premised on the view that DNA should be treated no differently from any other chemical compound, and that its purification from the body, using well-known techniques, renders it patentable by transforming it into something distinctly different in character. Many, however, including scientists in the fields of molecular biology and genomics, have considered this practice a "lawyer's trick"[1] that circumvents the prohibitions on the direct patenting of the DNA in our bodies but which, in practice, reaches the same result. The resolution of these motions is based upon long recognized principles of molecular biology and genetics: DNA represents the physical embodiment of biological information, distinct in its

[1] See, e.g., John M. Conley & Roberte Markowski, Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents, 85 J. Pat. & Trademark Off. Soc'y 301, 305 (2003).

essential characteristics from any other chemical found in nature. It is concluded that DNA's existence in an "isolated" form alters neither this fundamental quality of DNA as it exists in the body nor the information it encodes. Therefore, the patents at issue directed to "isolated DNA" containing sequences found in nature are unsustainable as a matter of law and are deemed unpatentable subject matter under 35 U.S.C. § 101.

Similarly, because the claimed comparisons of DNA sequences are abstract mental processes, they also constitute unpatentable subject matter under § 101.

The facts relating to molecular biology are fundamental to the patents at issue and to the conclusions reached. Consequently, in the findings which follow, the discussion of molecular biology precedes the facts concerning the development, application, and description of the patents. Following those facts are the conclusions which compel the partial grant of summary judgment to the Plaintiffs, the denial of Myriad's cross-motion, and the grant of the USPTO's motion for judgment on the pleadings.

I. PRIOR PROCEEDINGS

The complaint in this action was filed on May 12, 2009, alleging violations of 35 U.S.C. § 101; Article I, Section 8, Clause 8 of the United States Constitution; and the First and Fourteenth Amendments to the Constitution.

Defendants moved to dismiss the complaint which motion was denied by the opinion of November 1, 2009. See Assoc. for Molecular Pathology v. U.S. Patent and Trademark Office, 669 F. Supp. 2d 365 (S.D.N.Y. 2009). Plaintiffs were found to have the necessary standing to assert their declaratory judgment claims against the Myriad Defendants and the USPTO, and specific personal jurisdiction was found to exist over the Directors of the UURF by virtue of acts performed in their official capacity that were directed to the state of New York. It was also determined that this Court possessed the necessary subject matter jurisdiction to hear Plaintiffs' constitutional claims against the USPTO and that the complaint satisfied the pleading requirements set forth in Ashcroft v. Iqbal, 129 S. Ct. 1937 (2009).

Plaintiffs' motion for summary judgment and the cross-motions for summary judgment and judgment on the pleadings were heard and marked fully submitted on February 4, 2010.

II. THE PARTIES AND AMICI

Plaintiff Association for Molecular Pathology ("AMP") is a not-for-profit scientific society dedicated to the advancement, practice, and science of clinical molecular laboratory medicine and translational research based on the applications of genomics and proteomics. AMP members participate in basic and translational research aimed at broadening the understanding of gene/protein structure and function, disease processes, and molecular diagnostics, and provide clinical medical services for patients, including diagnosis of breast cancer. Sobel Decl. ¶¶ 2, 4-5.[2]

Plaintiff the American College of Medical Genetics ("ACMG") is a private, non-profit voluntary organization of clinical and laboratory geneticists. The

[2] For purposes of this opinion, references to the parties' declarations will be in the format [Declarant name] Decl. ¶ [paragraph number].

Fellows of the ACMG are doctoral level medical geneticists and other physicians involved in the practice of medical genetics. With more than 1300 members, the ACMG's mission is to improve health through the practice of medical genetics. In order to fulfill this mission, the ACMG strives to define and promote excellence in medical genetics practice and the integration of translational research into practice; promote and provide medical genetics education; increase access to medical genetics services and integrate genetics into patient care; and advocate for and represent providers of medical genetics services and their patients. Watson Decl. ¶¶ 2, 4-5.

Founded in 1922, plaintiff the American Society for Clinical Pathology ("ASCP") is the largest and oldest organization representing the medical specialty of pathology and laboratory medicine. ASCP is a not-for-profit entity organized for scientific and educational purposes and dedicated to patient safety, public health, and the practice of pathology and laboratory medicine and has 130,000 members working as pathologists and laboratory professionals. ASCP members design and interpret the tests that detect disease, predict outcome, and determine the appropriate therapy for the patient. The ASCP is

recognized for its excellence in continuing professional education, certification of laboratory professionals, and advocacy. Ball Decl. ¶¶ 2, 5.

Plaintiff the College of American Pathologists ("CAP") is a national medical society representing more than 17,000 pathologists who practice anatomic pathology and laboratory medicine in laboratories worldwide. The College's Commission on Laboratory Accreditation is responsible for accrediting more than 6,000 laboratories domestically and abroad, and approximately 23,000 laboratories are enrolled in CAP's proficiency testing programs. It is the world's largest association composed exclusively of board-certified pathologists and pathologists in training worldwide and is widely considered the leader in laboratory quality assurance. CAP is an advocate for high quality and cost-effective medical care. Scott Decl. ¶¶ 2, 4-5.

Plaintiff Haig Kazazian, M.D. ("Dr. Kazazian"), is the Seymour Gray Professor of Molecular Medicine in Genetics in the Department of Genetics at the University of Pennsylvania School of Medicine. He is a human genetics researcher and the previous chair of the Department. Dr.

Kazazian and plaintiff Arupa Ganguly, Ph.D. ("Dr. Ganguly"), designed tests to screen the *BRCA1* and *BRCA2* genes in their lab and provided screening to approximately 500 women per year starting in 1996. Drs. Kazazian and Ganguly ceased their *BRCA1/2* testing in response to cease-and-desist letters from Myriad relating to the patents-in-suit. Kazazian Decl. ¶¶ 1-5.

Plaintiff Dr. Ganguly is an Associate Professor in the Department of Genetics at the Hospital of the University of Pennsylvania. Dr. Ganguly's work previously included *BRCA1/2* screening for both research and clinical purposes. She ceased *BRCA1/2* screening following her receipt of cease-and-desist letters from Myriad accusing her lab of violating the patents-in-suit. Ganguly Decl. ¶¶ 1, 3-5.

Plaintiff Wendy Chung, M.D., Ph.D. ("Dr. Chung"), is an Associate Professor of Pediatrics and the Herbert Irving Professor of Pediatrics and Medicine in the Division of Molecular Genetics at Columbia University. Dr. Chung is a human geneticist whose current research includes research on the *BRCA1* and *BRCA2* genes. Because of the patents-in-suit, Dr. Chung currently cannot tell research subjects in

her studies the results of their *BRCA1/2* tests and cannot offer clinical *BRCA1/2* testing services. Chung Decl. ¶¶ 1-9, 11-13, 16.

Plaintiff Harry Ostrer, M.D. ("Dr. Ostrer"), is a Professor of Pediatrics, Pathology and Medicine and Director of the Human Genetics Program in the Department of Pediatrics at New York University School of Medicine. Dr. Ostrer's work has focused on understanding the genetic basis of development and disease, including disorders of sexual differentiation and genetic susceptibility to breast and prostate cancer and malignant melanoma. Dr. Ostrer is actively engaged in identifying genes that convey risk of breast cancer and that may mitigate the effects of mutations in the *BRCA1* and *BRCA2* genes. Dr. Ostrer is also the Director of the Molecular Genetics Laboratory of NYU Medical Center, one of the largest academic genetic testing laboratories in the United States. Because of the patents-in-suit, Dr. Ostrer currently cannot tell research subjects in his studies the results of their *BRCA1/2* tests and cannot offer clinical *BRCA1/2* testing services. Ostrer Decl. ¶¶ 1-4.

Plaintiff David Ledbetter, Ph.D. ("Dr.

Ledbetter"), is a Professor of Human Genetics and Director of the Division of Medical Genetics at the Emory University School of Medicine. Research in his laboratory focuses on the molecular characterization of human developmental disorders. Dr. Ledbetter directs the Emory Genetics Laboratory which provides testing services for individuals with or at risk for genetic diseases. Because of the patents-in-suit, Dr. Ledbetter cannot offer comprehensive *BRCA1/2* genetic testing to patients. Ledbetter Decl. ¶¶ 1-8, 16.

Plaintiff Stephen T. Warren, Ph.D. ("Dr. Warren"), is the William Patterson Timmie Professor of Human Genetics, Chairman of the Department of Human Genetics, and Professor of Biochemistry and Professor of Pediatrics at Emory University. He is a past President of the American Society of Human Genetics. Dr. Warren supervises genetic research at Emory and is responsible for the laboratories at the Emory Genetics Laboratory. These laboratories would offer *BRCA1/2* genetic testing but for the patents-in-suit. Ledbetter Decl. ¶¶ 1, 16.

Plaintiff Ellen Matloff, M.S. ("Ms. Matloff"), is Director of the Yale Cancer Genetic Counseling Program.

Ms. Matloff advises women on the desirability of obtaining an analysis of their genes to determine if the women have the genetic mutations that correlate with an increased risk of breast and/or ovarian cancer. If she determines that such an analysis is warranted and the individual woman concurs, Ms. Matloff arranges for the analysis and then advises the woman of the significance of the results. Ms. Matloff would like to have the option to send patient samples to laboratories other than Myriad Genetics for *BRCA1/2* sequencing. Matloff Decl. ¶¶ 1-4, 11.

Plaintiff Elsa W. Reich, M.S. ("Ms. Reich"), is a Professor in the Department of Pediatrics at New York University. She is a genetic counselor. She helps women decide whether to be tested for mutations in the *BRCA1* and *BRCA2* genes. If they need testing, she sends samples to Myriad and explains the results for the women. Ms. Reich would like to have the option to send patient samples to laboratories other than Myriad for *BRCA1/2* sequencing. Reich Decl. ¶¶ 1-3, 8.

Plaintiff Breast Cancer Action ("BCA") is a national organization of approximately 30,000 members based in San Francisco, California. BCA is dedicated to

representing the voices of people affected by breast cancer in order to inspire and compel the changes necessary to end the breast cancer epidemic. Its members include breast cancer survivors, family members of people diagnosed with breast cancer and other people affected by or concerned about breast cancer. BCA advocates for policy changes directed at achieving prevention, finding better treatments, and reducing the incidence of breast cancer, provides information about breast cancer to anyone who needs it via newsletters, web sites, e-mail and a toll-free number, and organizes people to get involved in advocacy to advance its policy goals. Brenner Decl. ¶¶ 1-3.

Plaintiff Boston Women's Health Book Collective, doing business as Our Bodies Ourselves ("OBOS"), is a non-profit, public interest women's health education, advocacy, and consulting organization. OBOS provides information about health, sexuality and reproduction from a feminist and consumer perspective. OBOS advocates for women's health and provides information to members of the public about genetic analysis. Norsigian Decl. ¶¶ 1-4.

Plaintiff Lisbeth Ceriani ("Ms. Ceriani") is a 43-year-old single mother who was diagnosed with cancer in

both breasts in May 2008. Ms. Ceriani is insured through MassHealth, a Medicaid insurance program for low-income people. Her oncologist and genetic counselor recommended that she obtain *BRCA1* and *BRCA2* genetic testing because she may need to consider further surgery in order to reduce her risk of ovarian cancer. However, Myriad will not accept the MassHealth coverage, and Ms. Ceriani is unable to pay the full cost out-of-pocket. Ceriani Decl. ¶¶ 1-6.

Plaintiff Runi Limary ("Ms. Limary") is a 32-year-old Asian-American woman who was diagnosed with aggressive breast cancer in 2005. Ms. Limary obtained *BRCA1/2* testing through Myriad and received the following result: "genetic variant of uncertain significance." Because of Myriad's patents, she is unable to pursue alternative testing options. Limary Decl. ¶¶ 1-5.

Plaintiff Genae Girard ("Ms. Girard") is a 39-year-old woman who was diagnosed with breast cancer in 2006. Shortly after her diagnosis, she obtained *BRCA1/2* genetic testing from Myriad and tested positive for a deleterious mutation on the *BRCA2* gene. She sought a second opinion of that test result but learned that Myriad is the only laboratory in the country that can provide full

BRCA1/2 sequencing. Girard Decl. ¶¶ 1-6.

Plaintiff Patrice Fortune ("Ms. Fortune") is a 48-year-old woman who was diagnosed with breast cancer in February 2009. Ms. Fortune is insured through Medi-Cal. Her oncologist and genetic counselor recommended that she obtain *BRCA1/2* genetic testing, including the supplemental testing that is offered by Myriad separate from its standard test, but told her that Myriad would not accept her insurance. Ms. Fortune is unable to pay the full cost out-of-pocket. Fortune Decl. ¶¶ 1-5.

Plaintiff Vicky Thomason ("Ms. Thomason") is a 52-year-old woman who was diagnosed with ovarian cancer in 2006. She obtained *BRCA1/2* genetic testing from Myriad in 2007 and was found to be negative for mutations covered by that test. Her genetic counselor advised her about additional *BRCA1/2* genetic testing offered by Myriad that looks for other large genetic rearrangements that are not included in Myriad's standard full sequencing test, but informed her that her insurance would not cover the full cost of that test. Ms. Thomason is unable to afford the extra cost. Thomason Decl. ¶¶ 1-8.

Plaintiff Kathleen Raker ("Ms. Raker") is a 41-year-old woman whose mother and maternal grandmother died from breast cancer. She obtained *BRCA1/2* genetic testing from Myriad in 2007 and was found to be negative for mutations covered by that test. Her genetic counselor advised her about additional *BRCA1/2* genetic testing offered by Myriad that looks for other large DNA rearrangements that are not included in Myriad's standard full sequencing test, but informed her that it was unclear whether her insurance would cover the full cost of that test. Ms. Raker is unable to afford the extra cost. Raker Decl. ¶¶ 1-9.

Defendant USPTO is an agency of the Commerce Department of the United States with its principal office in Alexandria, Virginia. USPTO Answer ¶ 27.

Defendant Myriad is a for-profit corporation incorporated in Delaware with its principal place of business in Salt Lake City, Utah. Myriad is the former co-owner of several of the patents-in-suit and the current exclusive licensee of the patents-in-suit. Myriad is the sole provider of full sequencing of *BRCA1* and *BRCA2* genes in the United States on a commercial basis. Myriad Answer

¶ 28.

The University of Utah Research Foundation, whose directors are named as defendants in their official capacity, is an owner or part-owner of each of the patents-in-suit. Myriad Answer ¶ 29.

Amici curiae American Medical Association, American Society of Human Genetics, American College of Obstetricians and Gynecologists, American College of Embryology, and The Medical Society of the State of New York are non-profit organizations representing physicians and medical students throughout the United States, including New York; professionals in the field of human genetics, including researchers, clinicians, academicians, ethicists, genetic counselors and nurses whose work involve genetic testing; women's health care professionals; and embryologists. These amici contend that the patents-in-suit are directed to unpatentable natural phenomena in violation of Article I, Section 8, Clause 8 of the Constitution, and 35 U.S.C. § 101, are unnecessary to promote innovation in genetic research, and violate medical and scientific ethics.

Amici curiae March of Dimes Foundation, Canavan Foundation, Claire Altman Heine Foundation, Breast Cancer Coalition, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, and National Tay-Sachs & Allied Diseases Association are non-profit organizations dedicated to advancing the treatment of a variety of genetic diseases, including breast cancer, Tay-Sachs, Spinal Muscular Dystrophy, Canavan disease, and other rare genetic disorders. These amici contend that Myriad's patents represent patents on natural phenomena and laws of nature, thereby restricting future research and scientific progress.

Amici curiae National Women's Health Network, Asian Communities for Reproductive Justice, Center for Genetics and Society, Generations Ahead, and Pro-Choice Alliance for Responsible Research are non-profit organizations seeking to improve the health of women; promote reproductive justice; encourage responsible use and governance of genetic, reproductive and biomedical technologies; promote policies on genetic technologies that protect human rights; promote accountability, safety, and social justice in biomedical research from a women's rights perspective. These amici contend that isolated DNA

constitutes an unpatentable product of nature whose patenting harms women by stifling innovation and interfering with patient access to medical testing and treatment. These amici also contend that human genes and the information contained therein constitute part of the common heritage of humanity, and patenting human gene sequences is contrary to both international law and treatises as well as the public trust doctrine.

Amici curiae The International Center for Technology Assessment, Indigenous People Council on Biocolonialism, Greenpeace, Inc., and Council for Responsible Genetics are non-profit organizations dedicated to assisting the public and policy makers in understanding how technology affects society, protecting the cultural heritage and genetic materials of indigenous peoples; addressing global environmental problems; and protecting the public interest and fostering public debate about the social, ethical, and environmental implications of genetic technologies. These amici contend that the patents-in-suit claim unpatentable products of nature and that gene patents have significant negative consequences, including privatization of genetic heritage in violation of fundamental precepts of common heritage, public domain, and

the public trust doctrine; creation of private rights of unknown scope and significance; facilitate the exploitation of indigenous peoples; and violation of patients' rights to informed consent.

Amicus curiae Biotechnology Industry Organization ("BIO") is the country's largest biotechnology trade association, representing over 1200 companies, academic institutions, and biotechnology centers in all 50 states. BIO members are involved in the research and development of biotechnological healthcare, agricultural, environmental, and industrial products. BIO member companies range from start-up businesses and university spin-offs to large Fortune 500 corporations. BIO contends that patents directed to isolated DNA fall within the categories of patent-eligible subject matter because they differ "in kind" from naturally-occurring DNA. The BIO also contends that patents such as the ones in dispute here provide incentives for investment in biotechnology that promotes the advancement of science.

Amicus curiae Boston Patent Law Association ("BPLA") is a non-profit association of attorneys and other intellectual property professionals. BPLA's members serve

a broad range of clients who rely on the patent system, including independent investors, corporations, investors, and non-profit and academic institutions, such as universities and research hospitals. BPLA contends that patents, including patents on gene-related inventions, promote innovation by protecting investments in the innovation process. It further contends that the patents-in-suit satisfy the requirements of 35 U.S.C. § 101 as well as the Constitution.

Amicus curiae Genetic Alliance ("GA") is a not-for-profit, tax-exempt health advocacy organization founded in 1986 (as the Alliance for Genetic Support Groups). It brings together diverse stakeholders that create novel partnerships in advocacy. By integrating individual, family, and community perspectives to improve health systems, Genetic Alliance seeks to revolutionize access to information to enable translation of research into services and individualized decision-making. GA contends that the wholesale abolition of patents on isolated DNA molecules and isolated purified natural substances is legally untenable and undesirable as public policy, because it would diminish the promise of genetic research for patients and negatively affect other areas of medicine.

Amicus curiae Rosetta Genomics, Inc. is a wholly owned subsidiary of amicus curiae Rosetta Genomics, Ltd., a molecular diagnostics company that provides diagnostic tests for cancer and which owns several patents claiming isolated nucleic acid sequences. Amicus curiae George Mason University ("George Mason") is a public university located in Virginia. Research conducted at George Mason has been incorporated into patent applications covering cancer diagnostics. These amici contend that the question of patentability of human gene sequences is appropriately left to Congress; that the patents-in-suit promote, rather than hinder innovation; and that the challenged patents are lawful under 35 U.S.C. § 101 and the Constitution.

Amicus curiae BayBio is an independent, non-profit 501(c)(6) trade association serving the life sciences industry in Northern California, and represents more than 330 companies involved in the research and development of treatments, cures, and diagnostics. Amicus curiae Celera Corporation is a manufacturer of diagnostic products that include gene-based products used in genetic testing. Amicus curiae The Coalition for 21st Century Medicine represents some of the world's most innovative

diagnostic technology companies, clinical laboratories, researchers, physicians, venture capitalists, and patient advocacy groups that share a common mission to develop advanced diagnostics that improve the quality of healthcare for patients. Amicus curiae Genomic Health, Inc., is a life sciences company committed to improving the quality of cancer treatment decisions through genomics-based clinical laboratory services and currently offers the Oncotype DX breast cancer assay, which predicts the likelihood of the recurrence of specific types of breast cancer and whether a patient will benefit from certain treatment strategies. Amicus curiae Qiagen, N.V. is a leading provider of innovative sample and assay technologies and products which are considered standard for use in molecular diagnostics, applied testing, and academic and pharmaceutical research and development. Amicus curiae Target Discovery, Inc. discovers, validates, and utilizes protein isoforms to improve clinical diagnosis and management of disease. Amicus curiae XDx, Inc., is a molecular diagnostics company focused on the discovery, development and commercialization of non-invasive gene expression testing in the areas of transplant medicine and autoimmunity through the use of modern genomics and bioinformatics technology. These amici contend that patent exclusivity is required for the

development of personalized medicine and that the challenged patents satisfy the requirements of 35 U.S.C. § 101 and the Constitution. In addition, the amici contend that the harm alleged by Plaintiffs can be redressed through traditional judicial remedies and do not require a finding that isolated DNA constitutes unpatentable subject matter.

Amicus curiae Kenneth Chahine, Ph.D. ("Professor Chahine"), is a Visiting Professor of Law at S.J. Quinney College of Law at the University of Utah. Professor Chahine contends that the scope of the claims-in-suit are sufficiently limited to avoid claiming products of nature and that the claims directed to isolated DNA and diagnostic process satisfy the requirements of patentable subject matter under 35 U.S.C. § 101.

Amicus curiae Kevin E. Noonan, Ph.D. ("Dr. Noonan"), is a patent attorney with McDonnell Boehnen Hulbert & Berghoff LLP. Dr. Noonan contends that isolated human DNA constitutes patentable subject matter and that a ban on patenting isolated human DNA would negatively affect the development of human therapeutics, the development of personalized medicine, and the scientific research in

general.

III. THE FACTS

The facts as set forth in this section are taken from the parties' respective statements and counterstatements pursuant to Local Civil Rule 56.1 and the affidavits submitted by the parties and amici and are not in dispute except where noted.

