No. 12-398

IN THE

Supreme Court of the United States

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,
Petitioners,

v.

MYRIAD GENETICS, INC., ET AL.,
Respondents.

On Writ Of Certiorari
To The United States Court Of Appeals
For The Federal Circuit

BRIEF FOR RESPONDENTS

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QUESTION PRESENTED

The claimed isolated molecules of deoxyribonucleic acid are particular molecular compositions designed based on the Myriad inventors' identification and characterization of the structure of the BRCA genes, and separated from other cellular content by the inventors based on those designs. These molecules are used to detect and analyze mutations in human tissue, which aid in determining a patient's genetic predisposition risk to breast and ovarian cancers.

The question presented is:

Did the Federal Circuit correctly apply 35 U.S.C. § 101 to conclude that these particular molecules are "product[s] of human ingenuity 'having a distinctive name, character [and] use,'" particularly where the general legal rule followed by courts for 30 years has been to allow such patent claims, where the U.S. Patent and Trademark Office ("USPTO") has issued similar patents since at least 1982 and confirmed in the 2001 *Utility Guidelines* that such isolated molecules are patent-eligible as human-made inventions under § 101, where investors and technology companies have placed significant reliance in these settled property rights over the last 30 years, where the alternative dividing line is indefensible under law or science, and where the challenged claims do not preempt or preclude the use of alternative technologies to identify a patient's cancer predisposition?

LIST OF PARTIES

Petitioners' brief correctly lists the parties to the Federal Circuit proceedings. *See* Pet. Br. i-ii. However, the Federal Circuit held that only one plaintiff, Dr. Harry Ostrer, had standing. Pet. App. 41a. Because this Court declined petitioners' certiorari request to review whether the remaining plaintiffs also had standing in this case, *see Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 694 (2012), Ostrer is the sole petitioner before this Court.

CORPORATE DISCLOSURE STATEMENT

No parent or publicly held company owns 10% or more of the stock of respondent Myriad Genetics, Inc. or of the University of Utah Research Foundation.

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JURISDICTION

Petitioners' jurisdictional statement omits that Myriad has always contested any live case or controversy between Myriad and Dr. Harry Ostrer, the only remaining petitioner. There is still no case or controversy. *See* pp. 17-22, *infra*.

STATEMENT

1. In passing the 1952 Patent Act, and in particular 35 U.S.C. § 101, "Congress intended statutory subject matter to 'include anything under the sun that is made by man.'" *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (quoting S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952); H. R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952)). "Made by man" means, for composition-of-matter claims, that they are "a product of human ingenuity." *Id.*

"[M]anifestations of . . . nature," such as a new plant found in the wild or the qualities of a naturally-occurring bacterium, *see Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948), are of course not "product[s] of human ingenuity," because they occur without aid of human faculties. But because "[e]verything that happens may be deemed 'the work of nature,' and any patentable composite exemplifies in its properties 'the laws of nature,'" *id.* at 134-35 (Frankfurter, J., concurring), it is important to define clearly the line between an unpatentable manifestation of nature and a patent-eligible composition. As this Court has held, the answer to that inquiry depends on whether the composition—even if created with naturally-occurring starting materials, and even if resembling or performing some of the same functions as something found in nature—was the result of "human ingenuity," *i.e.*, "invention."

Chakrabarty, 447 U.S. at 309; *see Mackay Radio & Tel. Co. v. Radio Corp. of Am.*, 306 U.S. 86, 94 (1939).

No one would doubt the patent-eligibility of a newly-created chemical composition that, when applied in a laboratory to a person's blood or tissue sample, could detect a mutation genetically predisposing her to a risk of breast or ovarian cancer, thereby allowing her to take proactive measures to prolong her life even before cancer actually strikes. That is what Myriad's patented molecules are—and they were never available to the world until Myriad's scientists applied their inventive faculties to a previously undistinguished mass of genetic matter in order to identify, define, and create the isolated DNA molecules.

