
**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,
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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**

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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:

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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)
<i>BRCA1/2</i>	Two genes (<i>BRCA1</i> and <i>BRCA2</i>) 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 [plaintiff’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 PGE₂ and PGE₃ [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 "distinct[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 initiate 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.

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Respectfully submitted,



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