A. The Development of Genetics as a Field of Knowledge

The field of genetics - the science of heredity and variation in living organisms - and the concept of units of heredity that could be transmitted from one generation to another originated in the 19th century from experiments with pea plants conducted by Gregor Mendel. Mendel showed that certain traits are passed on from parent to offspring as discrete entities and do not appear blended in the offspring. He hypothesized that it was the plant's genotype, or assortment of hereditary factors, that determined the plant's phenotype, or appearance. Mason Decl. ¶ 8. In 1909, this unit of inheritance was termed a "gene." Yet the gene remained an abstract concept until

1915, when it was shown that genes corresponded to physical spans of chromosomal material. Mason Decl. ¶ 9.

In 1944, scientists determined that the chemical compound known as deoxyribonucleic acid, or DNA,[3] served as the carrier for genetic information by demonstrating that DNA extracted from one strain of bacteria and transferred to another strain could transfer certain characteristics found in the first strain. Oswald Theodore Avery, et al., Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types: Induction of Transformation by a Desoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III, 79 J. Exp. Med. 137-158 (1944).

On April 25, 1953, James Watson and Francis Crick published their determination of the famous double-helix structure of DNA in the journal *Nature*. James D. Watson & Francis H.C. Crick, A Structure for Deoxyribose Nucleic Acid, 171 Nature 737-38 (1953). Dr. Crick subsequently contributed to the decryption of the genetic code and proposed "the central dogma" of molecular biology: (1)

[3] Scientists had learned to extract DNA from the body by removing it from the rest of the cellular material since as early as 1869. Ralf Dahm, Discovering DNA: Friedrich Miescher and the Early Years of Nucleic Acid Research, 122 Human Genetics 565-581, 567-68 (2008).

information is encoded in a segment of DNA, i.e., a gene; (2) transmitted through a molecule called RNA; and then (3) utilized to direct the creation of a protein, the building block of the body. Mason Decl. ¶ 10.

Our understanding of the DNA contained within our cells has since grown at an exponential rate and has included the landmark completion of the first full-length sequence of a human genome, containing 25,000 genes, as a result of the work performed by the Human Genome Project from 1990 to 2003. Sulston Decl. ¶¶ 11, 22. Access to the information encoded in our DNA has presented expansive new possibilities for future biomedical research and the development of novel diagnostic and therapeutic approaches. How this genomic information is best harnessed for the greater good presents difficult questions touching upon innovation policy, social policy, medical ethics, economic policy, and the ownership of what some view as our common heritage.

B. Molecular Biology and Gene Sequencing

An understanding of the basics of molecular biology is required to resolve the issues presented and to

provide the requisite insight into the fundamentals of the genome, that is, the nature which is at the heard of the dispute between the parties. What follows represents the standard undisputed knowledge of those in the field of molecular biology as set forth in the parties' 56.1 Statements and expert declarations. Citations are also made to two established texts in the field: Bruce Alberts, et al., *Molecular Biology of the Cell* (4th ed. 2002) ("*The Cell*") and James Watson, et al., *Molecular Biology of the Gene* (6th ed. 2008) ("*The Gene*").

1. DNA

DNA is a chemical molecule composed of repeating chemical units known as "nucleotides" or "bases." DNA is composed of four standard nucleotides: adenine, thymine, cytosine, and guanine. As shorthand, scientists denote nucleotides by the first letter of the names of their bases: "A" for adenine; "G" for guanine; "T" for thymine; and "C" for cytosine. These nucleotide units are composed of several chemical elements, namely carbon, hydrogen, oxygen, nitrogen, and phosphorus, and are linked together by chemical bonds to form a strand, or polymer, of the DNA molecule. Kay Decl. ¶¶ 14, 125; Linck Decl. ¶ 70.

Although it can exist as a single strand of nucleotides, DNA typically exists as a "double helix"[4] consisting of two intertwined strands of DNA that are chemically bound to each other. This structure is possible because of a property of DNA known as "base pair complementarity" or "base pairing," in which adenine on one strand of DNA always binds to thymine on the other strand of DNA, and guanine on one strand always bind to cytosine on the other strand. Kay Decl. ¶ 129. For example, if a portion of one strand of DNA has the nucleotide sequence ACTCGT, the corresponding section of DNA on the complementary strand will have the nucleotide sequence TGAGCA.

Genes are basic units of heredity found in all living organisms and are responsible for the inheritance of a discrete trait. Sulston Decl. ¶ 11. In molecular terms, a gene is composed of several, typically contiguous, segments of DNA. Kay Decl. ¶ 142. Each gene is typically thousands of nucleotides long and usually "encodes" one or more proteins, meaning it contains the information used by the body to produce those proteins. Some of the segments of DNA within a gene, known as "exons" or "coding

[4] It was the description of this famous "double-helix" structure that earned Watson and Crick the Nobel Prize.

sequences," contain sequences necessary for the creation of a protein, while other segments of DNA, known as "introns," are not necessary for the creation of a protein.[5] See Mason Decl. ¶ 11; Kay Decl. ¶ 151; Schlessinger Decl. ¶ 14. DNA encodes proteins by way of three nucleotide combinations, termed "codons," that correspond to one of twenty amino acids that constitute the building blocks of proteins. Sulston Decl. ¶¶ 14-15. For example, the codon adenine-thymine-guanine (ATG) encodes the amino acid methionine. Kay Decl. ¶ 158. However, because there are only twenty different amino acids but 64 possible codons that can be derived from combinations of the four DNA nucleotides, most amino acids are encoded by more than one DNA codon. *The Gene* at 37 & Table 2-3.

Together, the approximately 25,000 genes in the human body make up the human genome.[6] The genome, and the genes within it, are contained within almost every cell in the human body and define physical traits such as skin tone, eye color, and sex, in addition to influencing the development of conditions such as obesity, diabetes,

[5] Introns can contain regulatory sequences that affect the body's rate of production of the protein encoded by a gene. Kay Decl. ¶ 151.
[6] Genome is defined as "[t]he totality of genetic information belonging to a cell or an organism; in particular, the DNA that carries this information." *The Cell* at G:15.

Alzheimer's disease, and bipolar disorder. Mason Decl. ¶¶ 4-5; Sulston Decl. ¶¶ 10-11.

The linear order of DNA nucleotides that make up a polynucleotide, such as a gene, is referred to as the "nucleotide sequence," "DNA sequence," or "gene sequence."[7] Kay Decl. ¶ 126; Schlessinger Decl. ¶ 19; Linck Decl. ¶ 45; Sulston Decl. ¶ 16; Mason Decl. ¶ 13; Chung Decl. ¶ 10. Gene sequences constitute biological information insofar as they describe the structural and chemical properties of a particular DNA molecule and serve as the cellular "blueprint" for the production of proteins. Sulston Decl. ¶ 16; Kay Decl. ¶ 126; Schlessinger Decl. ¶ 19; Linck Decl. ¶¶ 45, 46. Genes and the information represented by human gene sequences are products of nature universally present in each individual, and the information content of a human gene sequence is fixed. While many inventive steps may be necessary to allow scientists to extract and read a gene sequence, it is undisputed that the ordering of the nucleotides is determined by nature. Sulston Decl. ¶ 10, 17; Ostrer Decl. ¶ 14; Chung Decl. ¶ 25; Ledbetter Decl. ¶ 27; Leonard Decl. ¶ 15.

[7] By analogy, if a gene is the equivalent of a word, then the nucleotide sequence is the equivalent of the word's spelling.

Scientists often use the term "wild-type" to refer to the "normal" human gene sequence, i.e. the sequence of a gene without any variations,[8] against which individuals' gene sequences are compared. Mason Decl. ¶ 17; Grody Decl. ¶ 46. Variations in the human genome are very common: aside from identical twins, the genomes of any two individuals are estimated to have one to five nucleotide differences for every 1000 nucleotides. Mason Decl. ¶ 14; Sulston Decl. ¶ 12.

Variations in the human genome, also known as "mutations," can occur at different scales. Small scale variations can be manifested as slight sequence differences between the same genes in different individuals. Thus, for example, if the wild-type sequence of a portion of a gene is represented by GACTCG, a variation of that sequence might omit the first C (resulting in GATCG) or contain an extra C at that point (resulting in GACCTCG) or reverse the order of two of the letters (e.g., GCATCG). Mason Decl. ¶ 16. Alternatively, there can be large scale variations,

[8] At the same time there is an increasing recognition that the notion of a single "normal" gene sequence may not be entirely accurate in light of the high frequency of variations in a gene's sequence between individuals. Mason Decl. ¶ 17. For purposes of this opinion, however, genes are treated as having a single "normal" DNA sequence.

such as the addition or deletion of substantial chromosomal regions. Thus, a particular gene may omit several hundred letters at one point or may add several hundred letters where they do not normally exist in the wild-type gene sequence. Even larger variations, known as structural variants, also can occur, involving the deletion or duplication of up to millions of nucleotides. Extra copies or missing copies of the genome that are larger than 1000 nucleotides are called "copy number variants" ("CNVs"). Mason Decl. ¶ 15, 18.

Some of these mutations have little or no effect on the body's processes, while other mutations, including those that appear to correlate with an increased risk of particular diseases, do interfere with the body's processes.[9] There are also variants of uncertain significance ("VUS"): variants whose effect on the body's processes, if any, is currently unknown. Mason Decl. ¶ 19; Sulston Decl. ¶ 18; Kay Decl. ¶ 76.

DNA as it is found in the human body - "native

[9] The correlation between a particular mutation and disease susceptibility is not self-evident from the mutation itself; rather, extensive statistical analysis is required to identify which alterations in the nucleotide sequence correlate with a particular medical condition, a process which may take many years. Kay Decl. ¶ 190.

DNA" or "genomic DNA" - is packaged, along with proteins, into complex structures known as chromosomes, which contain the vast majority of the genes located in the cells of the human body. Kay Decl. ¶ 131; Schlessinger Decl. ¶ 12. This mixture of DNA and proteins that makes up chromosomes is also referred to as chromatin. See *The Gene* at 135. Genes are organized on forty-six chromosomes (twenty-three of which are inherited from the mother, and twenty-three of which are inherited from the father) which together constitute the vast majority of the human genome.[10] Mason Decl. ¶ 5. The proteins within the chromosomes are bound[11] to the DNA molecules and modulate the structure and function of the DNA molecules to which they are associated. Kay Decl. ¶ 131; Schlessinger Decl. ¶ 12; *The Cell* at 198, 208, Fig. 4-24. This interaction between chromosomal proteins and native DNA is one method by which the body establishes which genes are inactive, which genes are active, and the level of activity. Kay Decl. ¶ 132. Some DNA in the body also undergoes chemical modifications, such

[10] A very small fraction of human genes are located in a cellular organelle known as the mitochondria. Kay Decl. ¶ 144; Schlessinger Decl. ¶ 23. Neither party appears to believe that a discussion of mitochondrial DNA bears much relevance to the legal issues presented.

[11] The ionic chemical bonds that exists between proteins and DNA molecules differ from the covalent chemical bonds which hold DNA itself together. See *The Cell* at 198 (describing DNA in the cell as "associated with proteins that fold and pack the fine DNA thread into a more compact structure."); id. at 208 Fig. 4-24 (demonstrating dissociation of histone proteins from DNA by high salt solution, indicating lack of covalent bond between DNA and histones).

as methylation,[12] which can affect the level of activity of a gene, but does not affect the nucleotide sequence of the gene. Kay Decl. ¶ 132; Mason Supp. Decl. ¶ 22.

2. Extracted and purified DNA

Native DNA may be extracted from its cellular environment, including the associated chromosomal proteins, using any number of well-established laboratory techniques. Grody Decl. ¶ 13; Leonard Decl. ¶ 33. A particular segment of DNA, such as a gene, contained in the extracted DNA may then be excised from the genomic DNA in which it is embedded to obtain the purified DNA of interest. Kay Decl. ¶¶ 133, 137. DNA molecules may also be chemically synthesized in the laboratory. Kay Decl. ¶¶ 17, 133, 137.

Although the parties use the term "isolated DNA" to describe DNA that is separated from proteins and other DNA sequences, the term "isolated DNA" possesses a specific legal definition reflecting its use in the patents-in-suit. To avoid any confusion for purposes of this fact recitation, the term "extracted DNA" will be used to refer

[12] Methylation refers to the addition of a small chemical group composed of one carbon atom and three hydrogen atoms (CH_3), known as a "methyl group," to the nucleotides of a segment of DNA. See *The Cell* at 430.

to DNA that has been removed from the cell and separated from other non-DNA materials in the cell (e.g., proteins); "purified DNA" will be used to refer to extracted DNA which has been further processed to separate the particular segment of DNA of interest from the other DNA in the genome; and "synthesized DNA" will be used to refer to DNA which has been synthesized in the laboratory.

As noted above, native DNA, unlike purified or synthesized DNA, is not typically found floating freely in cells of the body, but is packaged into chromosomes. Kay Decl. ¶¶ 131, 148. However, when DNA is copied, or replicated, in preparation for cell division, short segments of DNA are dissociated from the chromosomal proteins, although they are still contained within the cell. Similarly, when a particular portion of DNA is transcribed into RNA, segments of DNA exist dissociated from the proteins normally bound to it. Mason Supp. Decl. ¶ 23.

Purified or synthesized DNA may be used as tools for biotechnological applications for which native DNA cannot be used. Kay Decl. ¶¶ 134, 138; Schlessinger Decl. ¶ 27. For example, unlike native DNA, purified or

synthesized DNA may be used as a "probe,"[13] which is a diagnostic tool that a molecular biologist uses to target and bind to a particular segment of DNA, thus allowing the target DNA sequence to be detectable using standard laboratory machinery. Kay Decl. ¶ 135; Schlessinger Decl. ¶ 29. Purified or synthesized DNA can also be used as a "primer"[14] to sequence a target DNA, a process used by molecular biologists to determine the order of nucleotides in a DNA molecule, or to perform polymerase chain reaction ("PCR") amplification, a process which utilizes target-DNA specific primers to duplicate the quantity of target DNA exponentially. Critchfield Decl. ¶ 40; Kay Decl. ¶ 184.

During this process, the DNA molecule being used as a probe or a primer binds, or "hybridizes," to a specific nucleotide sequence of a DNA target molecule, such as the *BRCA1* or *BRCA2* gene. This sequence-specific binding of two strands of DNA results from the same base-pairing phenomenon which allows two complementary strands of DNA to form the double helix structure. As a result, a strand of isolated DNA being used as a primer with the sequence

[13] A probe is a DNA fragment that is usually between 100-1000 nucleotides long. Kay Decl. ¶ 135.
[14] A primer is a DNA fragment, usually between 15 and 30 nucleotides long, that binds specifically to a target DNA sequence. Kay Decl. ¶ 183.

ATGTCG, for example, will bind specifically to the portion of the target DNA molecule containing the nucleotide sequence TACAGC. The hybridization of a primer or probe to a DNA target, such as *BRCA1* or *BRCA2*, results in the formation of a "hybridization product" that either acts as a substrate for the enzymes used in the sequencing or amplification reaction or permits the detection of the target DNA. See Kay Decl. ¶¶ 138, 183; Schlessinger Decl. ¶ 30; *The Gene* at 105-06; 113-15.

The utility of purified *BRCA1/2* DNA molecules as biotechnological tools therefore relies on their ability to selectively bind to native or isolated *BRCA1/2* DNA molecules, which ability is a function of the isolated DNA's nucleotide sequence. Kay Decl. ¶ 138.

3. RNA

Ribonucleic acid ("RNA") is another nucleic acid found in cells. Like DNA, an RNA molecule is composed of a combination of four different nucleotides, three of which are the same bases incorporated into DNA: adenine, cytosine, and guanine. Unlike DNA, however, RNA utilizes uracil as the fourth nucleotide base, rather than thymine.

In addition, the sugar-phosphate backbone in RNA is chemically different from the sugar-phosphate backbone of DNA. Kay Decl. ¶ 170.

The creation of proteins, which do the work of the body, comprises two steps: transcription and translation. Transcription is the process by which a temporary copy of a particular DNA sequence, in the form of an RNA molecule, is generated. Mason Decl. ¶¶ 11-12; Kay Decl. ¶¶ 149, 150. During transcription, a discrete segment of DNA unwinds itself inside the cell and the bases of the DNA molecule act as "clamps" that hold the bases of the newly forming RNA molecule in place while the chemical bonds of its sugar-phosphate backbone are formed. Kay Decl. ¶ 150. Each nucleotide in the DNA strand corresponds to a nucleotide to be incorporated into the newly forming RNA molecule: adenine on the DNA molecule binds to and thereby acts as a clamp for RNA nucleotide uracil, thymine for adenine, guanine for cytosine, and cytosine for guanine. Kay Decl. ¶ 150. This newly generated RNA is termed "pre-messenger RNA" or "pre-mRNA" and, like the DNA from which it was generated, contains both introns and exons. In a process known as "splicing," the introns are physically cut out of the pre-mRNA by the cell and the

remaining RNA segments containing the exons are rejoined, or "ligated," together in consecutive order to form the final "messenger RNA," or "mRNA." Mason Decl. ¶ 11; Kay Decl. ¶ 151; Schlessinger Decl. ¶ 14. Pre-mRNAs can also undergo a process known as "alternative splicing," in which different combinations of exons from the same pre-mRNA molecule are ligated together to yield different final mRNA products.[15] Kay Decl. ¶ 152; Schlessinger Decl. ¶ 14.

During translation, an mRNA molecule serves as a template for the assembly of a protein. Kay Decl. ¶ 157. In a process that parallels the transcription of DNA, the mRNA bases, along with other proteins in the cell, serve as clamps to hold the corresponding amino acids in place while the chemical bonds between the individual amino acids are formed. Kay Decl. ¶ 157. The three-nucleotide codons originally found in DNA and copied into mRNA determine which amino acids are incorporated into the protein and the order in which they are incorporated. Kay Decl. ¶ 157.

[15] For example, a pre-mRNA molecule containing exons ("E") numbered 1-6, with introns ("I") between each exon whose structure is represented as follows: E1+I1+E2+I2+E3+I3+E4+I4+E5+I5+E6. After splicing, the introns would be removed to form an mRNA composed only of exons: E1+E2+E3+E4+E5+E6. On the other hand, the same pre-mRNA molecule might undergo alternative splicing to form final mRNAs with a variety of different exon compositions: for example, E1+E2+E5; E1+E3+E6; and E1+E4+E6.

4. cDNA

Complementary DNA, or "cDNA," is a type of DNA molecule generated from mRNA during a process known as "reverse transcription" which is catalyzed by a protein known as "reverse transcriptase." cDNA derives its name from the fact that it is "complementary" to the mRNA from which it is produced - that is, each base in the cDNA can bind to the corresponding base in the mRNA from which it is generated. Kay Decl. ¶ 161. Because it is derived from mRNA, a cDNA molecule represents an exact copy of one of the protein coding sequences encoded by the original genomic DNA. Leonard Decl. ¶ 75. In this respect, cDNA contains the identical protein coding informational content as the DNA in the body, even though differences exist in its physical form. Mason Decl. ¶ 32.

During reverse transcription, each base of the mRNA serves as a clamp for its complementary nucleotide to be incorporated into the new cDNA molecule while the chemical bonds between the nucleotides of the cDNA strand are formed. Much like transcription, uracil on the mRNA binds to and thereby acts as a clamp for the nucleotide adenine, adenine for thymine, guanine for cytosine, and

cytosine for guanine. Kay Decl. ¶ 165. The synthesis of cDNA from very long mRNA molecules, such as *BRCA1* and *BRCA2*, often does not result in a cDNA strand that is as long as the mRNA chain. Kay Decl. ¶ 166.

cDNA is typically generated by scientists in a laboratory. Kay Decl. ¶ 164, Linck Decl. ¶ 48. However, naturally occurring cDNAs, known as "pseudogenes," exist in the human genome and are structurally, functionally, and chemically identical to cDNAs made in the laboratory. Mason Supp. Decl. ¶¶ 18-21; Nussbaum Decl. ¶¶ 41-42.

cDNA possesses certain structural and functional differences from native DNA. In contrast to most forms of native DNA, cDNA does not contain non-coding intronic sequences because it is derived from mRNA in which the introns have been removed. As a result, the production of proteins from cDNA does not require RNA splicing, in contrast to the production of proteins from native DNA as described above. Some cDNAs cannot be used to produce proteins without the addition of certain regulatory sequences, although other cDNAs possess some of the necessary regulatory sequences. cDNAs also usually contain nucleotides corresponding to the so-called "poly A tail"

sequence found in mRNA, which native DNA does not possess. In addition, as mentioned above, native DNA is often (although not always) chemically modified in the body, e.g., by methylation, while cDNA generated in the laboratory is not so modified. Kay Decl. ¶¶ 168, 169; Mason Supp. Decl. ¶¶ 18-22; Nussbaum Decl. ¶¶ 41-42. cDNA also differs from mRNA in that it is a more stable compound and requires both transcription and translation to produce protein, rather than simply translation, as is the case with mRNA. Kay Decl. ¶ 171.

Much like purified DNA, cDNA can be used as a tool for biotechnological and diagnostic applications for which native DNA cannot be used. Kay Decl. ¶ 162. In addition, a scientist seeking to learn more about a protein of interest may transfer a cDNA encoding the protein into a recipient cell that does not normally express that protein. If the cDNA is operatively linked to particular "promoter" sequences that initiate transcription from the cDNA, the recipient cell will then express the protein of interest. Kay Decl. ¶ 163.