2. It has long been established that specific isolated molecules of deoxyribonucleic acid ("DNA") are patent-eligible. "Isolated" means that a human being has defined the molecule and separated it from the complex of genetic material that accompanies it in the body, or (as with complementary DNA, or cDNA) synthetically created the molecule in a laboratory. Such molecules may include recombinant, cloned, or synthesized DNA isolates. Pet. App. 19a-20a. This human design and action transforms the molecule's physical structure and alters its chemistry. JA413-19.

Two years after *Chakrabarty*, the USPTO granted the first human DNA-related patents. *See* Eric J. Rogers, *Can You Patent Genes? Yes and No*, 93 J. PAT. & TRADEMARK OFF. SOC'Y 19, 19 & n.3 (2010) (citing patents issued March 30 and December 14, 1982). Over the next 30-plus years, the USPTO and the courts reinforced the rule of patent-eligibility for

isolated DNA molecules, recognizing that creating a particular novel isolated molecule represents a patentable advancement over what existed in nature. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). The USPTO has granted over 40,000 patents drawn to genetic material, almost 3,000 of which are specifically directed to isolated DNA molecules. Indeed, the challenged Myriad patents began issuing 15 years ago (all will expire in the next two years). *See* Rogers, *supra*, at 19, 40; Pet. App. 61a-62a, 87a-88a; JA527-28.

In the mid-1990s, when DNA-related claims had been issuing for over a decade and upheld by the Federal Circuit, the USPTO evaluated its approach for compliance with § 101, and "to ensure that examination was of sufficiently high quality." JA519, 581. The USPTO held a public hearing, received comments, and in 1995 issued its initial guidelines for patent examiners. These guidelines concluded that "any 'non-naturally occurring manufacture or composition of matter'" is patent-eligible under § 101. *Utility Examination Guidelines*, 60 Fed. Reg. 36,263 (July 14, 1995); JA581-84.

In 2001, the USPTO again considered the rule that isolated molecules derived from genetic material can be patent-eligible. JA521-22. Following an extensive notice-and-comment process and further review of the statute and precedent, the USPTO promulgated another set of *Utility Guidelines*. 66 Fed. Reg. 1092 (Jan. 5, 2001). Under the USPTO's 2001 *Guidelines*,

so long as "the [patent] application discloses a specific, substantial, and credible utility for the claimed isolated and purified gene, the isolated and purified gene composition may be patentable." *Id.* at 1093.[1] The USPTO elaborated that "[a] patent on a gene covers the isolated and purified gene but does not cover the gene as it occurs in nature." *Id.*; *see also* JA522 (declaration of John Doll, later Commissioner for Patents, explaining the reasoning underlying the 2001 *Guidelines*). When a patent claims isolated DNA molecules, the USPTO requires a symbolic recitation of the nucleotide or amino acid sequence in what is called a "SEQ ID." *See* 37 C.F.R. §§ 1.821-1.825; *Manual of Patent Examining Procedure* §§ 2420 *et seq.* ("MPEP").

The USPTO's *Guidelines* followed the long-established rule that isolates or extracts of natural products may be patented.[2] The USPTO, and, ultimately, the courts, had long considered extracts

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[1] Petitioners have never challenged the utility of Myriad's claimed molecules. *E.g.*, Pet. Br. 9.