5. DNA sequencing

DNA sequencing is the process by which one "reads," or determines the ordering of the nucleotides within a DNA molecule. Sulston Decl. ¶ 20; Kay Decl. ¶ 138. In the context of a gene or a portion of the genome, sequencing is designed to illuminate the information that nature has dictated in that person's genome, and the sequencing process, by design, does not alter the information content of the native DNA sequence. Sulston Decl. ¶ 27; Mason Decl. ¶ 32. In that respect, sequencing is analogous to examining something through a microscope insofar as it makes visible something that exists in nature but is too small to be seen otherwise. Mason Decl. ¶ 23. Gene sequencing is used in diagnostic testing, such as Myriad's tests, to determine whether a gene contains mutations that have been associated with a particular condition. Sulston Decl. ¶ 24; Chung Decl. ¶ 10; Swisher Decl. ¶¶ 23-26; Mason Decl. ¶ 21. These mutations, along with any association with a propensity to develop a particular disease, are caused by nature. Chung Decl. ¶ 10; Mason Decl. ¶ 20; Sulston Decl. ¶¶ 19, 27; Ledbetter Decl. ¶ 26. Therefore, the significance of any person's gene sequence, including its relationship to any disease, is dictated by nature. Mason Decl. ¶ 32.

Sequencing is often used to identify single nucleotide substitutions or the insertion or deletion of a small number of nucleotides in a gene. Swisher Decl. ¶ 23; Kay Decl. ¶ 180. However, even full sequencing of an entire gene can miss large genomic rearrangements in which whole sections of the gene have been deleted or moved to a different part of the genome. Other tests have been developed that better detect these large rearrangements. Swisher Decl. ¶ 24; Ledbetter Decl. ¶¶ 16-17.

Sequencing native DNA first requires that cells of a tissue sample[16] be broken open to permit extraction of the DNA contained within the cells. Sulston Decl. ¶ 25. The extracted DNA of the entire genome contains over three billion nucleotides, of which the gene of interest comprises a very small portion. Kay Decl. ¶ 178. *BRCA1/2* sequencing by Myriad follows the typical process for sequencing extracted genomic DNA, which begins with obtaining a sufficient quantity of the *BRCA1/2* genomic DNA to permit its sequencing. Critchfield Decl. ¶ 40.

Under the current state of the art, the only

[16] Various types of patient samples can be used, e.g., blood, tumor tissue, or non-tumor tissue. Kay Decl. ¶ 186.

practical way to obtain a sufficient amount of *BRCA1/2* genomic DNA for mutation detection purposes is to PCR amplify the genomic DNA in segments. Critchfield Decl. ¶ 40. In order to design the necessary primers to PCR amplify the correct region of the genome, at least a portion of the sequence of the target DNA molecule must be known. Kay Decl. ¶ 184. Typically, each exon of the *BRCA1/2* genes, including a small adjacent portion of the flanking introns, is separately amplified by PCR into one or more amplified DNA fragments, also called "amplicons." The *BRCA1* and *BRCA2* genes have a total of 48 coding exons containing over 15,700 nucleotide base pairs. More than 50 amplicons are typically produced as part of Myriad's *BRCA1/2* testing. Critchfield Decl. ¶ 40.

Following PCR amplification of the target DNA, a sequencing reaction is performed to determine the nucleotide sequence of the amplicon. Kay Decl. ¶ 183. As with PCR, at least some of the target sequence must be known in order to design a primer specific to the target DNA to be sequenced. Kay Decl. ¶¶ 177, 179, 183. For this reason, primers that bind only to specific DNA sequences in the *BRCA1* and *BRCA2* genes permit the analysis of a patient's native DNA sequence to determine if the

nucleotide composition is the same or different from the nucleotide composition of the normal *BRCA1* and *BRCA2* gene. Kay Decl. ¶ 187. Gene sequencing also sometimes utilizes cDNA as the DNA template. Leonard Decl. ¶ 75.

The techniques required for gene sequencing are well-known and understood by scientists skilled in molecular biology, and scientists and clinicians sequence and analyze genes literally every day. Chung Decl. ¶¶ 10-11; Mason Decl. ¶ 22; Hegde Decl. ¶¶ 6-7. However, because sequencing requires knowledge of the sequence of a portion of the target sequence, some ingenuity and effort is required for the initial sequencing of a target DNA. See Kay Decl. ¶ 183; Klein Decl. ¶ 32-34.

C. The Development of the Patents-in-Suit

Breast cancer is the most frequently diagnosed cancer worldwide and is the leading cause of cancer death for women in Britain and the second leading cause of cancer death for women in the United States. Parthasarathy Decl. ¶ 8.[17] Ovarian cancer is the eighth most common cancer in

[17] Dr. Parthasarathy has researched the development of genetic testing for breast and ovarian cancer in the United States and Britain and has interviewed over 100 individuals involved in the process, including

women and causes more deaths in the Western world than any other gynecologic cancer. Swisher Decl. ¶ 10.

Throughout the 1980s, organizations dedicated to breast cancer awareness began efforts to increase public and governmental awareness of the breast cancer epidemic. In 1991, the U.S. Department of Defense created a research program devoted to breast cancer research. Over the years this funding has grown from less than $90 million during the fiscal year 1990 to more than $2.1 billion during the fiscal year 2008. Parthasarathy Decl. ¶ 10.

Throughout the 1980s, scientists from the United States, England, France, Germany, Japan, and other countries sought to be the first to identify DNA nucleotide sequences associated with breast cancer. Parthasarathy Decl. ¶ 11. In 1989, various European and American research laboratories participated in the International Breast Cancer Linkage Consortium (the "Consortium"), and in 1990, a group of researchers led by Mary-Claire King ("Dr. King") at the University of California, Berkeley, published a landmark paper demonstrating for the first time that a

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research scientists, officials at research institutions, health care professionals, patent office officials, bioethicists, and journalists. Parthasarathy Decl. ¶ 6.

gene linked to breast cancer, whose sequence was unknown but which was later designated Breast Cancer Susceptibility Gene 1 (*BRCA1*), was located on a region of chromosome 17. See Jeff M. Hall, et al., Linkage of Early-Onset Familial Breast Cancer to Chromosome 17q21, 250 Science 1684-89 (1990); Parthasarathy Decl. ¶ 11. Soon afterwards, research intensified as teams around the world, including groups led by Dr. King, Dr. Mark Skolnick ("Dr. Skolnick") (co-founder of Myriad), and Dr. Michael Stratton ("Dr. Stratton") (Institute for Cancer Research, London ("ICR")), focused in on this region of the genome in an attempt to be the first to determine the DNA sequence of *BRCA1*. Parthasarathy Decl. ¶ 11.

Dr. Skolnick, a 1968 economics graduate of the University of California, Berkeley, had become interested in the application of demography to the study of genetics while doing research for his Ph.D. in genetics, which he received from Stanford University in 1975. While reconstructing genealogies in Italy, he met three Mormons who were microfilming parish records and from whom he learned of the resources of the Utah Genealogical Society in Salt Lake City. Thereafter, in 1973, after an inquiry from the organizers of a cancer center at the University of

Utah, Dr. Skolnick suggested linking the Utah Mormon Genealogy with the Utah Cancer Registry. To further this effort, a familial cancer screening clinic was established and a program for mapping genes was developed. Skolnick Decl. ¶¶ 7, 11, 12.

Following publication of the King group's study relating to *BRCA1* in the fall of 1990, Dr. Skolnick and his collaborators concluded that additional resources would be required to compete with the team of Dr. Francis Collins, which had received a substantial grant from the National Institutes of Health ("NIH"), Skolnick Decl. ¶¶ 13, 14, and in 1991 Myriad was founded by Dr. Skolnick and a local venture capital group interested in genetics. Myriad received $5 million in funding in 1992, $8 million in 1993, and $9 million in 1994. Skolnick Decl. ¶ 16.

Locating the *BRCA1* gene relied on the use of linkage analysis, in which correlations between the occurrence of cancer and the inheritance of certain DNA markers among family members were used to identify, or "map," the physical location of, the *BRCA1* gene within the human genome. See '282 patent, col. 7:39-52. Once the physical location had been narrowed down to a sufficiently

small region of the genome, Myriad was able to directly analyze the sequence of the DNA in this region and identify the nucleotides comprising the *BRCA1* gene. See '282 patent, col. 7:53-8:7. Successful linkage analysis requires large and genetically informative families, or kindreds, and detailed family information, such as detailed genealogical records, are an important component to this analysis. Shattuck Decl. ¶¶ 10, 13; '282 patent, col. 8:16-29.

In September 1994, the group at Myriad, along with researchers from the National Institute for Environmental Health Sciences ("NIEHS") (a subdivision of the NIH), the University of Utah, McGill University, and Eli Lilly and Company announced that they had sequenced the *BRCA1* gene. See Yoshio Miki, et al., A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene *BRCA1*, 266 Science 66-71 (1994). In addition to funding the six NIEHS researchers who participated in the identification of *BRCA1*, the NIH had also provided approximately $2 million in funding to the University of Utah.[18] See id. at 71 n.52; Parthasarathy Decl. ¶ 18.

[18] According to the description of author associations, the first and second authors of the paper were associated with the University of Utah.

According to one analysis, the NIH contributed one-third of the funding for the identification of *BRCA1*. Parthasarathy Decl. ¶ 18.

A dispute subsequently arose between Myriad and the NIH over the NIEHS scientists' exclusion as co-inventors on the *BRCA1* patents. Parthasarathy Decl. ¶ 19. The NIH maintained that its scientists had conducted some of the most important work leading up to the sequencing of the gene, including identifying the sequences of two of the *BRCA1* gene fragments and assembling the complete *BRCA1* sequence. Id. Myriad agreed to include the names of the NIEHS researchers as inventors on its patent application and pay inventors' royalties, although no payments appear to have been made as of 2005. Id.

Following the isolation of *BRCA1*, scientists continued to search for a second gene also believed to be linked with breast and ovarian cancer.[19] Parthasarathy Decl. ¶ 12. Myriad collaborated with several research groups, including scientists at the University of Laval in Quebec, Canada, the Hospital for Sick Children in Toronto,

[19] The same positional cloning approach utilized to isolate the *BRCA1* gene was relied on to isolate the *BRCA2* gene. Tavtigian Decl. ¶ 4.

Canada, and the University of Pennsylvania in their search for this second gene. It also collaborated with a team of researchers led by Dr. Stratton at the ICR which, in November 1995, identified a mutation in breast cancer patients that appeared to be located in the as-yet unpublished *BRCA2* gene. Dr. Stratton ended the collaboration with Myriad upon learning of Myriad's plans to patent the *BRCA2* gene sequence. Sulston Decl. ¶ 30.

On December 21, 1995, Myriad filed for patents on the *BRCA2* gene in both the U.S. and Europe. Tavtigian Decl. ¶ 5. The next day, the Stratton group published its identification of the *BRCA2* gene in the journal *Nature*, and Myriad submitted the sequence of *BRCA2* to GenBank, an international depository of gene sequence information. Parthasarathy Decl. ¶ 12; Tavtigian Decl. ¶ 9; Richard Wooster, et al., Identification of the Breast Cancer Susceptibility Gene *BRCA2*, 378 Nature 789-92 (1995). Subsequent analysis of the *BRCA2* sequence from the Stratton group indicated that while they had correctly sequenced the primary portion of the *BRCA2* gene, their published sequence had errors in both ends of the *BRCA2* gene. Tavtigian Decl. ¶¶ 7-10. Nonetheless, the consensus among the scientific community is that the Stratton group, rather than Myriad,

was the first to sequence the *BRCA2* gene. Parthasarathy Decl. ¶ 13.

The isolation of the *BRCA1/2* genes required considerable effort on the part of Myriad and its collaborators as well as ingenuity in overcoming technical obstacles associated with the isolation process. However, the process and techniques used were well understood, widely used, and fairly uniform insofar as any scientist engaged in the search for a gene would likely have utilized a similar approach. Parthasarathy Decl. ¶ 19; Tavtigian Decl. ¶ 13.

D. Application of the Patents-in-Suit

Mutations in the *BRCA1/2* genes correlate with an increased risk of breast and ovarian cancer. Women with *BRCA1* and *BRCA2* mutations face up to an 85% cumulative risk of breast cancer, as well as up to a 50% cumulative risk of ovarian cancer. Love Decl. ¶ 10; Parthasarathy Decl. ¶ 9. In addition, among the 10-15% of ovarian cancer cases that are inherited genetically, 80% of women diagnosed under the age of 50 carry mutations in their *BRCA1* genes and 20% carry mutations in their *BRCA2* genes. The women with

inherited *BRCA1* mutations have a 40-52% cumulative risk of ovarian cancer by the time they reach 70 years old. For women with inherited *BRCA2* mutations, the risk is approximately 15-25%. Swisher Decl. ¶ 11. Male carriers of mutations are also at an increased risk for breast and prostate cancer. Love Decl. ¶ 10.

The existence of *BRCA1/2* mutations is therefore an important consideration in the provision of clinical care for breast and/or ovarian cancer. A patient will not only learn of her risk for hereditary breast and ovarian cancer, but also can gain information that may be useful in determining prevention and treatment options. This information is useful for women who are facing difficult decisions regarding whether or not to undergo prophylactic surgery, hormonal therapy, chemotherapy, and other measures. Swisher Decl. ¶ 12; Love Decl. ¶ 11. Testing results for the *BRCA1/2* genes can be an important factor in structuring an appropriate course of cancer treatment, since certain forms of chemotherapy can be more effective in treating cancers related to *BRCA1/2* mutations. Swisher Decl. ¶ 13; Love Decl. ¶ 18.

1. Myriad's *BRCA1/2* testing

Myriad offers multiple forms of *BRCA1/2* testing to the general public. Its standard test, called Comprehensive BRACAnalysis, originally only consisted of the full sequencing of the *BRCA1/2* genes. Swisher Decl. ¶¶ 29-30; Reich Decl. ¶ 10; Parthasarathy Decl. ¶ 26; Critchfield Decl. ¶ 49. In 2002, Myriad supplemented its full sequencing analysis with a large rearrangement panel ("LRP") for detecting five common large rearrangement mutations which is now included in the Comprehensive BRACAnalysis. Critchfield Decl. ¶¶ 49, 51. In 2006, Myriad began offering a supplemental test to Comprehensive BRACAnalysis called the BRACAnalysis Rearrangement Test ("BART"), which, according to Myriad, can detect virtually all large rearrangement mutations in the *BRCA1* and *BRCA2* genes.[20] Swisher Decl. ¶¶ 29-30; Reich Decl. ¶ 10; Parthasarathy Decl. ¶ 26; Critchfield Decl. ¶ 51.

2. Funding for Myriad's *BRCA1/2* tests

The Myriad tests are available to clinicians and

[20] Myriad also offers other more limited forms of *BRCA1/2* genetic testing. Swisher Decl. ¶¶ 29-30; Reich Decl. ¶ 10; Parthasarathy Decl. ¶ 26

patients at a cost of over $3000 per test. In 2008, the total cost to Myriad of providing these tests was $32 million with resulting revenues of $222 million. See Myriad Genetics, Inc., Annual Report (Form 10-K), at 27 (Aug. 28, 2008). In Ontario, where the regional public healthcare plan is ignoring Myriad's patent, the testing for breast cancer is performed for a third of Myriad's cost. See CBC News, Ontario to Offer New Genetic Test for Breast, Ovarian Cancer (Jan. 8, 2003), available at http://www.cbc.ca/health/story/2003/01/06/test_genetic030106.html.

Plaintiffs have noted several instances where women have been unable to obtain funding for all of Myriad's testing services. For example, Myriad refused to process Ms. Ceriani's sample because it did not accept coverage by Ms. Ceriani's insurance carrier. Unable to pay for Myriad's tests, and unable to find scholarship programs to fund her testing, Ms. Ceriani has not been tested. Ceriani Decl. ¶¶ 5-7. Ms. Fortune's insurance carrier is not accepted by Myriad, and Ms. Fortune is also unable to pay the full out-of-pocket cost of Myriad's test. Fortune Decl. ¶ 5.

Myriad's BART test is not covered by a number of insurers, and unless a patient is one of a limited number of "high risk patients" who meet certain clinical criteria established by Myriad, a patient must pay an extra fee for BART testing. Swisher Decl. ¶¶ 29-30; Reich Decl. ¶ 10; Parthasarathy Decl. ¶ 26; Critchfield Decl. ¶ 52. As a result of the cost of BART testing, the test is unavailable to women who would otherwise choose to utilize the test. Swisher Decl. ¶¶ 30-31; Reich Decl. ¶ 10. For example, Ms. Raker is unable to afford the extra cost for BART testing and has not been tested for large genomic rearrangements, despite the advice of her genetic counselor. Raker Decl. ¶¶ 7-11. Similarly, Ms. Thomason has been unable afford the BART testing recommended by her genetic counselor. Thomason Decl. ¶¶ 6-9.

Myriad has pursued Medicaid coverage for years, but has been unable to secure "participating provider" status in 25 states which would allow it to offer testing to that state's Medicaid patients. Myriad also has a financial assistance program which provides free testing to low-income and uninsured patients who meet certain economic and clinical requirements. In addition, Myriad provides free testing to independent non-profit institutions. In

particular, Ms. Ceriani may be eligible to receive BRACAnalysis testing at no charge through the non-profit organization Cancer Resource Foundation, for which Myriad has provided free testing since 2009. Rusconi Decl. ¶¶ 4-6; Critchfield Decl. ¶ 33; Ogaard Decl. ¶¶ 4-6. Currently, 90% of the tests Myriad performs are covered by insurance at over 90% of the test cost. Critchfield Decl. ¶¶ 32, 33, 52, 53.

A number of researchers, clinicians, and molecular pathologists have the personnel, equipment, and expertise to sequence and analyze genes, including the *BRCA1* and *BRCA2* genes, at a lower cost than Myriad's testing. Kazazian Decl. ¶¶ 8, 11; Matloff Decl. ¶ 12; Ostrer Decl. ¶¶ 8-9; Ledbetter Decl. ¶¶ 16-18. For example, the *BRCA1/2* testing previously conducted by the Yale DNA Diagnostics Laboratory and the University of Pennsylvania Genetic Diagnostic Laboratory ("GDL") cost less than what Myriad charges, and testing by OncorMed, a one-time competitor, was cheaper than Myriad's testing. Matloff Decl. ¶ 7; Kazazian Decl. ¶ 8; Parthasarathy Decl. ¶ 24. However, on a "cost per exon" basis, Myriad's BRACAnalysis test costs less than testing for other genes performed by the GDL at the University of Pennsylvania and

Drs. Ledbetter and Warren at Emory University. See infra; Critchfield Decl. ¶ 35.

3. Myriad's enforcement of the patents-in-suit

During the mid-to-late-1990s, Drs. Kazazian and Ganguly offered, for a fee, screening services for *BRCA1* mutations through the GDL at the University of Pennsylvania. Kazazian Decl. ¶ 4; Ganguly Decl. ¶ 3. The screening methodology utilized by Drs. Kazazian and Ganguly differed from the testing method used by Myriad, but involved using isolated DNA encoding *BRCA1* or *BRCA2*. Kazazian Decl. ¶ 9; Parthasarathy Decl. ¶ 23. At some point during this period, Dr. Skolnick advised Dr. Kazazian that Myriad planned to stop the *BRCA1/2* testing being conducted at the GDL. Kazazian Decl. ¶ 6. On May 29, 1998, Myriad offered Dr. Kazazian a collaborative license in connection with the '473, '999, '001, '282, and '441 patents. Ganguly Decl. Ex. 2. However, the license covered only single mutation tests and multiple mutation panels of up to four mutations to allow for testing of patients of Ashkenazi Jewish descent. Ganguly Decl. ¶ 5. Myriad subsequently sent cease and desist letters to Dr.

Kazazian and the University of Pennsylvania. On August 26, 1998, O'Melveny & Myers LLP gave notice to Dr. Kazazian of infringement in the absence of a license. Ganguly Decl. Ex. 3. Myriad subsequently sued the University of Pennsylvania in November 1998 for infringement of the patents-in-suit. See Myriad Genetics v. Univ. of Pennsylvania, 2:98-cv-00829 (D. Utah) (filed November 19, 1998). On June 10, 1999, Myriad's general counsel, Christopher Wright, sent a letter to the University of Pennsylvania seeking written assurances that Dr. Kazazian and the University of Pennsylvania had ceased *BRCA1/2* clinical testing. Ganguly Decl. Ex. 4. This demand was repeated in a September 22, 1999 letter from Myriad to the University of Pennsylvania. Ganguly Decl. Ex. 6.

As a result of Myriad's efforts to enforce its patents against the University of Pennsylvania, the GDL no longer conducts *BRCA1/2* screening for research or as part of its clinical practice. Kazazian Decl. ¶ 5; Ganguly Decl. ¶¶ 8-9; Parthasarathy Decl. ¶ 28. However, sometime between 1999 and 2000, Dr. Critchfield, on behalf of Myriad, informed Dr. Kazazian that he is free to conduct academic research on the *BRCA1/2* genes, including

sequencing the genes and detecting mutations in the genes. Critchfield Decl. ¶ 22.

In May 1998, Myriad offered Dr. Ostrer a license agreement to conduct diagnostic *BRCA1/2* genetic testing. The proposed license would permit Dr. Ostrer to conduct single mutation tests and multiple mutation panels (up to four mutations) for patients of Ashkenazi Jewish descent only. Dr. Ostrer declined the offer as too narrow to allow him to perform any meaningful *BRCA1/2* testing. Ostrer Decl. ¶ 7.

On September 15, 1998, Myriad also notified Dr. Barbara Weber ("Dr. Weber"), a principal investigator on the Cancer Genetics Network Project ("CGNP") sponsored by the National Cancer Institute ("NCI"), that Myriad's patent position might impact research sponsored by NCI. As a result of that letter, the GDL at the University of Pennsylvania ceased conducting *BRCA1/2* analysis for Dr. Weber. Ganguly Decl. ¶ 12, Ex. 7. According to Myriad, the GDL's involvement in CGNP was to provide DNA testing on *BRCA1/2* genes for a fee, similar to the activity of any commercial core lab. Critchfield Decl. ¶ 21. In September 1999, Myriad also requested that Georgetown University, one

of the other cancer centers participating in the CGNP, to cease sending genetic samples to the GDL for *BRCA1/2* analysis. Ganguly Decl. ¶ 13.

In December 2000, the director of the Yale DNA Diagnostics Lab received a cease and desist letter concerning *BRCA1/2* genetic testing being conducted by the lab. As a result of the letter, the lab ceased *BRCA1/2* genetic testing. Matloff Decl. ¶ 7. In 2005, Dr. Matloff sought permission from Myriad for the Yale DNA Diagnostics Lab to conduct screening for mutations caused by large rearrangements, which Myriad was not conducting at the time. Her request was denied. Matloff Decl. ¶ 8.

Myriad was also involved in a series of lawsuits in the late 1990s against Oncormed, another company undertaking *BRCA*-related testing, regarding patents that covered various aspects of the *BRCA1* gene sequence. Parthasarathy Decl. ¶ 27. Myriad eventually purchased Oncormed's patents and testing services in 1998. Id.

E. Disputed Issues

1. The impact of Myriad's patents on *BRCA1/2* testing

According to Plaintiffs, Myriad's patents and its position as the sole provider of *BRCA1/2* testing has hindered the ability of patients to receive the highest-quality breast cancer genetic testing and has impeded the development of improvements to *BRCA1/2* genetic testing. Plaintiffs first note deficiencies in the genetic testing services offered by Myriad, alleging that in the several years prior to the addition of the LRP, the testing done by Myriad did not reveal all known mutations in the *BRCA1/2* genes or utilize known methodologies that would have revealed these additional mutations.[21] Chung Decl. ¶ 19; Matloff Decl. ¶ 8; Swisher Decl. ¶ 26; Ledbetter Decl. ¶ 16; Parthasarathy Decl. ¶ 29. As a result, Myriad's test may have reported false negative results during this period. Plaintiffs also cite a study published in 2006 in the Journal of the American Medical Association that concluded that 12% of those from high risk families with breast cancer and with negative test results from Myriad carried cancer-predisposing genomic deletions or duplications in one of those genes. Swisher Decl. ¶¶ 25-

[21] For example, the Myriad test received by Ms. Thomason, Ms. Raker, and Ms. Limary did not look for all known large rearrangements in the *BRCA* genes. Thomason Decl. ¶ 6; Raker Decl. ¶¶ 7-8; Limary Decl. ¶ 7.

26. Plaintiffs also note that the sensitivity and specificity of the BART test has not been validated by comparing the results of BART testing with Multiplex Ligation Dependent Probe Amplification ("MLPA") testing commonly used by researchers. Swisher Decl. ¶¶ 32, 33.

According to Plaintiffs, other labs are in a position to offer more comprehensive testing than Myriad's standard testing services and would use newer testing methods with improved testing quality and efficiency. These labs would also include large rearrangement testing after a negative test result is received from full sequencing. Ledbetter Decl. ¶¶ 17-18; Chung Decl. ¶ 18; Ostrer Decl. ¶ 9. In addition, labs would perform genetic testing on tumor specimens preserved in paraffin from deceased family members, which Myriad does not regularly perform even though, according to Plaintiffs, such testing can often provide valuable genetic information for living relatives and is often necessary for accurate test interpretation. Chung Decl. ¶ 24.

According to Myriad, however, its full sequencing test has been recognized as the "gold standard" for *BRCA1/2* mutation testing, and it continues to improve

its testing process. Critchfield Decl. ¶ 37. Myriad contends that it researched and developed a commercially viable high quality test for detecting large rearrangements as soon as it and the research community recognized the need for such testing, and continues work towards a test capable of detecting all large rearrangement mutations, including extremely rare ones. Critchfield Decl. ¶¶ 49, 50. According to Myriad, *BRCA1/2* studies conducted by outside researchers confirmed that the BART test exhibited superior performance over other methods for mutation detection, including the MLPA kit often used by academic researchers.[22] Critchfield Decl. ¶ 51.

According to Plaintiffs, the lack of independent *BRCA1/2* analysis also undermines the ability of the scientific community to determine the meaning of VUS results, which are reported disproportionately for members of minority groups, and whose significance would be more extensively analyzed by other labs. Chung Decl. ¶ 20-21; Ostrer Decl. ¶ 12; Matloff Decl. ¶ 9. Myriad, however, asserts that it has undertaken significant efforts to determine the clinical importance of VUSs by establishing

[22] In addition, Myriad states that the MLPA kit is for research use only, is not approved for clinical testing by the FDA, and is incapable of detecting certain smaller rearrangements. Critchfield Decl. ¶¶ 49, 50.

an in-house review committee for variant classification and developing a systematic approach to providing clinical interpretations for detected sequence variants based on generally accepted scientific data and analysis of its own database. In addition, clarification of any VUS previously reported to a patient is immediately provided to the patient and her doctor. According to Myriad, the VUS reporting rate has decreased markedly, with a 50% decrease in major ethnic groups between 2002 and 2006, and a total of 850 VUSs for about 21,000 patients have been clarified, including 502 VUSs for 13,127 patients since the beginning of 2008. Myriad also asserts that it has made critical data available to researchers to assist in the analysis of VUSs and which have the potential of improving the diagnostic testing for other genes. Critchfield Decl. ¶¶ 57-59.

Plaintiffs contend that as a result of the patents-in-suit, *BRCA1/2* genetic testing is one of the very few tests performed as part of breast cancer care and prevention for which a doctor or patient cannot get a second confirmatory test done through another laboratory. Love Decl. ¶ 12. In particular, women who receive a positive result cannot confirm the lab's findings or seek a

second opinion on the interpretation of those results.[23] Ledbetter Decl. ¶ 23; Ostrer Decl. ¶ 11. According to Myriad, absent any doubts regarding the accuracy of the original test, resequencing the patient's genes by another laboratory would be an unnecessary waste of resources, and Myriad has never prohibited a second interpretation of the results of its diagnostic tests. Critchfield Decl. ¶ 64; Reilly Decl. ¶¶ 54, 55. In addition, there are multiple laboratories available to conduct confirmatory *BRCA1/2* testing pursuant to patent licenses granted by Myriad, including both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Critchfield Decl. ¶ 62. That confirmatory testing, however, is limited to the confirmation of certain, specific positive test results; the remaining types of positive test results as well as all negative test results are excluded from such testing services. Matloff Decl. ¶¶ 9, 10.

Whether the patents at issue impact the testing

[23] For example, Ms. Girard sought but was unable to obtain confirmatory testing of her Myriad test results that indicated the presence of a deleterious mutation in her *BRCA2* gene. A second opinion would also be important for her immediate family's screening options. Girard Decl. ¶¶ 4-9. Similarly, Ms. Ceriani and Ms. Fortune would both want a second opinion concerning their *BRCA1/2* status before taking major surgical steps. Ceriani Decl. ¶¶ 9, 11; Fortune Decl. ¶ 7.

for *BRCA1/2* mutations favorably or unfavorably is an issue of factual dispute not resolvable in the context of the instant motions.

2. The impact of gene patents on the advancement of science and medical treatment

There exists a deep disagreement between the parties concerning the effects of gene patents on the progression of scientific knowledge.

According to Plaintiffs, data sharing is the key to the future of genetic discoveries and bioinformatics, and gene patents impede research aimed at identifying the role of genes in medical conditions. Sulston Decl. ¶¶ 36, 38. Plaintiffs assert that this understanding has wide acceptance, noting that from the beginning of the Human Genome project,[24] most scientists and even some private companies recognized the importance of keeping the genome freely available to all. For example, in 1994, the pharmaceutical company Merck funded a massive drive to generate gene sequences and place them into public

[24] The Human Genome Project was an international project initiated in 1990 with the aim of sequencing an entire human genome and in which Sir John Sulston, a Nobel laureate, actively participated. Sulston Decl. ¶¶ 5, 22.

databases, thereby making them difficult to patent. Sulston Decl. ¶¶ 22, 29. In 1996, a group of 50 of the most prominent geneticists who were involved with the sequencing of the human genome adopted the Bermuda principles which included the mandate that all "human genome sequence information should be freely available and in the public domain in order to encourage research and development and to maximize its benefit to society." Sulston Decl. ¶ 33. The proliferation of intellectual property rights directed to genetic material has also been postulated to contribute to a phenomenon dubbed "the tragedy of the anti-commons," in which numerous competing patent rights held by independent parties prevents any one party from engaging in productive innovation. See, e.g., Michael A. Heller & Rebecca S. Eisenberg, Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 Science 698 (1998) (citing Michael A. Heller, The Tragedy of the Anticommons: Property in the Transition from Marx to Markets, 111 Harv. L. Rev. 621 (1998)).

According to Dr. Fiona Murray ("Dr. Murray"), who received a grant to research the impact of gene patenting on scientific research and commercialization, 4382 of the 23,688 genes listed in the database of the National Center

for Biotechnology Information ("NCBI") - nearly 20% of human genes - are explicitly claimed as United States intellectual property. Murray Decl. ¶ 6. After devising a study to gauge the impact of gene patenting on public knowledge that utilized the time lag between publication of papers on a gene sequence and the issuance of a patent claiming that gene sequence, Dr. Murray concluded that the Myriad patents have negatively impacted the public knowledge of the *BRCA1* and *BRCA2* genes by 5-10%. Murray Decl. ¶¶ 7-15, 20.

Plaintiffs have cited other studies to demonstrate the chilling effect of gene patents on the advancement of both genetic research and clinical testing. A survey of laboratory directors in the United States conducted by Dr. Mildred Cho (the "Cho study") found that 53% decided not to develop a new clinical test because of a gene patent or license, and 67% believed that gene patents decreased their ability to conduct research. Cho Decl. ¶ 10. This correlated with a study conducted by the American Society of Human Genetics that reported that 46% of respondents felt that patents had delayed or limited their research. Cho Decl. ¶ 11. The Cho study also revealed that of those who stopped performing a clinical test

because of a gene patent or license, the largest number stopped doing *BRCA1* and *BRCA2* testing (with the same number having stopped Apolipoprotein E testing). Cho Decl. ¶ 16. Specifically, the survey found that nine labs had ceased performing *BRCA1/2* genetic testing as a result of the patents-in-suit. In addition to labs that have ceased performing *BRCA1/2* genetic testing, labs have avoided or refrained from developing tests for *BRCA1* and *BRCA2* as a result of the patents held by Myriad. Ostrer Decl. ¶ 6; Ledbetter Decl. ¶¶ 14-16. Studies of other gene patents have also revealed that labs frequently stop developing or offering clinical tests for disease as a result of gene patents. For example, a purportedly valid scientific survey of labs in the United States found a 26% drop in the number of labs performing testing for hemochromatosis as a result of gene patents. Cho Decl. ¶¶ 18-20.

Researchers, clinicians, and pathologists are aware that Myriad has sent cease and desist letters in connection with the patents-in-suit and that Myriad prohibits clinical testing of the *BRCA1/2* genes. Kazazian Decl. ¶¶ 5-11; Ganguly Decl. ¶¶ 4-14; Chung Decl. ¶ 15; Hegde Decl. ¶ 10; Matloff Decl. ¶¶ 5-7; Ostrer Decl. ¶¶ 4-7; Swisher Decl. ¶ 28; Hubbard Decl. ¶¶ 7-8; Kant Decl. ¶

4; Ledbetter Decl. ¶ 13; Reich Decl. ¶¶ 3, 5; Parthasarathy Decl. ¶¶ 28-31. Myriad also does not permit researchers to tell patients involved in research the results of their *BRCA1/2* testing, leading physicians involved in breast cancer care and research unable to meet their ethical obligations to provide genetic test results to research subjects, when requested. Ostrer Decl. ¶ 10; Chung Decl. ¶ 13, 14. In addition to the direct benefits to the patient of knowing the results of their testing, such disclosure would also provide valuable insights into patient behavior that would enhance patient care. Ostrer Decl. ¶ 10. The AMA has also expressed its belief that the "[t]he use of patents . . . or other means to limit the availability of medical procedures places significant limitation on the dissemination of medical knowledge, and is therefore unethical." American Medical Association, Opinion 9.095 - The Use of Patents and Other Means to Limit Availability of Medical Procedures, (adopted June 1995), available at http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion9095.shtml. In addition, others have argued that human genes are the common heritage of mankind whose use should not be restricted by patent grants. See, e.g., Pilar A. Ossorio, The Human Genome as Common Heritage:

Common Sense or Legal Nonsense?, 35 J.L. Med. & Ethics 425, 426 (2007); Melissa L. Sturges, Who Should Hold Property Rights to the Human Genome? An Application of the Common Heritage of Humankind, 13 Am. U. Int'l L. Rev. 219, 245 (1997); Barbara Looney, Should Genes Be Patented? The Gene Patenting Controversy: Ethical and Policy Foundations of an International Agreement, 26 Law & Pol'y Int'l Bus. 231 (1994); Hubert Curien, The Human Genome Project and Patents, 254 Science 1710, 1710-12 (1991).

According to Plaintiffs, Myriad has withheld critical data concerning genetic predisposition to breast cancer from the Breast Cancer Information Core ("BIC"), an international, open access online database that is a central repository for information about the *BRCA1/2* genes and their genetic variants. The BIC facilitates the identification of deleterious mutations (i.e. those associated with a higher risk of cancer), provides a mechanism to collect and distribute data about genetic variants, and plays an important role in helping to elucidate the significance of those variants through its collection of data. Swisher Decl. ¶¶ 15, 17, 18; Chung Decl. ¶ 22; Ostrer Decl. ¶ 13. Although the value of the BIC comes from the amount and quality of data provided by

the scientific community, Myriad, according to Plaintiffs, has not contributed any data to BIC in the past two years. Sulston Decl. ¶ 36; Swisher Decl. ¶¶ 19-21; Ostrer Decl. ¶¶ 12-13; Chung Decl. ¶¶ 21-22; Ledbetter Decl. ¶ 20.

Plaintiffs also assert that gene patents impede the development of improved genetic testing. For example, as new sequencing technologies offer the possibility of faster and less expensive sequencing of a patient's genes, patents on one or more genes may impede scientists' ability to develop a comprehensive test for complex diseases or provide a person with an analysis of his or her entire genome. Sulston Decl. ¶ 38; Ledbetter Decl. ¶ 24. In addition, Plaintiffs assert that gene patents interfere with the ability of physicians and researchers to investigate complex diseases. For example, *BRCA1/2* may be associated with cancers other than breast and ovarian cancer, but so long as the patents on these genes remain, no one will be able to include these genes in tests for other disease predispositions. Ledbetter Decl. ¶¶ 24-25. Gene patents similarly impede the development and improvement of tests for diseases by geneticists. Ledbetter Decl. ¶¶ 14-15. Plaintiffs also assert that allowing only a single lab to offer testing means that the

one lab dictates the standards for patient care in testing for that disease; in contrast, patient care is promoted when more than one lab offers a particular genetic test, utilizing different methodologies, since this can ensure the quality of the testing and accuracy of the test results. Chung Decl. ¶ 23; Ledbetter Decl. ¶ 23; Reich Decl. ¶¶ 9, 11; Ostrer Decl. ¶ 11; Parthasarathy Decl. ¶ 31.

Plaintiffs further assert that gene patents are not necessary to create incentives for initial discoveries or the development of commercial applications, including diagnostic tests. Cho Decl. ¶ 25; Leonard Decl. ¶¶ 20-21. Patents have not been necessary for the rapid introduction of genetic testing, as evidenced by genetic testing that has been offered prior to the issuance of a patent. Cho Decl. ¶ 21. In support of this assertion, Plaintiffs cite a study of gene patents issued in the United States for genetic diagnostics that showed that 67% of these patents were issued for discoveries funded by the U.S. government. Cho Decl. ¶ 22. Similarly, another study showed that 63% of patents on gene sequences resulted from federally supported research. Leonard Decl. ¶ 22. As previously noted, the NIH provided $2 million in research grants to

the University of Utah, or approximately one-third of the total funding, for the identification of the *BRCA1* sequence. Parthasarathy Decl. ¶ 18.

Myriad has contested these assertions and disputes the idea that patenting of isolated human DNA conflicts with the advancement of science. According to Myriad, the quid pro quo of the patent system is that inventors, in exchange for a limited period of patent exclusivity, must provide a sufficient description of the patented invention so that others may improve upon it. Reilly Decl. ¶ 24; Doll Decl. ¶ 44. Furthermore, according to Myriad, its policy and practice has been and still is to allow scientists to conduct research studies on *BRCA1* and *BRCA2* freely, the result of which has been the publication of over 5,600 research papers on *BRCA1* and over 3,000 research papers on *BRCA2*, representing the work of over 18,000 scientists. Critchfield Decl. ¶¶ 3, 13; Li Decl. ¶¶ 3-6; Baer Decl. ¶¶ 3-6; Parvin Decl. ¶¶ 3-6; Sandbach Decl. ¶¶ 3-7.

According to Myriad, patents on isolated DNA, including the patents-in-suit, actually promote research and advance clinical development to the benefit of

patients. Reilly Decl. ¶¶ 38, 43; Critchfield Decl. ¶¶ 2-18, 65, 68; Linck Decl. ¶¶ 27-28, 71, 73; Tavtigian Decl. ¶¶ 14-17; Doll Decl. ¶¶ 45-46; Schlessinger Decl. ¶¶ 31-32. Myriad has contended that gene patents are essential for obtaining capital investment in the development and commercialization of technological breakthroughs. Linck Decl. ¶¶ 27, 28; Reilly Decl. ¶ 16; Doll Decl. ¶ 46. In support, Myriad has cited a survey published in 2009 by the BIO of 150 biotechnology member companies in the therapeutic and diagnostic healthcare industry stating that the majority of companies (61%) generally in-licensed projects that are in the pre-clinical or Phase I stage of development, and thus still require substantial R&D investment and commercialization risk by the licensee. A substantial majority (77%) of the respondents without approved products indicated that they expect to spend 5-15 years and over $100 million developing a commercial product. Myriad asserts that these expenditures dwarf any initial research funding by the federal government. Reilly Decl. ¶ 22. In particular, Myriad notes that a significant amount of private investment led to its identification of the *BRCA1* and *BRCA2* sequences, with the expectation of patent protection providing an incentive to fund the research into the determination of the gene sequences.

Skolnick Decl. ¶¶ 14-16. Therefore, Myriad asserts that absent the promise of a period of market exclusivity provided by patents and the infusion of venture and risk capital derived therefrom, companies such as Myriad that capitalize on innovation simply would not be created and their products would not be brought to market or the clinic. Reilly Decl. ¶¶ 18, 34, 51, 52, 62; Critchfield Decl. ¶¶ 67, 68; Linck Decl. ¶ 73.

Myriad also notes that it has made over 20,000 submissions to the BIC database, making it the largest contributor to the database. It has also published the largest clinical series of mutation risk in the *BRCA1/2* genes based on its testing data and has tabulated and posted the data on Myriad's website, where it is freely available to researchers throughout the world. Critchfield Decl. ¶¶ 11, 12.

According to Myriad, the majority of academic researchers operating laboratories (as opposed to Clinical Laboratory Improvement Amendments ("CLIA")-certified laboratories) do not believe that they should share test results with subjects outside of the standard clinical setting. Reilly Decl. ¶¶ 57-59.

As the declarations submitted by the parties make clear, there exists a sharp dispute concerning the impact of patents directed to isolated DNA on genetic research and consequently the health of society. As with the dispute concerning the effect of the patents-in-suit on *BRCA1/2* genetic testing, the resolution of these disputes of fact and policy are not possible within the context of these motions.

IV. THE PATENTS

A. Summary of the Patents

The subjects of this declaratory judgment action are fifteen claims contained in seven patents issued by the USPTO:[25] claims 1, 2, 5, 6, 7, and 20 of U.S. patent 5,747,282 (the "'282 patent"); claims 1, 6, and 7 of U.S. patent 5,837,492 (the "'492 patent"); claim 1 of U.S. patent 5,693,473 (the "'473 patent"); claim 1 of U.S. patent 5,709,999 (the "'999 patent"); claim 1 of U.S.

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

patent 5,710,001 (the "'001 patent"); claim 1 of U.S. patent 5,753,441 (the "'441 patent"); and claims 1 and 2 of U.S. patent 6,033,857 (the "'857 patent").[26]

The claims-in-suit may be divided into two types of claims: composition claims and method, or process, claims. Independent claim 1 of the '282 patent is representative of the group of composition claims and claims:

> An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

This claim is therefore directed to an isolated DNA molecule possessing a nucleotide sequence that translates into the BRCA1 protein. Because most amino acids can result from the translation of more than one DNA codon, multiple DNA sequences correspond to the nucleotide sequence claimed by this claim. Claim 2 of the '282 patent is dependent on claim 1 but contains an additional limitation that identifies the specific *BRCA1* nucleotide

[26] For purposes of understanding what the claim terms would have meant to a person of ordinary skill in the art at the time of the application for the patents, an application date of August 1994 is presumed for the '282, '473, '999, '001, and '441 patents and December 1995 for the '492 and '857 patents.

sequence of the claimed DNA.[27] Claims 5 and 6 of the '282 patent are directed to fragments as short as 15 nucleotides of the DNA molecules claimed in claims 1 and 2 of the '282 patent.[28] Finally, claim 7 of the '282 patent and claim 1 of the '473 patent are directed to isolated DNA possessing one of the specified mutant *BRCA1* gene sequences.[29]

Claims 1, 6, and 7 of the '492 patent are also composition claims covering isolated DNA molecules containing certain specified nucleotide sequences relating to the *BRCA2* gene. Claim 1 is directed to an isolated DNA molecule encoding the BRCA2 protein.[30] Like claim 1 of the '282 patent, claim 1 of the '492 patent is directed to multiple possible DNA sequences as a result of the

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[27] Claim 2 of the '282 patent reads: "The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

[28] Claim 5 of the '282 patent claims: "An isolated DNA having at least 15 nucleotides of the DNA of claim 1."
Claim 6 of the '282 patent reads: "An isolated DNA having at least 15 nucleotides of the DNA of claim 2."