[2] *See, e.g.*, U.S. Patent Nos. 644,077 (1900) (pure acetyl salicylic acid (aspirin)); 1,898,199 (1933) (isolated digitalis—a substance obtained from the foxglove plant for the treatment of heart conditions); 2,105,486 (1938) (whooping-cough vaccine derived from bacterial extracts); 2,698,843 (1955) (antimicrobial composition extracted and purified from a corn fungus); 3,929,992 (1975) (Rapamycin—an immunosuppressant produced by a soil bacterium and used to prevent rejection of transplanted organs); 3,983,140 (1976) (cholesterol-lowering compound purified from a Penicillium sp.); 5,135,864 (1992) (the HIV virus).

or isolates of natural products to be both patent-eligible *and* patentable. *See, e.g.*, *Kuehmstead v. Farbenfabriken of Elberfeld Co.*, 179 F. 701 (7th Cir. 1910) (aspirin); *In re Kratz*, 592 F.2d 1169 (C.C.P.A. 1979) (substantially pure 2-methyl-2-pentenoic acid (2M2PA)—the molecule that imparts strawberries' distinctive flavor and odor—mixed with an adjuvant); *In re Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970) (substantially pure PGE2 and PGE3 (prostaglandins)); *Merck Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958) (purified vitamin B12 obtained from extracts of streptomyces cultures); *Parke-Davis & Co. v. H.K. Mulford & Co.*, 196 F. 496 (2d Cir. 1912) (substantially pure adrenalin derived from cow glands).

3. Countless companies and investors have risked billions of dollars to research and develop advances under this promise of stable patent protection. *See* Letter from Eric Y. Drogin & Robert A. Armitage to David J. Kappos re: Genetic Diagnostic Testing 5 (Apr. 16, 2012), *available at* www.uspto.gov/aia_implementation/gene-comment-aba.pdf. One was a small Utah start-up, Helix Technologies. In the mid-1990s, scientists at Helix, now known as Myriad Genetics, successfully identified, defined, and isolated the BRCA molecules, and disclosed their creation and utilities to the world. This momentous scientific advancement displayed Myriad's inventors' significant scientific skill, insight, and invention.

Genes in the body are chemically connected in unbroken strands of DNA wrapped around proteins to form chromosomes. By 1990, it had been hypothesized that at least one very large chromosomal location correlated with susceptibility

to breast and ovarian cancers, but there was much confusion in the field at that time over any more particular location. JA479-80, 493, 499, 747. "Given the confusion, a skilled artisan would not have known in which chromosomal region to look for the *BRCA1* gene." JA480, 747.

Myriad succeeded where others failed by applying its genetic-mapping technology to define and locate the precise genetic regions associated with mutations predisposing a patient to breast and ovarian cancers. JA481-83, 484-87 (a collaborating scientist described this technique as "the closest thing to magic"). These regions came to be known as the "BRCA1 gene" and the "BRCA2 gene." JA498-501. This stage of the inventive process itself depended on an enormous amount of human judgment, including how to define the beginning and end of these genes. JA480-90, 495-99, 507-11.

Building on this foundation, Myriad then studied the BRCA genes to identify their particular structures, attributes, and characteristics. Once it deciphered this information, it sought to improve existing techniques for diagnosing an individual's hereditary cancer risk by designing isolated DNA molecules and producing them in the laboratory (by manufacturing or synthesis). JA481-90, 495-99, 506-11. These applications of human ingenuity yielded new, never-before-available molecules that can now be used to detect mutations associated with a risk of hereditary breast or ovarian cancer (the principal cancers associated with mutations in the BRCA1 and BRCA2 regions of the genome).

As the patents describe, the specific isolated BRCA1 and BRCA2 molecules, once defined, were

either separated from surrounding genomic and cellular matter at precise locations chosen by the Myriad inventors, or assembled in a laboratory (in the case of cDNA). Pet. App. 14a; *e.g.*, JA748, 755. Their human inventive choices defined the particular isolated molecules, free from genetic and other surrounding material, to enable their utility outside the body in ways that naturally-occurring DNA in the body lacks. Pet. App. 18a; JA413-19, 468-69. To function within the body, a gene cannot be isolated, but must be physically bound to other genes, nucleic acids, and proteins within the chromosome.