[29] Claim 7 of the '282 patent reads: "An isolated DNA selected from the group consisting of: (a) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having T at nucleotide position 4056; (b) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having an extra C at nucleotide position 5385; (c) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having G at nucleotide position 5443; and (d) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having 11 base pairs at nucleotide positions 189-199 deleted."
Claim 1 of the '473 patent reads: "An isolated DNA comprising an altered BRCA1 DNA having at least one of the alterations set forth in Tables 12A, 14, 18 or 19 with the proviso that the alteration is not a deletion of four nucleotides corresponding to base numbers 4184-4187 in SEQ. ID. NO:1."

[30] Claim 1 of the '492 patent reads: "An isolated DNA molecule coding for a BRCA2 polypeptide, said DNA molecule comprising a nucleic acid sequence encoding the amino acid sequence set forth in SEQ ID NO:2."

redundancy of the DNA codons. Claim 6 of the '492 patent, however, is considerably broader than claim 1 and is directed to any DNA nucleotide encoding any mutant BRCA2 protein that is associated with a predisposition to breast cancer.[31] Claim 7 of the '492 patent depends on claim 6, but is restricted to the mutated forms of the *BRCA2* nucleotide sequence set forth in the specification.[32] As a result of the breadth of these composition claims, they reach isolated *BRCA1/2* DNA obtained from any human being.

Claim 1 of the '999 patent is representative of the group of method claims. It claims:

> A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from a group consisting of the alterations set forth in Tables 12A, 14, 18, or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1.

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[31] Claim 6 of the '492 patent reads: "An isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide set forth in SEQ ID NO:2, wherein said mutated form of the BRCA2 polypeptide is associated with susceptibility to cancer."

[32] Claim 7 of the '492 patent reads: "The isolated DNA molecule of claim 6, wherein the DNA molecule comprises a mutated nucleotide sequence set forth in SEQ ID cNO:1."

Thus, claim 1 of the '999 patent covers the process of identifying the existence of certain specific mutations in the *BRCA1* gene by "analyzing" the sequence of the *BRCA1* DNA, RNA, or cDNA made from *BRCA1* RNA obtained from a human sample.

Most of the remaining method claims-in-suit are similarly structured and directed to the comparison of gene sequences. Claim 1 of the '001 patent claims a method for determining whether a human tumor sample contains a mutation in the *BRCA1* gene by "comparing" the sequence of the *BRCA1* gene from the tumor with the sequence of the *BRCA1* gene from a non-tumor sample from the same person.[33] Claim 1 of the '441 patent and claim 1 of the '857 are both directed to the same process, differing only as to whether the claimed method is directed to *BRCA1* ('441) or *BRCA2* ('857). Both of these independent claims are directed to the process of determining whether an individual has

[33] Claim 1 of the '001 patent reads: "A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises gene comparing a first sequence selected form [sic] the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample."

inherited an altered *BRCA1* or *BRCA2* gene by "comparing" the individual's *BRCA1* or *BRCA2* gene sequence with the wild-type *BRCA1* or *BRCA2* gene sequence.[34] Claim 2 of the '857 patent covers a method for determining whether an individual has a predisposition for breast cancer by "comparing" the individual's *BRCA2* gene sequence with the known wild-type *BRCA2* gene sequence.[35]

Finally, claim 20 of the '282 patent claims a method for determining the effectiveness of a potential cancer therapeutic comprising growing cells carrying an altered *BRCA1* gene known to cause cancer in the presence and absence of a potential cancer therapeutic, comparing the growth rates of the cells, and concluding that a slower

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[34] Claim 1 of the '441 patent reads: "A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises comparing germline sequence of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a sequence of BRCA1 cDNA made from mRNA from said sample with germline sequences of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA1 cDNA, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject." Claim 1 of the '857 patent claims: "A method for identifying a mutant BRCA2 nucleotide sequence in a suspected mutant BRCA2 allele which comprises comparing the nucleotide sequence of the suspected mutant BRCA2 allele with the wild-type BRCA2 nucleotide sequence, wherein a difference between the suspected mutant and the wild-type sequences identifies a mutant BRCA2 nucleotide sequence."

[35] Claim 2 of the '857 patent reads: "A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the germline sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from said subject with the germline sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the germline sequence of the BRCA2 gene or the sequence of its mRNA of the subject indicates a predisposition to said cancer."

growth rate in the presence of the potential therapeutic indicates that it is indeed a cancer therapeutic.[36]

B. Construction of the Claims[37]

1. Legal standard

Before considering the patent-eligibility of a patent claim, the disputed terms in the claims must be construed in order ensure the scope of the claims 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."). Courts are charged with interpreting disputed

[36] Claim 20 of the '282 patent reads: "A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer n 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."

[37] In addition to the claim terms discussed below, the parties also dispute the proper interpretation of the method claims – i.e., whether they may be construed to encompass certain transformative steps. Because this issue is broader in scope than simple claim term definition, it is addressed *infra* in Section VII.D.

claim terms as a matter of law. Markman v. Westview Instruments, Inc., 517 U.S. 370, 384-85 (1996).

In interpreting the meaning of claim terms, "words of a claim are generally given their ordinary and customary meaning" to a person of ordinary skill in the art at the time of invention (i.e., the effective filing date of the patent application). Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (internal citations and quotation marks omitted). "Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." Id. at 1313. Thus, the Federal Circuit has emphasized the importance of "intrinsic" evidence in claim construction: the words of the claim themselves, the written description in the patent's specification, and, when necessary, the history of the patent application's prosecution before the USPTO. Id. at 1314-17.

The process of claim construction begins with the language of the claims themselves. The language of the claim is what the patentee chose to use to "'particularly

point[] out and distinctly claim[] the subject matter which the applicant regards as his invention.'" Id. at 1311-12 (quoting 35 U.S.C. § 112, ¶ 2). Thus, "the claims themselves provide substantial guidance as to the meaning of particular claim terms." Id. at 1314. In addition to the particular claim being examined, the context provided by other claims may be helpful as well. "For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." Id. at 1314-15.

Claim language must also be read in the context of the specification. Id. at 1315. As the Federal Circuit has made clear, "claims, of course, do not stand alone. Rather, they are part of 'a fully integrated written instrument,' consisting principally of a specification that concludes with the claims." Id. (quoting Markman v. Westview Instruments, Inc., 52 F.3d 967, 978 (Fed. Cir. 1995)). "For that reason, claims 'must be read in view of the specification, of which they are a part.'" Id. (quoting Markman, 52 F.3d at 979). The specification "is always highly relevant to the claim construction analysis. Usually it is dispositive; it is the single best guide to

the meaning of a disputed term." Id. (quoting Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Moreover, when the patentee "act[s] as his or her own lexicographer" and includes an explicit definition of a claim term in the specification, that definition is dispositive over any ordinary meaning. Id. at 1319 (internal citation and quotation marks omitted); see also Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1344 (Fed. Cir. 1998).

In relying on the specification to interpret claim terms, the Federal Circuit has also "repeatedly warned against confining the claims" to the embodiments described in the specification. Phillips, 415 F.3d at 1323. The mistake of "reading a limitation from the written description into the claims" is "one of the cardinal sins of patent law." Id. at 1320 (quoting SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1340 (Fed. Cir. 2001)).

Courts may also utilize the prosecution history which "consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent . . . . [T]he prosecution

history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." Id. at 1317 (internal citations omitted). However, the prosecution history "often lacks the clarity of the specification and thus is less useful for claim construction purposes." Id.

Lastly, courts may rely on extrinsic evidence such as dictionaries, treatises, and expert testimony, which may serve to provide a source of "accepted meaning of terms used in various fields of science and technology," or by providing "background on the technology at issue." Id. at 1317-18. However, such "extrinsic" evidence is "less significant than the intrinsic record in determining the legally operative meaning of the claim language." Id. at 1317 (internal citations and quotation marks omitted). The use of extrinsic evidence may not be used to contradict the meaning of the claim terms as evidenced by the intrinsic evidence. Id. at 1317-19; see also Biagro W. Sales, Inc. v. Grow More, Inc., 423 F.3d 1296, 1302 (Fed. Cir. 2005).

2. Resolution of the disputed claim terms

a. "DNA" and "isolated DNA"

The parties approach the terms "DNA" and "isolated DNA" from opposing perspectives.[38] Plaintiffs contend that the term "DNA" means "a sequence of nucleic acids, also referred to as nucleotides" and therefore constitutes a "nucleotide sequence" or a "polynucleotide." Pl. Br. at 10.[39] Myriad disputes Plaintiffs' definition of "DNA" insofar as Plaintiffs' definition suggests that the term "DNA" refers merely to information, that is, "a description of the linear order of nucleotide units that make up the polynucleotide." Myriad Br. at 15. Myriad

[38] The degree to which the parties actually disagree on the meaning of the discussed claim terms is unclear; however, to the extent some disagreement has been noted by the parties, this section seeks to resolve them.

[39] For purposes of this opinion, "Pl. Br." refers to Plaintiffs' Memorandum of Law in Support of Motion for Summary Judgment; "Myriad Br." refers to Myriad Defendants' Memorandum of Law (1) in Support of Their Motion for Summary Judgment and (2) in Opposition to Plaintiffs' Motion for Summary Judgment; "Pl. Reply" refers to the Memorandum of Law (1) in Further Support of Plaintiffs' Motion for Summary Judgment Against All Defendants and (2) in Opposition to the Myriad Defendants' Motion for Summary Judgment and (3) in Opposition to Defendant United States Patent and Trademark Office's Motion for Judgment on the Pleadings; "Myriad Reply" refers to Myriad Defendants' Memorandum in Reply to Plaintiffs' Opposition to Myriad Defendants' Motion for Summary Judgment; and "USPTO Reply" refers to the Reply Memorandum of Law in Further Support of Defendant United States Patent and Trademark Office's Motion for Judgment on the Pleadings and in Opposition to Plaintiffs' Motion for Summary Judgment.

instead argues that "DNA" refers to "a real and tangible molecule, a chemical composition made up of deoxyribonucleotides linked by a phosphodiester backbone." Myriad Br. at 14.

As its name implies, DNA, or deoxyribonucleic acid, is an acid - a tangible, chemical compound. As Myriad correctly notes, the specifications make clear that "DNA," as used in the patents, refers to the physical manifestation of the acid, one that may be "substantially separated from other cellular components which naturally accompany a gene." '473 patent, col. 19:8-9; '282 patent, col. 19:10-11; '492 patent, col. 17:64-65. Despite the description of the term "DNA" set forth in the briefs, this understanding of the meaning of "DNA" is shared by both Plaintiffs' and Myriad's declarants. See Kay ¶ 125; Linck ¶ 45; Schlessinger ¶ 12; Grody ¶ 10; Leonard ¶ 30.

The term "isolated DNA" is defined by Plaintiffs as "a fragment of DNA substantially separated from other cellular components and other DNA." Pl. Br. at 10. Myriad disputes Plaintiffs' definition insofar as it implies that fragments of DNA exist free-floating in the cell, separate from other cellular components, such as proteins and the

other DNA in the chromosome. Myriad Br. at 16. The patent specifications expressly define "isolated DNA" as a DNA molecule "which is substantially separated from other cellular components which naturally accompany a native human sequence [such as] human genome sequences and proteins" and "includes recombinant or cloned DNA isolates and chemically synthesized analogs or analogs biologically synthesized by heterologous systems." '473 patent, col. 19:6-15; '282 patent, col. 19:8-18; '492 patent, col. 17:62-18:5.

"Isolated DNA" is therefore construed to refer to a segment of DNA nucleotides existing separate from other cellular components normally associated with native DNA, including proteins and other DNA sequences comprising the remainder of the genome, and includes both DNA originating from a cell as well as DNA synthesized through chemical or heterologous biological means.

b. "BRCA1" and "BRCA2"

Plaintiffs define the term "BRCA1" as "a particular fragment of DNA found on chromosome 17 that

relates to a person's predisposition to develop breast and ovarian cancer." Pl. Br. at 11. Similarly, Plaintiffs define the term "BRCA2" as "a particular fragment of DNA found on chromosome 13 that relate[s] to a person's predisposition to develop breast and ovarian cancer." Pl. Br. at 14. As with Plaintiffs' proposed definition of "isolated DNA," Myriad argues that these definitions are inconsistent with the patents' definition of "BRCA1" and "BRCA2" as "cancer-predisposing gene[s], some alleles of which cause susceptibility to breast and ovarian cancers" because they suggest that the *BRAC1* and *BRCA2* genes are not integrated into a chromosome, but are broken, detached, or otherwise easily removed from their respective chromosomes. Myriad Br. at 16.

The specifications of the patents-in-suit define the terms "BRCA1" and "BRCA2" as "a human breast cancer predisposing gene . . . some alleles of which cause susceptibility to cancer, in particular breast and ovarian cancer." '282 patent, col. 4:33-36; see also '282 patent, col. 1:22-23; '492 patent, col. 1:20-21, 4:28-29. Further, neither party disputes that "genes" refer to segments of DNA incorporated into chromosomes.

"BRCA1" is therefore construed to refer to a human gene, normally integrated into chromosome 17, some alleles of which cause susceptibility to breast and ovarian cancer. Similarly, "BRCA2" is construed to refer to a human gene, normally integrated into chromosome 13, some alleles of which cause susceptibility to breast and ovarian cancer.

V. CONCLUSIONS OF LAW

A. The Summary Judgment Standard

Summary judgment is granted only where there exists no genuine issue of material fact and the moving party is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(c); see Celotex Corp. v. Catrett, 477 U.S. 317, 322-23 (1986); SCS Commc'ns, Inc. v. Herrick Co., 360 F.3d 329, 338 (2d Cir. 2004). The courts do not try issues of fact on a motion for summary judgment, but, rather, determine "whether the evidence presents a sufficient disagreement to require submission to a jury or whether it is so one-sided that one party must prevail as a matter of law." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 251-52 (1986).

"The party seeking summary judgment bears the burden of establishing that no genuine issue of material fact exists and that the undisputed facts establish [its] right to judgment as a matter of law." Rodriguez v. City of New York, 72 F.3d 1051, 1060-61 (2d Cir. 1995). In determining whether a genuine issue of material fact exists, a court must resolve all ambiguities and draw all reasonable inferences against the moving party. See Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 587-88 (1986); Gibbs-Alfano v. Burton, 281 F.3d 12, 18 (2d Cir. 2002). However, "the non-moving party may not rely simply on conclusory allegations or speculation to avoid summary judgment, but instead must offer evidence to show that its version of the events is not wholly fanciful." Morris v. Lindau, 196 F.3d 102, 109 (2d Cir. 1999) (internal quotation marks omitted).

Summary judgment is appropriate where the moving party has shown that "little or no evidence may be found in support of the nonmoving party's case. When no rational jury could find in favor of the nonmoving party because the evidence to support its case is so slight, there is no genuine issue of material fact and a grant of summary

judgment is proper." Gallo v. Prudential Residential Servs., L.P., 22 F.3d 1219, 1223-24 (2d Cir. 1994) (internal citations omitted).

B. 35 U.S.C. § 101 and Its Scope

Section 101 of Title 35, United States Code, 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.

In interpreting this language, the Supreme Court has observed that "Congress plainly contemplated that the patent laws would be given wide scope." Diamond v. Chakrabarty, 447 U.S. 303, 308 (1980); see also J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124, 131 (2001) ("[W]e are mindful that this Court has already spoken clearly concerning the broad scope and applicability of § 101.").

However, this broad reading of § 101 and statutory patent eligibility is not without limits. "The Supreme Court has recognized that scientific principles and laws of nature, even when for the first time discovered, have existed throughout time, define the relationship of man to his environment, and, as a consequence, ought not to be the subject of exclusive rights to any one person." In re Meyer, 688 F.2d 789, 795 (C.C.P.A. 1982) (citing Leroy v. Tatham, 55 U.S. 155, 175 (1852)). Specifically, the Supreme Court has recognized three categories of subject-matter that fall outside the scope of § 101: "The laws of nature, physical phenomena, and abstract ideas have been held not patentable." Chakrabarty, 447 U.S. at 309; see also Diamond v. Diehr, 450 U.S. 175, 185 (1981). "The rule that the discovery of a law of nature cannot be patented rests, not on the notion that natural phenomena are not processes, but rather on the more fundamental understanding that they are not the kind of 'discovery' that the statute was enacted to protect." Parker v. Flook, 437 U.S. 584, 593 (1978).

The exclusion of products of nature[40] as patentable subject matter under § 101 also reflects the Supreme Court's recognition that "[p]henomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." Gottschalk v. Benson, 409 U.S. 63, 67 (1972). Thus, as Justice Breyer has observed, "the reason for this exclusion is that sometimes *too much* patent protection can impede rather than 'promote the Progress of Science and useful Arts,' the constitutional objective of patent and copyright protection." Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 126-27 (2006) (Breyer, J., dissenting) (quoting U.S. Const., Art. I, § 8, cl. 8.) (emphasis in original). For these reasons, "manifestations of laws of nature [are] free to all men and reserved

[40] Myriad distinguishes between "laws of nature," "natural phenomena," and "abstract ideas," which it concedes are not patentable, and "products of nature," for which it appears to argue no prohibition to patentability exists. Although the distinction between these two categories is unclear, it is well established that "products of nature" are not patentable. See, e.g., Chakrabarty, 447 U.S. at 13 (stating that relevant distinction for § 101 patentability is "between products of nature, whether living or not, and human-made inventions"); Gen. Elec. Co. v. De Forest Radio Co., 28 F.2d 641, 642 (3d Cir. 1928) (noting that "a patent cannot be awarded for a discovery or for a product of nature, or for a chemical element"); In re Marden, 47 F.2d 957, 957 (C.C.P.A. 1931) (concluding that "[u]ranium is a product of nature, and the appellant is not entitled to a patent on the same, or upon any of the inherent natural qualities of that metal"); In re Marden, 47 F.2d 958, 959 (C.C.P.A. 1931) (stating that "pure vanadium is not new in the inventive sense, and, it being a product of nature, no one is entitled to a monopoly of the same").

exclusively to none." Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

The inquiry into an invention's patent eligibility is a fundamental one, and as such, "[t]he obligation to determine what type of discovery is sought to be patented must precede the determination of whether that discovery is, in fact, new or obvious." Flook, 437 U.S. at 593; see also In re Bilski, 545 F.3d 943, 950 (Fed. Cir. 2008) (en banc), cert. granted, 129 S. Ct. 2735 (2009) ("Whether a claim is drawn to patent-eligible subject matter under § 101 is a threshold inquiry, and any claim of an application failing the requirements of § 101 must be rejected even if it meets all of the other legal requirements of patentability." (citing In re Comiskey, 499 F.3d 1365, 1372 (Fed. Cir. 2007)); Prometheus Labs. v. Mayo Collaborative Servs., 581 F.3d 1336, 1343 (Fed. Cir. 2009) (noting that in determining patent eligibility, "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." (citing Bilski, 545 F.3d at 958)). Consistent with this approach, the courts have rejected patent claims even when the purported invention was highly

beneficial or novel, or the research and work that went into identifying it was costly or time-consuming. See, e.g., Funk Bros., 333 U.S. at 130; Am. Fruit Growers, Inc. v. Brodgex Co., 283 U.S. 1, 11-13 (1931); Gen. Elec. Co. v. De Forest Radio Co., 28 F.2d 641, 642-43 (3d Cir. 1928).

The distinction between the § 101 inquiry into patentable subject matter and the other requirements for patentability set forth in Title 35 is of particular importance in evaluating the authorities cited by the parties and the arguments presented. The discussion of § 101 in In re Bergy, 596 F.2d 952 (C.C.P.A. 1979) by the late Honorable Giles S. Rich, one of the authors of the 1952 Patent Act, is particularly informative in clarifying the proper scope of a § 101 analysis. There, Judge Rich stated what considerations were salient - and importantly, what considerations were not - in a § 101 analysis:

> Section 101 states three requirements: novelty, utility, and statutory subject matter. The understanding that these three requirements are separate and distinct is long-standing and has been universally accepted. . . . Thus, the questions of whether a particular invention is novel or useful are questions wholly apart from whether the invention falls into a category of statutory subject matter. *Of the three requirements stated in § 101, only two, utility and statutory subject matter, are applied under § 101.* As we shall show, in 1952 Congress voiced

> its intent to consider the novelty of an invention under § 102 where it is first made clear what the statute means by "new," notwithstanding the fact that this requirement is first named in § 101.

Id. at 960-61 (emphasis added). Judge Rich further cautioned that "statements in the older cases must be handled with care lest the terms used in their reasoning clash with the reformed terminology of the present statute; lack of meticulous care may lead to distorted legal conclusions." Id. at 959. The Supreme Court subsequently affirmed this understanding of the § 101 analysis in Diehr, noting that while it had been argued that "novelty is an appropriate consideration under § 101," "[t]he question . . . of whether a particular invention is novel is 'wholly apart from whether from whether the invention falls into a category of statutory subject matter.'" 450 U.S. at 189-90 (quoting Bergy, 596 F.2d at 961); see also Bilski, 545 F.3d at 958 ("So here, it is irrelevant to the § 101 analysis whether Applicants' claimed process is novel or non-obvious.").

Accordingly, in considering whether the patents-in-suit comply with § 101, the proper analysis requires determining (1) whether the claimed invention possesses

utility; and (2) whether the claimed invention constitutes statutory subject matter, that is, whether it is a "process, machine, manufacture, or composition of matter, or any new and useful improvement thereof," 35 U.S.C. § 101, or whether the claimed invention instead falls within the judicially created "products of nature" exception to patentable subject matter, i.e., "laws of nature, natural phenomenon, and abstract ideas," Chakrabarty, 447 U.S. at 309. In contrast, the question of whether an invention is "new" or "novel" over the prior art is a question addressed by § 102 and falls outside of the scope of the present § 101 analysis. Because it is undisputed that the claimed compositions and methods possess utility, the sole task of this Court is to resolve whether the claimed compositions and methods constitute statutory subject matter or fall within the judicially created products of nature exception to patentable subject matter.

C. The Composition Claims Are Invalid Under 35 U.S.C. § 101

As noted, the issue presented by the instant motions with respect to the composition claims is whether or not claims directed to isolated DNA containing naturally-occurring sequences fall within the products of

nature exception to § 101. Based upon the reasons set forth below, it is concluded that the composition claims-in-suit are excepted.

1. Consideration of the merits of Plaintiffs' challenge is appropriate.

Myriad offers several arguments for why this Court should not engage the substance of Plaintiffs' claims, but should instead dismiss them out of hand. Foremost among them is Myriad's assertion that Plaintiffs' claims should be dismissed in light of the "carefully considered policy of the USPTO," which is "entitled to great respect from the courts." Myriad Br. at 26. In so arguing, Myriad notes the presumption of validity afforded to patents, see 35 U.S.C. § 282, and the USPTO's prior consideration of the eligibility of gene-related patents, see Utility Examination Guidelines 66 Fed. Reg. 1092, 1092-99 (Jan. 5, 2001), as well as the Supreme Court's statements in J.E.M. Ag Supply, 534 U.S. 124.

The Federal Circuit has previously held that it owes no deference to USPTO legal determinations. See, e.g., Arnold P'ship v. Dudas, 362 F.3d 1338, 1340 (Fed. Cir. 2004) ("This court reviews statutory interpretation,

the central issue in this case, without deference.").
While Congress has created a presumption of validity for issued patents, approximately 40% of patents challenged in the courts have been found invalid, demonstrating that this presumption is far from absolute. See Institute for Intellectual Property & Information Law, University of Houston Law Center, Patstats.org, Full Calendar Year 2008 Report,
http://www.patstats.org/2008_Full_Year_Posting.rev3.htm (indicating that 40% of all validity determinations in federal court in 2008 found the challenged patent invalid); Paul F. Morgan & Bruce Stoner, Reexamination v. Litigation - Making Intelligent Decisions in Challenging Patent Validity, 86 J. Pat. & Trademark Off. Soc'y 441-461 (2004) (citing USPTO statistics showing that 74% of patents previously issued by the Patent Office and later challenged through the reexamination process were either canceled or changed by the USPTO). Moreover, the lack of Congressional action to specifically prohibit gene patents in response to the USPTO's prior grant of such patents does not preclude their review by the courts. For example, in Bilski, 545 F.3d 943, the Federal Circuit set out a test for the patentability of method claims that potentially will invalidate thousands of patents on business method patents,

despite Congress' silence concerning the patentability of such methods. Finally, while the Supreme Court in J.E.M. Ag Supply noted the USPTO's practice of issuing patents on sexually reproducing plants in concluding that such plants represented patentable subject matter under § 101, that passing observation was neither dispositive nor central to the Court's holding and does not establish a rule of judicial deference to the USPTO's practices. See J.E.M. Ag Supply, 534 U.S. at 144-45. Indeed, the judicial deference urged by Myriad is difficult to reconcile with the courts' consideration of the substantive issues presented in cases such as Chakrabarty and indeed, J.E.M. Ag Supply itself.

Moreover, in the absence of a § 101 challenge to patent validity, the fact that courts have previously upheld the validity of patents directed to biological products in response to § 102 and/or § 103 challenges has no bearing on the present inquiry. See, e.g., In re Kubin, 561 F.3d 1351 (Fed. Cir. 2009) (considering obviousness of claims); In re O'Farrell, 853 F.2d 894 (Fed. Cir. 1988) (same). The Patent Act sets out patent invalidity as an issue to be raised by the parties, see 35 U.S.C. § 282, and it would be erroneous to treat a case involving DNA-related patents as holding that isolated human genes constitute

patentable subject matter under § 101. Were that the case, the Supreme Court could have proceeded with its consideration of Metabolite Labs., after it granted certiorari and the parties and amici had fully briefed the issue of patentable subject matter eligibility, rather than dismissing certiorari as improvidently granted based on the parties' failure to raise the § 101 issue below. 548 U.S. 124.

Finally, Myriad's suggestion that invalidating the patents-in-suit would constitute an unconstitutional taking in violation of the Fifth Amendment of the Constitution or a violation of the United States' obligations under the Agreement on Trade-Related Aspects of Intellectual Property Rights ("TRIPS") is unpersuasive. Myriad's novel takings argument runs counter to a long history of invalidation of patent claims by the courts and is unsupported by legal precedent. Similarly, Articles 8.1 and 27.3 of TRIPS permit governments to incorporate public health concerns into their intellectual property laws and to exclude from patentability diagnostic, therapeutic, or surgical methods as well as particular inventions on the grounds of public interest. As a result, invalidation of the patents-in-suit would constitute neither a

constitutional violation nor a conflict with the United States' treaty obligations.

2. Patentable subject matter must be "markedly different" from a product of nature

Supreme Court precedent has established that products of nature do not constitute patentable subject matter absent a change that results in the creation of a fundamentally new product. In American Fruit Growers, the Supreme Court rejected patent claims covering fruit whose skin had been treated with mold-resistant borax. Acknowledging that the "complete article is not found in nature," and "treatment, labor and manipulation" went into producing the fruit, the Court nonetheless held that the fruit did not become an "article of manufacture" unless it "possesses a new or distinctive form, quality, or property" compared to the naturally-occurring article.[41] 283 U.S. at 11. The Court went on to observe:

[41] Myriad argues that American Fruit Growers was decided on novelty grounds, rather than subject matter patentability. See Myriad Br. at 26. However, the Court's novelty discussion was restricted to its analysis of the process claims. Am. Fruit Growers, 283 U.S. at 13-14 ("If it be assumed that the process claims under consideration cover an invention, we think this lacked novelty when application was made for the patent August 13, 1923"). In contrast, its rejection of the composition claims was based on an analysis of subject matter patentability. See id. at 11 ("Is an orange, the rind of which has become impregnated with borax, through immersion in a solution, and thereby resistant to blue mold decay, a 'manufacture,' or manufactured article, within the meaning of section 31, title 35, U.S. Code?").

> Manufacture implies a change, but every change is not manufacture, and yet every change in an article is the result of treatment, labor, and manipulation. But something more is necessary . . . . There must be transformation; a new and different article must emerge having a distinctive name, character, or use.

Id. at 12-13 (quoting Anheuser-Busch Brewing Ass'n v. United States, 207 U.S. 556, 562 (1908)) (internal citation and quotation marks omitted).

Similarly, in Funk Brothers, the Supreme Court considered whether a mixture of several naturally-occurring species of bacteria was patentable.[42] 333 U.S. at 128-31. Each species of bacteria in the mixture could extract nitrogen from the air for plant usage. While the patent holder had created a mixture by selecting and testing for strains of bacteria that did not mutually inhibit one another, the Court concluded that the patent holder "did not create a state of inhibition or of non-inhibition in the bacteria. Their qualities are the work of nature. Those qualities are of course not patentable." Id. at 130.

[42] Myriad suggests that the Supreme Court's holding in Funk Brothers was premised on an obviousness determination, rather than patentable subject matter. Subsequent Supreme Court opinions, however, have treated the holding in Funk Brothers as a statement of patentable subject matter. See Chakrabarty, 447 U.S. at 309-10; Flook, 437 U.S. at 591-92; Benson, 409 U.S. at 67-68.

Most recently, the Supreme Court addressed the application of § 101 to product claims in Diamond v. Chakrabarty, 447 U.S. 303. In Chakrabarty, the Court considered whether a "live, human-made micro-organism is patentable subject matter under 35 U.S.C. § 101." Id. at 305. The microorganism in question was a bacterium that had been genetically engineered to break down multiple components of crude oil and possessed considerable utility in the treatment of oil spills. Id. In concluding that the man-made bacterial strain was patentable, the Court observed that the claim "is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter - a product of human ingenuity 'having a distinctive name, character [and] use.'" Id. at 309-10 (quoting Hartranft v. Wiegmann, 121 U.S. 609, 615 (1887)). The Court went on to contrast the Chakrabarty bacterium with the bacterial mixture at issue in Funk Brothers, stating that in Chakrabarty's case, "the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own . . . ."

Id. at 310.[43] This requirement that an invention possess "markedly different characteristics" for purposes of § 101 reflects the oft-repeated requirement that an invention have "a new or distinctive form, quality, or property" from a product of nature. Am. Fruit Growers, 283 U.S. at 11; In re Merz, 97 F.2d 599, 601 (C.C.P.A. 1935) ("[M]ere purification of known materials does not result in a patentable product," unless "the product obtained in such a case had properties and characteristics which were different in kind from those of the known product rather than in degree.").

Courts have also specifically held that "purification" of a natural compound, without more, is insufficient to render a product of nature patentable. In The American Wood-Paper Co. v. The Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566 (1874), the Supreme Court held that refined cellulose, consisting of purified pulp derived from wood and vegetable, was unpatentable because it was "an extract obtained by the decomposition or disintegration

[43] Although Chakrabarty is often cited for the proposition that "anything under the sun that is made by man" is patentable, id. at 309, that phrase is a misleading quotation from the legislative history of the Patent Act of 1952. The full quote clearly acknowledges the statutory limitations to patentable subject matter: "A person may have 'invented' a machine or a manufacture, which may include anything under the sun made by man, but it is not necessarily patentable under section 101 unless the conditions of the title are fulfilled." H.R. Rep. No. 1923, 82d Cong., 2d Sess. 6 (1952).

of material substance." Id. at 593. As the Court observed:

> There are many things well known and valuable in medicine or in the arts which may be extracted from divers[e] substances. But the extract is the same, no matter from what it has been taken. A process to obtain it from a subject from which it has never been taken may be the creature of invention, but the thing itself when obtained cannot be called a new manufacture.

Id. at 593-94.[44] Similarly, in Cochrane v. Badische Anilin & Soda Fabrik, 111 U.S. 293 (1884), the Court rejected a patent on an artificial version of a natural red dye called alizarine that was produced by manipulating another compound through acid, heat, water or distillation. See generally, id. Although the artificial version of the dye was of a brighter hue than the naturally occurring dye, the Court concluded that "[c]alling it artificial alizarine did not make it a new composition of matter, and patentable as such . . . ." Id. at 311 (citing Am. Wood-Paper, 90 U.S. (23 Wall.) at 593).

In General Electric, 28 F.2d at 642, the Third Circuit Court of Appeals considered the patentability of

[44] Given the posture of the challenge to the patent's validity, the Court rested its holding on the fact that the patent in question was invalid as non-novel. Id.

purified tungsten, which possessed superior characteristics and utility over its brittle, naturally-occurring form. The court first noted that "[i]f it is a natural thing then clearly, even if [the patentee] was the first to uncover it and bring it into view, he cannot have a patent for it because a patent cannot be awarded for a discovery or for a product of nature, or for a chemical element." Id. The court went on to state:

> Naturally we inquire who created pure tungsten. Coolidge? No. It existed in nature and doubtless has existed there for centuries. The fact that no one before Coolidge found it there does not negative its origin or existence.
>
> The second part of the claim reads: "Having ductility and high tensile strength." Did Coolidge give those qualities to "substantially pure tungsten"? We think not for it is now conceded that tungsten pure is ductile cold. If it possess that quality now it is certain that it possessed it always.

Id. at 643. The Court of Customs and Patent Appeals ("C.C.P.A."), the precursor to the Federal Circuit Court of Appeals,[45] subsequently relied on General Electric in

[45] The decisions of the C.C.P.A. remain binding precedent in patent cases. 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").

rejecting patents claiming purified uranium and vanadium. See In re Marden, 47 F.2d 957, 957-58 (C.C.P.A. 1931) ("Marden I"); In re Marden, 47 F.2d 958, 1059 (C.C.P.A. 1931) ("Marden II") ("The quality of purity of vanadium or its ductility is a quality of a natural product and as such is not patentable."). Similarly, in Ex Parte Latimer, the Patent Commissioner refused to allow a patent on pine needle fibers that were better suited for textile production, even though it was necessary to remove the needle from its sheath and other resinous material. 1889 Dec. Comm'r Pat. 123, 125 (1889) ("Nature made them so and not the process by which they are taken from the leaf or needle.").

Myriad argues that purification of "'naturally occurring' compounds that 'do not exist in nature in pure form' renders such compounds patent-eligible." Myriad Br. at 21 (quoting In re Bergstrom, 427 F.2d 1394, 1401 (C.C.P.A. 1970)). However, Myriad cites no Supreme Court authority that would rebut the authorities presented by Plaintiffs, nor do the cited cases support Myriad's position.

Myriad has relied heavily on the holding of the Honorable Learned Hand in Parke-Davis & Co. v. H.K. Mulford Co., 189 F.2d 95 (S.D.N.Y. 1911).[46] In Parke-Davis, Judge Hand considered a challenge to the validity of a patent claiming an adrenaline compound that had been isolated and purified from animal suprarenal glands. Id. at 97. It had been known that suprarenal glands in powdered form had hemostatic, blood-pressure-raising and astringent

[46] The invocation of Judge Hand is frequently practiced in this Circuit. See, e.g., United States v. Rigas, 583 F.3d 108, 121 n.3 (2d Cir. 2009) (quoting Learned Hand for the proposition that appellate courts may not find facts); United States v. Parker, 554 F.3d 230 (2d Cir. 2009) (quoting Learned Hand for his formulation of the requirements of conspiracy); In re City of New York, 522 F.3d 279, 284 (2d Cir. 2008) (citing Learned Hand for his formulation of negligence); In re Hyman, 501 F.3d 61, 67 (2d Cir. 2007) (quoting at length Learned Hand's inconclusive discussion of the meaning of the word "defalcation" in 11 U.S.C. § 523(a)(4)); United States v. Brand, 467 F.3d 179, 190 (2d Cir. 2006) (quoting Learned Hand's definition of inducement by the government); In re Enron Corp., 419 F.3d 115, 123 (2d Cir. 2005) (quoting Learned Hand's critique of statutes of limitations); Shannon v. Jacobowitz, 394 F.3d 90, 95 (2d Cir. 2005) (quoting Learned Hand's instruction that "[w]ords are not pebbles in alien juxtaposition . . . ."); Danahy v. Buscaglia, 134 F.3d 1185, 1189 (2d Cir. 1998) (quoting Learned Hand on the rationale for qualified immunity). See also, Remarks of the Honorable John M. Walker, Jr. Upon Receiving the Learned Hand Medal for Excellence in Federal Jurisprudence, 76 St. John's L. Rev. 595, 596 (2002) ("Judge Hand is widely considered to have been one of the four greatest judges of the first half of the twentieth century."); James L. Oakes, Personal Reflections on Learned Hand and the Second Circuit, 47 Stan. L. Rev. 387 (1995); Gerald Gunther, Learned Hand: the Man and the Judge (1994); Kathryn Griffin, Judge Learned Hand and the Role of the Federal Judiciary (1973); Marvin Schick, Learned Hand's Court (1970); Marcia Nelson, ed., The Remarkable Hands: An Affectionate Portrait (1983); Hershel Shanks, ed., The Art and Craft of Judging: The Decisions of Judge Learned Hand (1968). Although Judge Hand once turned his back on the author of this opinion arguing before him on behalf of the Government, his opinion in Parke-Davis deserves careful review but brings to mind that oft repeated adage "Quote Learned, but follow Gus." See Oakes, 47 Stan. L. Rev. at 389 n.175. This author, confronted by genomics and molecular biology, also emphatically empathizes with Judge Hand's complaint in Parke-Davis about his lack of knowledge of the rudiments of chemistry. See Parke-Davis, 189 F. at 114.

properties, but could not be used for those purposes in gross form. The isolated adrenaline, however, possessed the desired therapeutic properties and could be administered to humans.

Although Myriad argues that the holding in Parke-Davis establishes that the purification of a natural product necessarily renders it patentable, the opinion, read closely, fails to support such a conclusion. The question before the court in Parke-Davis was one of novelty (a modern-day § 102 question), not of patentable subject matter (the § 101 question before this Court). In framing the issue, Judge Hand observed that, "[the validity of the claims] is attacked, first, because they are *anticipated* in the art; and second, for a number of technical grounds which I shall take up in turn." Id. at 101 (emphasis added). He went on to conclude that the patented purified extract was not, in fact, different from the prior art "only for a degree of purity," but rather was a different chemical substance from that found in the prior art. Id. at 103 (observing that "no one had ever isolated a substance [adrenaline] which was not in salt form" and that "the [claimed] base [form of adrenaline] was an original production of [the patentee's]"). Thus, Judge Hand held

that the purified adrenaline was not anticipated by the prior art, namely, the ground paradrenal gland that was known to possess certain beneficial properties. See Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156, 162 (4th Cir. 1958) ("It was further held [in Parke-Davis] that the invention was not anticipated, though the principle was known to exist in the suprarenal glands.").

Only after concluding that the claimed purified adrenaline was novel over the prior art did Judge Hand offer, as dicta, the statement to which Myriad cites: "But, even if it were merely an extracted product without change, there is no rule that such products are not patentable." Id. at 103. While the accuracy of this statement at the time was written is dubious in light of American Wood-Paper (to which Judge Hand did not cite) it is certainly no longer good law in light of subsequent Supreme Court cases, which, as noted above, require that a claimed invention possess "markedly different characteristics" over products existing in nature in order for it to constitute patentable subject matter.[47] Chakrabarty, 447 U.S. at 310; see also Funk Bros., 333 U.S. at 130-32. By the same token, Judge

[47] Notwithstanding Judge Hand's reputation, see supra note 46, his opinion in Parke-Davis was one of a district court judge and does not supersede contrary statements of the law by the C.C.P.A. or the Supreme Court.

Hand's suggestion that a claimed invention was patentable since it was a "new thing commercially and therapeutically," Parke-Davis, 189 F.2d at 103, is firmly contradicted by subsequent case law establishing that "it is improper to consider whether a claimed element or step in a process is novel or nonobvious, since such considerations are separate requirements" when evaluating whether a claim is patent-eligible subject matter. Prometheus, 581 F.3d at 1343; see also Bergy, 596 F.2d at 960-61. Such an approach would also be inconsistent with the Supreme Court's rejection of the patentability of the commercially useful mixture of bacteria in Funk Brothers, the refined cellulose in American Wood-Paper, and the electromagnetic communication devices in O'Reilly v. Morse, 56 U.S. (15 How.) 62 (1853).

The distinction between considerations of novelty and patentable subject matter similarly undermines Myriad's reliance on Bergstrom and In re Kratz, 592 F.2d 1169 (C.C.P.A. 1979), both of which presented issues of novelty and anticipation rather than the question of patentable subject matter. In Bergstrom, the C.C.P.A. considered an appeal from a rejection by the Board of Patent and Interferences ("BPAI") of a patent claiming the purified

prostaglandins PGE_2 and PGE_3 that had been extracted from human or animal prostate glands. 427 F.2d at 1398. Although the BPAI cited § 101 in its rejection, the C.C.P.A. recognized the issue as a § 102 question of novelty. Id. at 1400 ("Tested by the conventional evidentiary criteria or 'conditions for patentability' relevant to the present factual situation which Congress has expressed in the various provisions of 35 U.S.C. § 102, appellants are undoubtedly correct, for the Patent Office has not been able to . . . establish that the claimed subject matter lacks 'novelty.'"); see also id. at 1401 ("[T]he fundamental error in the board's position, as we see it, is the analysis and answer it gave to the sole issue it accurately posed - whether the claimed pure materials are novel as compared with the less pure materials of the reference." (internal citation and quotation marks omitted)). Indeed, the C.C.P.A. itself has subsequently recognized that Bergstrom is properly viewed as a case concerning novelty. Bergy, 596 F.2d at 961 ("Our research has disclosed only two instances in which rejections for lack of novelty were made by the PTO under § 101 . . . . In In re Bergstrom we in effect treated the rejection as if it had been made under § 102, observing in the process that 'The word "new" in § 101 is defined and to

be construed in accordance with the provisions of § 102.'" (internal citation omitted)).

Kratz examined the rejection of a patent claiming a substantially purified chemical compound naturally occurring in strawberries, called 2-methyl-2-pentenoic acid ("2M2PA"). 592 F.2d at 1170. The patentee had appealed from the BPAI's determination that the purified compound was obvious over the prior art under § 103. See id. Although there was some discussion about whether the composition claimed was a naturally-occurring compound, the C.C.P.A. did not view the question before it as a § 101 inquiry. Instead, the court treated the appeal as a question of novelty and anticipation pursuant to § 102.[48] See, e.g., id. at 1174 ("It should be clear that an anticipation rejection in such a case is necessarily based on a dual footing.").[49]

[48] The differences between the test applied in Kratz and the "markedly different" requirement set forth in Chakrabarty and other Supreme Court precedent further demonstrates that the Kratz court was engaged in a § 102 anticipation analysis and not a § 101 statutory subject matter analysis. See id. at 1174 (requiring, for a finding of anticipation, that "the natural composition must inherently contain the naturally occurring compound" and that "the claim must be of sufficient breadth to encompass both the known natural composition and the naturally occurring compound.").

[49] Bergy, also cited by Myriad, considered the question of whether microorganisms constituted patentable subject matter, an issue subsequently addressed by the Supreme Court in Chakrabarty. It did not address the patentability of purified natural products, and its citation to Merck and Parke-Davis was only for the purpose of noting

Finally, Merck & Co., Inc. v. Olin Mathieson Chem. Corp., 253 F.2d 156, cited by Myriad, is entirely consistent with the principle set forth in Funk Brothers and American Fruit Growers that something derived from a product of nature must "possess a new or distinctive form, quality, or property" in order to become patentable subject matter. Am. Fruit Growers, 283 U.S. at 11. In Merck, the Fourth Circuit considered the validity of a patent claiming a Vitamin B_{12} composition useful for treating pernicious anemia. Id. at 157. Although naturally occurring Vitamin B_{12} produced in cows had known therapeutic properties and was commercially available, the court found the purified B_{12} composition, which was obtained from a microorganism, patentable. In upholding the validity of the patent, the court held:

> Every slight step in purification does not produce a new product. What is gained may be the old product, but with a greater degree of purity. Alpha alumina purified is still alpha alumina, In re Ridgway, 76 F.2d 602,[] and ultramarine from which floatable impurities have been removed is still ultramarine, In re Merz, 97 F.2d 599 . . . .

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that courts had upheld patents on pharmaceutical compounds such as vitamin B_{12} and adrenaline. See Bergy, 596 F.2d at 974-75 & n.13.

Id. at 163. Because the court concluded that the purified B_{12} was more than a "mere advance in the degree of purity of a known product," it determined that the claimed invention was entitled to patent protection. Id. at 164.

In sum, the clear line of Supreme Court precedent and accompanying lower court authorities, stretching from American Wood-Paper through to Chakrabarty, establishes that purification of a product of nature, without more, cannot transform it into patentable subject matter. Rather, the purified product must possess "markedly different characteristics" in order to satisfy the requirements of § 101.

3. The claimed isolated DNA is not "markedly different" from native DNA

The question thus presented by Plaintiffs' challenge to the composition claims is whether the isolated DNA claimed by Myriad possesses "markedly different characteristics" from a product of nature.[50] Chakrabarty, 447 U.S. at 310. In support of its position, Myriad cites

[50] The parties do not appear to dispute that isolated DNA claimed in the patents-in-suit are "useful" for purposes of § 101.

several differences between the isolated DNA claimed in the patents and the native DNA found within human cells. None, however, establish the subject matter patentability of isolated *BRCA1/2* DNA.

The central premise of Myriad's argument that the claimed DNA is "markedly different" from DNA found in nature is the assertion that "[i]solated DNA molecules should be treated no differently than other chemical compounds for patent eligibility," Myriad Br. at 26, and that the alleged "difference in the structural and functional properties of isolated DNA" render the claimed DNA patentable subject matter, Myriad Br. at 31.

Myriad's focus on the chemical nature of DNA, however, fails to acknowledge the unique characteristics of DNA that differentiate it from other chemical compounds. As Myriad's expert Dr. Joseph Straus observed: "Genes are of double nature: On the one hand, they are chemical substances or molecules. On the other hand, they are physical carriers of information, i.e., where the actual biological function of this information is coding for proteins. Thus, inherently genes are multifunctional." Straus Decl. ¶ 20; see also *The Cell* at 98, 104 ("Today the

idea that DNA carries genetic information in its long chain of nucleotides is so fundamental to biological thought that it is sometimes difficult to realize the enormous intellectual gap that it filled. . . . DNA is relatively inert chemically."); Kevin Davies & Michael White, *Breakthrough: The Race to Find the Breast Cancer Gene* 166 (1996) (noting that Myriad Genetics' April 1994 press release described itself as a "genetic information business"). This informational quality is unique among the chemical compounds found in our bodies, and it would be erroneous to view DNA as "no different[]" than other chemicals previously the subject of patents.[51]

Myriad's argument that all chemical compounds, such as the adrenaline at issue in Parke-Davis, necessarily conveys some information ignores the biological realities of DNA in comparison to other chemical compounds in the body. The information encoded in DNA is not information

[51] Myriad and many of the amici suggest that the invalidation of the patents-in-suit will result in the decimation of the biotechnology industry. See, e.g., Myriad Br. at 28-29 (suggesting that a finding that DNA is unpatentable subject matter will invalidate patents to important chemical compounds such as the anticancer drug Taxol (paclitaxel) and leave "little to nothing" of the United States biotechnology industry). The conclusions reached in this opinion concerning the subject matter patentability of isolated DNA, however, are based on the unique properties of DNA that distinguish it from all other chemicals and biological molecules found in nature. As a result, Myriad's predictions for the future of the U.S. biotechnology industry are unfounded.

about its *own* molecular structure incidental to its biological function, as is the case with adrenaline or other chemicals found in the body. Rather, the information encoded by DNA reflects its primary biological function: directing the synthesis of *other* molecules in the body - namely, proteins, "biological molecules of enormous importance" which "catalyze biochemical reactions" and constitute the "major structural materials of the animal body." O'Farrell, 854 F.2d at 895-96. DNA, and in particular the ordering of its nucleotides, therefore serves as the physical embodiment of laws of nature - those that define the construction of the human body. Any "information" that may be embodied by adrenaline and similar molecules serves no comparable function, and none of the declarations submitted by Myriad support such a conclusion. Consequently, the use of simple analogies comparing DNA with chemical compounds previously the subject of patents cannot replace consideration of the distinctive characteristics of DNA.

In light of DNA's unique qualities as a physical embodiment of information, none of the structural and functional differences cited by Myriad between native *BRCA1/2* DNA and the isolated *BRCA1/2* DNA claimed in the

patents-in-suit render the claimed DNA "markedly different." This conclusion is driven by the overriding importance of DNA's nucleotide sequence to both its natural biological function as well as the utility associated with DNA in its isolated form. The preservation of this defining characteristic of DNA in its native and isolated forms mandates the conclusion that the challenged composition claims are directed to unpatentable products of nature.

Myriad argues that the § 101 inquiry into the subject matter patentability of isolated DNA should focus exclusively on the differences alleged to exist between native and isolated DNA, rather than considering the similarities that exist between the two forms of DNA. See, e.g., Myriad Reply at 8-9 ("[T]he observation that isolated DNA and native DNA share this single property [i.e. the same protein coding sequences] is irrelevant to the critical issue of whether there are *differences* in their properties. It is the *differences* that are legally relevant to the novelty inquiry under Section 101, not the properties held in common." (emphasis in original)); Myriad Br. at 8. Setting aside the fact that considerations such as novelty are irrelevant for § 101 purposes, see Bergy,

596 F.2d at 960-61, Myriad offers no authorities supporting such an approach. To the contrary, the Supreme Court has held that "[i]n determining the eligibility of [a] claimed process for patent protection under § 101, [the] claims must be considered as a whole." Diehr, 450 U.S. at 188. Similarly, the Federal Circuit has expressly held that "[i]n the final analysis under § 101, the claimed invention, as a whole, must be evaluated for what it is." In re Grams, 888 F.2d 835, 839 (Fed. Cir. 1989) (quoting In re Abele, 684 F.2d 902, 907 (C.C.P.A. 1982)).

Were Myriad's approach the law, it is difficult to discern how any invention could fail the test. For example, the bacterial mixture in Funk Brothers was unquestionably different from any preexisting bacterial mixture; yet the Supreme Court recognized that a patent directed to the mixture, considered as a whole, did no more than patent "the handiwork of nature." 333 U.S. at 131. There will almost inevitably be some identifiable differences between a claimed invention and a product of nature; the appropriate § 101 inquiry is whether, considering the claimed invention as a whole, it is sufficiently distinct in its fundamental characteristics from natural phenomena to possess the required "distinctive

name, character, [and] use." Chakrabarty, 447 U.S. at 309-10.

None of Myriad's arguments establish the distinctive nature of the claimed DNA. Myriad's argument that association of chromosomal proteins with native DNA establishes the existence of "structural differences" between native and isolated DNA relies on an incorrect comparison between isolated DNA and *chromatin*, which are indeed different insofar as chromatin includes chromosomal proteins normally associated with DNA. The proper comparison is between the claimed isolated DNA and the corresponding native DNA, and the presence or absence of chromosomal proteins merely constitutes a difference in purity that cannot serve to establish subject matter patentability. See Gen. Elec., 28 F.2d at 642-43; Marden I, 47 F.2d at 957-58; Marden II, 47 F.2d at 1059.

Myriad also attempts to rely on its assertion that native DNA contains intron sequences that are absent in the claimed *BRCA1/2* DNA. However, some of the claims, such as claim 1 of the '282 patent, are directed broadly to DNA "coding for a BRCA1 polypeptide." Native *BRCA1* DNA, by definition, encodes the BRCA1 protein; thus claim 1 of the

'282 patent would cover purified *BRCA1* DNA possessing the exact same structure found in the human cell, introns and all.[52] See also '492 patent, claim 1 (similarly claiming isolated DNA "coding for a BRCA2 polypeptide"). In addition, several of the composition claims are directed to isolated DNA containing as few as 15 nucleotides of the *BRCA1* coding sequence, see, e.g., '282 patent, claims 5 & 6, and at least some of these short DNA sequences will be found within a single exon of the native *BRCA1* gene sequence. See Adam Pavlicek, et al., Evolution of the Tumor Suppressor *BRCA1* Locus in Primates: Implications for Cancer Predisposition, 13 Human Molecular Genetics 2737, 2737 (2004) (noting *BRCA1* exons range from 37 to 3427 nucleotides in length). Therefore, for these small DNA fragments, the existence of introns in native *BRCA1* DNA is completely irrelevant to the question of structural differences when comparing these short DNA molecules with native *BRCA1* DNA.

More generally, the fact that the *BRCA1/2* cDNA molecules covered by the composition claims-in-suit contain only the protein coding exons and not the introns found in

[52] To the extent a claim reads on unpatentable subject matter, the entire claim must be deemed invalid. See Titanium Metals Corp. of Am. v. Banner, 778 F.2d 775, 782 (Fed. Cir. 1985).

native DNA does not render these cDNAs and their native counterparts "markedly different." The splice variants represented by these cDNAs are the result of the naturally-occurring splicing of pre-mRNA into mature mRNA. Therefore, not only are the coding sequences contained in the claimed DNA identical to those found in native DNA, the particular arrangement of those coding sequences is the result of the natural phenomena of RNA splicing. Finally, at least in the case of *BRCA1*, the claimed cDNA sequences are actually found in the human genome in the form of a naturally occurring pseudogene. See Mason Supp. Decl. ¶ 18.[53]

Myriad's argument that the functional differences between native and isolated DNA demonstrates that they are "markedly different" relies on the fact that isolated DNA may be used in applications for which native DNA is unsuitable, namely, in "molecular diagnostic tests (e.g., as probes, primers, templates for sequencing reactions), in

[53] Native DNA is sometimes methylated, but that methylation is preserved when the DNA is extracted and purified. Nussbaum Decl. ¶ 20. Since the claimed "isolated DNA" includes DNA extracted and purified from the body, methylation of DNA in the body does not distinguish native DNA from the claimed DNA. In addition, DNA in the body also exists in a non-methylated state, just as the synthesized DNA claimed in the patents would not be methylated. More importantly, while methylation affects the transcription of a gene in the body, it does not have any impact on the genetic information contained within the DNA. Indeed, DNA is demethylated and remethylated as it passes from the germline of one generation to the next. Nussbaum Decl. ¶ 28.

biotechnological processes (e.g. production of pure *BRCA1* and *BRCA2* protein), and even in medical treatments (e.g. gene therapy)." Myriad Reply at 9; see also Myriad Br. at 30-32.

Isolated DNA's utility as a primer or a molecular probe (for example, for Southern blots) arises from its ability to "target and interact with other DNA molecules," that is, the ability of a given DNA molecule to bind exclusively to a specific DNA target sequence. Myriad Br. at 33; see Kay Decl. ¶ 138. Thus, for example, a 24 nucleotide segment of isolated *BRCA1* DNA can be used as a primer because it will bind only to its corresponding location in the *BRCA1* gene. However, the basis for this utility is the fact that the isolated DNA possesses the identical nucleotide sequence as the target DNA sequence,[54] thus allowing target specific hybridization between the DNA primer and the portion of the target DNA molecule possessing the corresponding sequence. Kay Decl. ¶¶ 135-36, 138. In contrast, another 24 nucleotide segment of DNA possessing the same nucleotide composition but a different

[54] To be precise, the isolated single-stranded DNA molecule utilized as a primer or probe has the identical sequence as the complementary DNA strand to the DNA strand containing the target DNA sequence. The description in the text is meant to serve as a short-hand description of this relationship.

nucleotide sequence would not have the same utility because it would be unable to hybridize to the proper location in the *BRCA1* gene.[55] Indeed, Myriad implicitly acknowledges this fact when it states that the usefulness of isolated DNA molecules "is based on their ability to target and interact with other DNA molecules, which is a function of *their own individual structure and chemistry*." Myriad Br. at 33 (emphasis added). Therefore, the cited utility of the isolated DNA as a primer or probe is primarily a function of the nucleotide sequence identity between native and isolated *BRCA1/2* DNA.

Similarly, the utility of isolated DNA as a sequencing target relies on the preservation of native DNA's nucleotide sequence. Indeed, one need look no further than Myriad's BRACAnalysis testing, which relies on the sequencing of isolated DNA (i.e. the PCR amplified exons of *BRCA1/2*), to determine the sequence of the corresponding DNA coding sequences found in the cell. The entire premise behind Myriad's genetic testing is that the claimed isolated DNA retains, in all relevant respects, the identical nucleotide sequence found in native DNA. The use

[55] The same reasoning applies with respect to the use of isolated DNA as a probe. See Kay Decl. ¶¶ 135-36.

of isolated *BRCA1/2* DNA in the production of BRCA1/2 proteins or in gene therapy also relies on the identity between the native DNA sequences and the sequences contained in the isolated DNA molecule. Were the isolated *BRCA1/2* sequences different in any significant way, the entire point of their use - the production of BRCA1/2 proteins - would be undermined.

While the absence of proteins and other nucleotide sequences is currently required for DNA to be useful for the cited purposes, the purification of native DNA does not alter its essential characteristic – its nucleotide sequence – that is defined by nature and central to both its biological function within the cell and its utility as a research tool in the lab. The requirement that the DNA used be "isolated" is ultimately a technological limitation to the use of DNA in this fashion, and a time may come when the use of DNA for molecular and diagnostic purposes may not require such purification. The nucleotide sequence, however, is the defining characteristic of the isolated DNA that will always be required to provide the sequence-specific targeting and protein coding ability that allows isolated DNA to be used for the various applications cited by Myriad. For these

reasons, the use of isolated DNA for the various purposes cited by Myriad does not establish the existence of differences "in kind" between native and isolated DNA that would establish the subject matter patentability of what is otherwise a product of nature. See Am. Fruit Growers, 283 U.S. at 11.

Finally, the isolated *BRCA1/2* DNA claimed in Myriad's patents bears comparison to the bacterial mixture in Funk Brothers. In explaining why the claimed mixture of bacteria did not constitute an invention, the Court observed that the first part of the claimed invention was the "[d]iscovery of the fact that certain strains of each species of these bacteria can be mixed without harmful effect to the properties of either" which was "a discovery of their qualities of non-inhibition. It is no more than the discovery of some of the handiwork of nature and hence is not patentable." 33 U.S. at 131. The Court went on to observe that the second part of the claimed invention was "[t]he aggregation of select strains of the several species into one product[,] an application of that newly-discovered natural principle. But however ingenious the discovery of that natural principle may have been, the

application of it is hardly more than an advance in the packaging of the inoculants." Id.

According to Myriad, the invention claimed in its patents required the identification of the specific segments of chromosomes 17 and 13 that correlated with breast and ovarian cancer (*BRCA1* and *BRCA2*) followed by the isolation of these sequences away from other genomic DNA and cellular components. Myriad Reply at 6 ("By identifying these particular *BRCA* DNAs and isolating them away from other genomic DNA and other cellular components, the inventors created the claimed isolated *BRCA* DNA molecules."). Like the discovery of the mutual non-inhibition of the bacteria in Funk Brothers, discovery of this important correlation was a discovery of the handiwork of nature - the natural effect of certain mutations in a particular segment of the human genome. And like the aggregation of bacteria in Funk Brothers, the isolation of the *BRCA1* and *BRCA2* DNA, while requiring technical skill and considerable labor, was simply the application of techniques well-known to those skilled in the art. See Parthasarathy Decl. ¶ 19. The identification of the *BRCA1* and *BRCA2* gene sequences is unquestionably a valuable scientific achievement for which Myriad deserves

recognition, but that is not the same as concluding that it is something for which they are entitled to a patent. See Funk Bros., 33 U.S. at 132 ("[O]nce nature's secret of the non-inhibitive quality of certain strains of the [nitrogen-fixing bacteria] was discovered, the state of the art made the production of a mixed inoculant a simple step. Even though it may have been the product of skill, it certainly was not the product of invention.").

Because the claimed isolated DNA is not markedly different from native DNA as it exists in nature, it constitutes unpatentable subject matter under 35 U.S.C. § 101.

D. The Method Claims are Invalid Under 35 U.S.C. § 101

"Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." Benson, 409 U.S. at 67. However, "'an application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.'" Bilski, 545 F.3d at 953 (quoting Diehr, 450 U.S. at 187). In Bilski, the Federal Circuit

set forth "the definitive test to determine whether a process claim is tailored narrowly enough to encompass only a particular application of a fundamental principle rather than pre-empt the principle itself." Id. at 954. Under this "machine or transformation" test, "[a] claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." Id. In addition, "the use of a specific machine or transformation of an article must impose meaningful limits on the claim's scope to impart patent-eligibility," and "the involvement of the machine or transformation in the claimed process must not merely be insignificant extra-solution activity." Id. at 961-62. In other words, the "transformation must be central to the purpose of the claimed process." Id. at 962. In particular, the Bilski court held that "adding a data-gathering step to an algorithm is insufficient to convert that algorithm into a patent-eligible process." Id. at 963 (citing Grams, 888 F.2d at 840; Meyer, 688 F.2d at 794). "A requirement simply that data inputs be gathered - without specifying how - is a meaningless limit on a claim to an algorithm because every algorithm inherently require the gathering of data inputs." Id. (citing Grams, 888 F.2d at 839-40).

"Further, the inherent step of gathering data can also fairly be characterized as insignificant extra-solution activity." Id. (citing Flook, 437 U.S. at 590).

1. The claims for "analyzing" and "comparing" DNA sequences are invalid under § 101

Claim 1 of the '999 patent is directed to the process of "analyzing" a *BRCA1* sequence and noting whether or not the specified naturally-occurring mutations exist. The claimed process is not limited to any particular method of analysis and does not specify any further action beyond the act of "analyzing." Similarly, claim 1 of the '001, '441, and '857 patents as well as claim 2 of the '857 patents are directed to "comparing" two gene sequences to see if any differences exist and do not specify any limitations on the method of comparison.

Myriad argues that these method claims should not be viewed as mental processes because they incorporate a transformation step and therefore satisfy the "transformation" prong of the Bilski "machine or transformation" test. In support of its position, Myriad relies primarily on the Federal Circuit's holding in

Prometheus, 581 F.3d 1336. There, the Federal Circuit considered a patent containing claims directed to methods for calibrating the proper dosage of thiopurine drugs by measuring metabolites in subjects having gastrointestinal disorders. Id. at 1343-50. The patentees had discovered a correlation between metabolite levels in a patient's blood and the therapeutic efficacy of a dose of the drug. Based on this correlation, the patentees claimed methods 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. A representative claim asserted by the patentee in Prometheus claimed:

> A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,
>
> wherein the level of 6-thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and

> wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

Id. at 1340.

In concluding that the claimed methods satisfied the requirements of § 101, the Federal Circuit held that the relevant transformation for purposes of the "machine or transformation" test was the transformation of the human body as well as the chemical and physical changes of the drug's metabolites. Id. at 1346 (stating that "claims to methods of treatment," were "always transformative when a defined group of drugs is administered to the body to ameliorate the effects of an undesired condition"). Because the transformative steps were central to the claimed treatment methods, they satisfied the "machine or transformation" test. Id. at 1346-47. The court went on to hold that the "determining" step alone was transformative and central to the claimed methods since "determining the levels of [the metabolites] 6-TG or 6-MMP in a subject necessarily involves a transformation, for those levels cannot be determined by mere inspection." Id. at 1347.

Myriad argues that just as the act of "determining" metabolite levels in Prometheus was found to involve the transformation of human blood, so too should "analyzing" or "comparing" *BRCA1/2* gene sequences be construed to incorporate physically transformative steps (i.e. the isolation and sequencing of DNA[56]) that would satisfy the Bilski "machine or transformation" test. Myriad further asserts that these transformations are "central to the purpose of the claims," id. at 1347, because "Myriad's method claims each require the transformation of a tissue or blood sample in order to isolate the patient's DNA." Myriad Br. at 35.

The claims in Prometheus, however, are distinguishable from the method claims in dispute here. In Prometheus, "determining metabolite levels in the clinical samples taken from patients" was found to be transformative because the act of "determining metabolite levels" was itself construed to include the extraction and measurement of metabolite concentrations, such as high pressure liquid chromatography. See Prometheus, 581 F.3d at 1347. Indeed,

[56] The challenged method claims are also directed to analyzing and comparing RNA and cDNA sequences, but for purposes of this opinion, the discussion will be framed in terms of analyzing and comparing DNA sequences.

neither party in Prometheus disputed that "determining" metabolite levels in samples taken from patients was, in and of itself, transformative.[57] Id.

In contrast, the language of the method claims-in-suit and the plain and ordinary meanings of the terms "analyzing" or "comparing" establish that the method claims-in-suit are directed only to the abstract mental processes of "comparing" or "analyzing" gene sequences. Although Myriad asserts that the challenged method claims are directed to comparing DNA molecules rather than DNA sequences, the language of the claims belies such an interpretation. While the *purpose* of the claimed method is, for example, to "detect a germline alteration in a BRCA1 gene," see '999 patent, col. 161:17-18, the *method* actually claimed is "analyzing a *sequence* of a BRCA1 gene." '999 patent, col. 161: 20-21 (emphasis added); see also '001 patent, col. 144:2-17 ("A method . . . which comprises gene comparing a first sequence selected from the group consisting of a BRCA1 gene from said tumor sample . . . with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample . . . wherein a

[57] The issue with respect to the "determining" step was not whether it was transformative, but whether that transformation was central to the claimed invention. Id.

difference in the sequence of the BRCA1 gene . . . indicates a somatic alteration in the BRCA1 gene."); '857 patent, col. 169:40-45 ("A method . . . which comprises comparing the nucleotide sequence of the suspected mutant BRCA2 allele with the wild-type BRCA2 nucleotide sequence . . . .").

Similarly, the inclusion of the phrases "from a human subject" or "from a nontumor sample" in the claims serve only to specify the identity of the DNA or RNA sequence to be "analyzed" or "compared," i.e., from a human sample as opposed to an animal sample or cell culture, and do not, as Myriad argues, establish that the claims should be read to include the physical transformations associated with obtaining DNA from those sources.[58] In addition, the passages from the '999 specification cited by Myriad describing the process by which DNA sequences are obtained cannot serve to redefine the scope of the challenged claims

[58] Whether acts are "transformative" in the context of the "machine or transformation" test for process claims is distinct from the question of whether those acts would render the resulting product patentable subject matter. See, e.g., Am. Wood-Paper, 90 U.S. (23 Wall.) at 593-94 (noting that a party may be entitled to a patent on a process for purifying a natural product but not the final product itself if the final product is not different "in kind" from the natural product); Merz, 97 F.2d at 601 (same). Therefore the description of DNA purification and sequencing as "transformative acts" in the context of the challenged process claims is not inconsistent with the conclusion that the isolated DNAs claimed in the challenged patents constitute unpatentable subject matter.

without violating the prohibition against importing claim limitations from the specification. See Phillips, 415 F.3d at 1320.

By the same token, the transformative steps associated with isolating and sequencing DNA described in the unchallenged dependent claims cannot be used to establish that the challenged claims include transformative events. To do so would violate the doctrine of claim differentiation, which presumes that "different words or phrases used in separate claims . . . indicate that the claims have different meanings and scope." Karlin Tech., Inc. v. Surgical Dynamics, Inc., 177 F.3d 968, 972 (Fed. Cir. 1999). Because claim differentiation "prevents the narrowing of broad claims by reading into them the limitations of narrower claims," Clearstream Wastewater Sys., Inc. v. Hydro-Action, Inc., 206 F.3d 1440, 1446 (Fed. Cir. 2000), the dependent claims serve only to illustrate the breadth of the challenged claims and reinforce the conclusion that what is claimed are mental processes independent of any physical transformations. See Phillips, 415 F.3d at 1314-15 ("[T]he presence of a dependent claim that adds a particular limitation gives rise to a

presumption that the limitation in question is not present in the independent claim.").[59]

Myriad also argues that because isolating and sequencing DNA are required for "analyzing" or "comparing" DNA sequences, Prometheus allows those transformative acts to be incorporated into the process claims for purposes of the § 101 analysis. See Myriad Reply at 12. Myriad thus seeks to rely on transformations not actually claimed by the method claims-in-suit to satisfy the Bilski "machine or transformation" test. Neither Prometheus nor any other authority supports such an expansive approach to the application of this test. Prometheus held only that the term "determining," as used in the claims at issue, referred to acts that included manipulations that satisfied the "machine or transformation" test. Id. Nowhere did Prometheus suggest that preparatory physical transformations required for the performance of, but not included in, claims directed to mental processes should be incorporated into the claim for purposes of the § 101 analysis. Not only would such an approach be inconsistent

[59] The patent examiner's reasons for allowance, cited by Myriad, are precisely the legal conclusions concerning the patentability of the claimed methods being challenged by Plaintiffs. Moreover, the examiner's reasons of allowance cannot serve to define the scope of claim terms. See ACCO Brands, Inc. v. Micro Sec. Devices, Inc., 346 F.3d 1075, 1079 (Fed. Cir. 2003).

with the prohibition on the importation of claim limitations from the specification, it would effectively vitiate the limitations to claiming mental processes provided by the "machine or transformation" test since "to use virtually any natural phenomenon for virtually any useful purpose could well involve the use of empirical information obtained through an unpatented means that might have involved transforming matter." Metabolite Labs., 548 U.S. at 136 (Breyer, J., dissenting). Therefore the preparatory transformations relating to obtaining DNA sequences cannot be relied on to satisfy the requirements of § 101.

Even if the challenged method claims were read to include the transformations associated with isolating and sequencing human DNA, these transformations would constitute no more than "data-gathering step[s]" that are not "central to the purpose of the claimed process." Bilski, 545 F.3d at 962-63. In Grams, the Federal Circuit considered a patent directed to a method of diagnosing an abnormal condition in an individual. The claimed method consisted of two steps: (1) "performance of clinical laboratory tests on an individual to obtain data for the parameters," and (2) "analyz[ing] that data to ascertain

the existence and identity of an abnormality . . . ." 888 F.2d at 837. Concluding that the essence of what was claimed was the mathematical algorithm for analyzing the clinical data, and that the sole physical process - laboratory testing - was merely data-gathering to obtain clinical data, the court held the patent invalid under § 101 for claiming a mathematic algorithm. Id. at 840.

The method claims-in-suit present a closely analogous situation. The essence of what is claimed is the identification of a predisposition to breast cancer based on "analyzing" or "comparing" *BRCA1/2* gene sequences. See, e.g., '857 patent, claim 2 ("A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the [BRCA2 gene sequence] from said subject with the [] sequence of the wild-type BRCA2 gene . . . ."). As in Grams, isolation and sequencing of DNA from a human sample, even if incorporated into the method claims-in-suit, would represent nothing more than data-gathering steps to obtain the DNA sequence information on which to perform the claimed comparison or analysis. Moreover, in the absence of a specified method for isolating and sequencing DNA, "[a] requirement simply that data inputs be gathered - without specifying how - is a

meaningless limit on a claim to an algorithm because every algorithm inherently requires the gathering of data inputs." Bilski, 545 F.3d at 963 (citing Grams, 888 F.2d at 839-40). Consequently, even if the method claims-in-suit were construed to include the physical transformations associated with isolating and sequencing DNA, they would still fail the "machine or transformation" test under § 101 for subject matter patentability.

2. The claim for "comparing" the growth rate of cells is invalid under § 101.

Claim 20 of the '282 patent is directed to "comparing" the growth rates of cells in the presence or absence of a potential cancer therapeutic. Specifically, the claim recites a method for identifying potential cancer therapeutics by utilizing cells into which an altered *BRCA1* gene known to cause cancer has been inserted. Thus modified to mimic cancerous cells in the body, these cells are then grown in either the presence or absence of a potential cancer therapeutic, and the growth rates of the cells are compared to determine the effect of the potential therapeutic.

Unlike the method claims directed to "analyzing" or "comparing" DNA sequences, claim 20 arguably recites certain transformative steps, such as the administration of the test compound.[60] However, the essence of the claim, when considered in its entirety, is the act of comparing cell growth rates and concluding that "a slower growth of said host cell in the presence of said compound is indicative of a cancer therapeutic." '282 patent, col. 156:25-27.

This claimed "process" is, in fact, the scientific method itself, and claim 20 seeks to patent a basic scientific principle: that a slower rate of cell growth in the presence of a compound indicates that the

[60] It is questionable whether the two transformations cited by Myriad are relevant transformations for purposes of the § 101 inquiry. Under Prometheus, the administration of a test compound is transformative only if it effects a change in cell growth. See Prometheus, 581 F.3d at 1346 (finding "administering" of a drug transformative since it resulted in changes to both the patient and the drug metabolites). If the test compound had no effect on the cells, it is unclear whether there would be any basis to view its administration as working a "transformation" since there would be no transformation with respect to the cells (i.e. there was no change in their growth rate) and there would also presumably be no transformation with respect to the test drug (i.e. it was not metabolized).

The other alleged "transformation" cited by Myriad is the insertion of DNA into cells to create the "transformed eukaryotic cell" for treatment with the test compound. Kay Decl. ¶ 57. Even more that its expansive interpretation of the method claims for analyzing DNA sequences for § 101 purposes, Myriad's attempt to rely on transformations associated with the creation of a starting product for its claimed process is unsupported by the law and demonstrates the limitlessness of Myriad's interpretation of Prometheus and the "machine or transformation" test.

compound may be a cancer therapeutic. The recited transformative steps, as in Grams, represent nothing more than preparatory, data-gathering steps to obtain growth rate information and do not render the claimed mental process patentable under § 101. See Grams, 888 F.2d at 840 ("The presence of a physical step in the claim to derive data for the algorithm will not render the claim statutory").[61]

E. The Constitutional Claims Against the USPTO Are Dismissed

As determined above, the patents issued by the USPTO are directed to a law of nature and were therefore improperly granted. The doctrine of constitutional avoidance, which states that courts should not reach unnecessary constitutional questions, thereby becomes applicable. See, e.g., Allstate Ins. Co. v. Serio, 261 F.3d 143, 149-50 (2d Cir. 2001) ("It is axiomatic that the federal courts should, where possible, avoid reaching constitutional questions.") (citing Spector Motor Serv., Inc. v. McLaughlin, 323 U.S. 101 (1944) ("If there is one doctrine more deeply rooted than any other in the process

[61] Because Plaintiffs' motion for summary judgment with respect to its claims against Myriad is granted on the basis of 35 U.S.C. § 101, its Constitutional claims need not be addressed.

of constitutional adjudication, it is that we ought not to pass on questions of constitutionality . . . unless such adjudication is unavoidable")); see also Ashwander v. TVA, 297 U.S. 288, 347 (1936) (Brandeis, J., concurring) ("[I]f a case can be decided on either of two grounds, one involving a constitutional question, the other a question of statutory construction or general law, the Court will decide only the latter."). This doctrine bears on the consideration of Plaintiffs' claims that the USPTO's policy permitting the grant of the Myriad patents violates Article I, Section 8, Clause 8 and the First Amendment of the Constitution.

The Plaintiffs have not addressed these authorities and have contended that "the doctrine of constitutional avoidance is inapplicable" because the invalidation of Myriad's claims pursuant to 35 U.S.C. § 101 "will not necessarily invalidate the USPTO's policy [in granting the patents]." Pl. Reply at 43. However, a decision by the Federal Circuit or the Supreme Court affirming the holding set forth above would apply to both the issued patents as well as patent applications and would be binding on all patent holders and applicants, as well as the USPTO. See Koninklijke Philips Electronics N.V. v.

Cardiac Science, 590 F.3d 1326, 1337 (Fed. Cir. 2010) ("We remind the district court and the [USPTO] Board that they must follow judicial precedent. . . ."). Thus, to the extent the USPTO examination policies are inconsistent with a final, binding ruling, the USPTO would conform its examination policies to avoid issuing patents directed to isolated DNA or the comparison or analysis of DNA sequences. See USPTO Reply Memo, at 4.

With the holding that the patents are invalid, the Plaintiffs have received the relief sought in the Complaint and the doctrine of constitutional avoidance precludes this Court from reaching the constitutional claims against the USPTO. See Allstate Ins. Co. v. Serio, 261 F.3d 143, 149-50 (2d Cir. 2001); USPTO Br. at 4. Plaintiffs' claims for constitutional violations against the USPTO are therefore dismissed without prejudice.

VIII. CONCLUSION

For the reasons set forth above, Plaintiffs' motion for summary judgment is granted in part, Myriad's motion for summary judgment is denied, the USPTO's motion for judgment on the pleadings is granted, and the claims-in-suit are declared invalid pursuant to 35 U.S.C. § 101.

Submit judgment on notice.

It is so ordered.

New York, N.Y.
April 2, 2010

ROBERT W. SWEET
U.S.D.J.

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

----------X

ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,

Plaintiffs,

09 Civ. 4515 (RWS)

-against-

O R D E R

UNITED STATES PATENT AND TRADEMARK OFFICE, ET AL.,

Defendants.

----------X

Sweet, D.J.

To correct an inadvertent omission, the Opinion filed on March 29, 2010 is hereby amended by inserting the following paragraph at page 21:

"Amicus curiae Genetic Alliance ("GA") is a not-for-profit, tax-exempt health advocacy organization founded in 1986 (as the Alliance for Genetic Support Groups). It brings together diverse stakeholders that create novel partnerships in advocacy. By integrating individual, family, and community perspectives to improve health systems, Genetic Alliance seeks to revolutionize access to information to enable translation of research into services and individualized decision-making. GA contends that the wholesale abolition of patents on isolated DNA molecules and

isolated purified natural substances is legally untenable and undesirable as public policy, because it would diminish the promise of genetic research for patients and negatively affect other areas of medicine."

The Amended Opinion will be filed forthwith.

It is so ordered.

New York, NY
April 7, 2010

ROBERT W. SWEET
U.S.D.J.

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 BAKER,

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.

09 Civ. 4515 (RWS)
ECF Case

JUDGMENT

Plaintiffs 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, 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, and Kathleen Baker ("Plaintiffs") having moved for summary judgment pursuant to Fed. R. Civ. P. 56; and

Defendant United States Patent and Trademark Office ("Defendant USPTO") having moved for judgment on the pleadings pursuant to Fed. R. Civ. P. 12(c); and

Defendants 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 ("the Myriad Defendants") having moved for summary judgment pursuant to Fed. R. Civ. P. 56; and

The Court having issued its Amended Opinion on April 5, 2010, granting Plaintiffs' motion for summary judgment in part; and granting Defendant USPTO's motion for judgment on the pleadings; and denying the Myriad Defendants' motion for summary judgment, it is

ORDERED, ADJUDGED AND DECREED: That for the reasons stated in the Court's Amended Opinion dated April 5, 2010:

Claims 1, 2, 5, 6, 7, and 20 of United States Patent 5,747,282 are invalid; and

Claims 1, 6, and 7 of United States Patent 5,837,492 are invalid; and

Claim 1 of United States Patent 5,693,473 is invalid; and

Claim 1 of United States Patent 5,709,999 is invalid; and

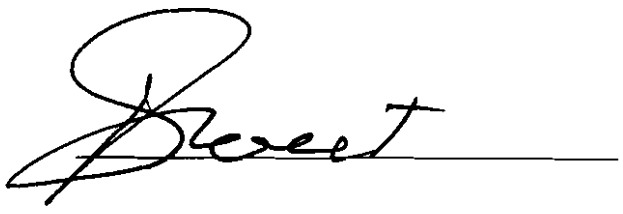
Claim 1 of United States Patent 5,710,001 is invalid; and

Claim 1 of United States Patent 5,753,441 is invalid; and

Claims 1 and 2 of United States Patent 6,033,857 are invalid; and

Plaintiffs' claims against Defendant USPTO are dismissed without prejudice.

Dated: New York, New York
April 19, 2010



PARTIES ENTITLED TO BE
NOTIFIED OF ENTRY OF JUDGMENT

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(2) American College of Medical Genetics
(3) American Society for Clinical Pathology
(4) College of American Pathologists
(5) Haig Kazazian, MD
(6) Arupa Ganguly, PhD
(7) Wendy Chung, MD, PhD
(8) Harry Ostrer, MD
(9) David Ledbetter, PhD
(10) Stephen Warren, PhD
(11) Ellen Matloff, M.S.
(12) Elsa Reich, M.S.
(13) Breast Cancer Action
(14) Boston Women's Health Book Collective
(15) Lisbeth Ceriani
(16) Runi Limary
(17) Genae Girard
(18) Patrice Fortune
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(5) Jack Brittain

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(7) Raymond Gesteland

(8) James U. Jensen

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(10) Thomas Parks

(11) David W. Pershing

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CERTIFICATE OF SERVICE

This is to certify that on April 9, 2010, a true and correct copy of the foregoing document has been served on all counsel of record via email and US mail.

Barry R. Satine

United States District Court
Southern District of New York
Office of the Clerk
U.S. Courthouse
500 Pearl Street, New York, N.Y. 10007-1213

Date:

In Re:

-v-

Case #: ( )

Dear Litigant,

Enclosed is a copy of the judgment entered in your case.

Your attention is directed to Rule 4(a)(1) of the Federal Rules of Appellate Procedure, which requires that if you wish to appeal the judgment in your case, you must file a notice of appeal within 30 days of the date of entry of the judgment (60 days if the United States or an officer or agency of the United States is a party).

If you wish to appeal the judgment but for any reason you are unable to file your notice of appeal within the required time, you may make a motion for an extension of time in accordance with the provision of Fed. R. App. P. 4(a)(5). That rule requires you to show "excusable neglect" or "good cause" for your failure to file your notice of appeal within the time allowed. Any such motion must first be served upon the other parties and then filed with the Pro Se Office no later than 60 days from the date of entry of the judgment (90 days if the United States or an officer or agency of the United States is a party).

The enclosed Forms 1, 2 and 3 cover some common situations, and you may choose to use one of them if appropriate to your circumstances.

The Filing fee for a notice of appeal is $5.00 and the appellate docketing fee is $450.00 payable to the "Clerk of the Court, USDC, SDNY" by certified check, money order or cash. **No personal checks are accepted.**

J. Michael McMahon, Clerk of Court

by: _____

, Deputy Clerk

United States District Court
Southern District of New York
Office of the Clerk
U.S. Courthouse
500 Pearl Street, New York, N.Y. 10007-1213

----------X

-V-

NOTICE OF APPEAL

civ. ( )

----------X

Notice is hereby given that _____ (party)
hereby appeals to the United States Court of Appeals for the Second Circuit from the Judgment [describe it]

entered in this action on the _____ (day) day of _____ (month) , _____ (year) .

_____ (Signature)

_____ (Address)

_____ (City, State and Zip Code)

Date: _____ ( ) _____ - _____ (Telephone Number)

Note: You may use this form to take an appeal provided that it is received by the office of the Clerk of the District Court within 30 days of the date on which the judgment was entered (60 days if the United States or an officer or agency of the United States is a party).

FORM 1

United States District Court
Southern District of New York
Office of the Clerk
U.S. Courthouse
500 Pearl Street, New York, N.Y. 10007-1213

----------X

-V-

MOTION FOR EXTENSION OF TIME TO FILE A NOTICE OF APPEAL

civ. ( )

----------X

Pursuant to Fed. R. App. P. 4(a)(5), _____ respectfully
(party)
requests leave to file the within notice of appeal out of time. _____
(party)
desires to appeal the judgment in this action entered on _____ but failed to file a
(day)
notice of appeal within the required number of days because:

[Explain here the "excusable neglect" or "good cause" which led to your failure to file a notice of appeal within the required number of days.]

_____
(Signature)

_____
(Address)

_____
(City, State and Zip Code)

Date: _____ ( ) _____-_____
(Telephone Number)

Note: You may use this form, together with a copy of Form 1, if you are seeking to appeal a judgment and did not file a copy of Form 1 within the required time. If you follow this procedure, these forms must be received in the office of the Clerk of the District Court no later than 60 days of the date which the judgment was entered (90 days if the United States or an officer or agency of the United States is a party).

FORM 2

United States District Court
Southern District of New York
Office of the Clerk
U.S. Courthouse
500 Pearl Street, New York, N.Y. 10007-1213

----------X

-V-

NOTICE OF APPEAL
AND
MOTION FOR EXTENSION OF TIME

civ. ( )

----------X

1. Notice is hereby given that _____ hereby appeals to
(party)
the United States Court of Appeals for the Second Circuit from the judgment entered on _____.
[Give a description of the judgment]

2. In the event that this form was not received in the Clerk's office within the required time

_____ respectfully requests the court to grant an extension of time in
(party)
accordance with Fed. R. App. P. 4(a)(5).

a. In support of this request, _____ states that
(party)
this Court's judgment was received on _____ and that this form was mailed to the
(date)
court on _____ .
(date)

_____
(Signature)

_____
(Address)

_____
(City, State and Zip Code)

Date: _____ ( ) _____ - _____
(Telephone Number)

Note: You may use this form if you are mailing your notice of appeal and are not sure the Clerk of the District Court will receive it within the 30 days of the date on which the judgment was entered (60 days if the United States or an officer or agency of the United States is a party).

FORM 3

United States District Court
Southern District of New York
Office of the Clerk
U.S. Courthouse
500 Pearl Street, New York, N.Y. 10007-1213

----------X

-V-

AFFIRMATION OF SERVICE

civ. ( )

----------X

I, _____, declare under penalty of perjury that I have served a copy of the attached _____

_____

upon _____

_____

whose address is: _____

_____

Date: _____
New York, New York

_____
(Signature)

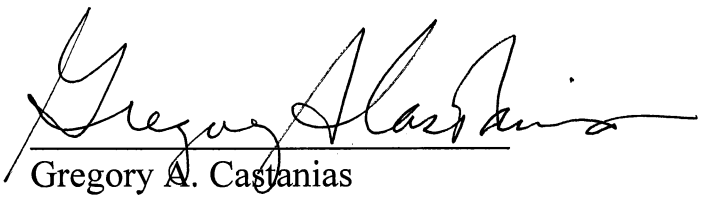
_____
(Address)

_____
(City, State and Zip Code)

CERTIFICATE OF SERVICE

The undersigned counsel hereby certifies that two copies of the Brief for Appellants were served by UPS (overnight delivery) and e-mail on October 22, 2010, upon the following counsel for Plaintiffs-Appellees:

Christopher A. Hansen, Esq.
American Civil Liberties Union Foundation
125 Broad Street—18th Floor
New York, NY 10004



Gregory A. Castanias
Attorney For Appellants

CERTIFICATE OF COMPLIANCE

1. This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B), because it contains 13,996 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii) and Federal Circuit Rule 32(b).

2. This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6), because it has been prepared in a proportionally spaced typeface using Microsoft Word 2003 in Times New Roman 14 point font.

Dated: October 22, 2010

Gregory A. Castanias
Attorney For Appellants