Two critical uses of the claimed molecules are to "probe" for target DNA in a patient sample or to "prime" the production of copies of the target DNA in the laboratory. *E.g.*, 753, 756. When so used, these isolated molecules are designed to "zero-in" on and bind to (hybridize) the BRCA gene in the much larger genome in the human sample—akin to finding "a grain of sand" within the Empire State Building. JA436-37. This hybridization can only take place because of the natural "pairing" quality of the molecule's nucleotide bases (the bases denoted "A" and "T" bind with one another, as do the bases denoted "G" and "C"), *in combination with* the human ingenuity involved in designing those particular molecules. Probes and primers thus function because of the *differences* from native DNA brought about by the ingenuity of Myriad's inventors. JA135, 415-18,

473-75, 524-25, 564-65, 595-601, 603, 608-11.[3] DNA molecules in the body (native DNA), by contrast, cannot be used as probes or primers, because they are chemically bound up with other matter. *See generally* Bruce Alberts et al., MOLECULAR BIOLOGY OF THE CELL 98-99, 291-93, 296-98 (3d ed. 1994).

4. To recoup its vast investment in creating these new molecules, Myriad uses them as part of a molecular testing service for targeted isolation and sequencing of a patient's BRCA DNA. Myriad's BRAC*Analysis*® test, conducted on a patient's blood or oral-rinse sample, filled a long-felt need by drastically improving accuracy in determining

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[3] To be used as a "probe," an isolated molecule is typically "tagged" with a marker (*e.g.*, a radioactive or fluorescent compound) so that it can be detected once it binds (hybridizes) with the targeted area of the human sample. JA413-19, 473-75, 525, 595-96, 598-601, 610-11; Bruce Alberts et al., MOLECULAR BIOLOGY OF THE CELL 295-96 (3d ed. 1994).

As a "primer," the isolated DNA molecule is used in a reiterative process called a polymerase chain reaction ("PCR"). Like probes, primers are designed to bind to the target BRCA DNA in the human sample. In PCR, the primer is combined with, *inter alia*, the human sample and a heat-stable enzyme (that does not exist in the human body). The free reactive end of the bound primer serves as a starting point for PCR to synthesize a copy of the target DNA. The reaction is repeated to "amplify"—exponentially duplicate—DNA copies of the target. JA413-19, 473-75, 353, 432, 597. The resulting high concentration of the DNA copies allows scientists to better analyze and ascertain the sequence of the target DNA in the patient's sample to detect a genetic mutation. JA353; Alberts, *supra*, at 316-17.

patients' predisposition to hereditary breast and ovarian cancers. JA341, 350-51, 356-57. Myriad also spent hundreds of millions of dollars over the past 20 years educating patients, doctors, medical associations, and insurers (including Medicare and Medicaid) about genetic testing, and it provides free testing for patients in need. JA344-47, 535-37. Moreover, Myriad has dedicated staff to help patients navigate the complexities of insurance coverage and reduce their out-of-pocket expenses, so that over 90% of BRAC*Analysis*® tests are covered by insurance at over 90% of the cost, with those patients paying less than $100 on average. JA344, 348. Today, because of Myriad's inventions and its investments—secured by the promise of a limited period of patent protection—high-quality BRCA testing, widely approved by doctors and insurers, has been conducted on over one million patients.[4] JA346-49, 351-55.

Those of ordinary skill could not have created Myriad's patented molecules in the mid-1990s. One of Myriad's principal competitors followed conventional wisdom by cloning large pieces of human DNA, rather than Myriad's counterintuitive approach of using smaller pieces, which required many more clones and was thought at the time to be a "mistake." JA484-86. The competitor's large clones,

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[4] Ostrer incorrectly implies that only 130 million Americans have access to BRAC*Analysis®*, Pet. Br. 45, but that counts only those with private insurance. The test is also covered under Medicare and Medicaid. JA347-48, 536.

however, "had a deletion at the site of the BRCA1 gene," so their research would never have succeeded in defining the molecule now known as BRCA1 to permit further study for isolation. JA485. Their leader eventually acknowledged these flaws, described Myriad's identification of the BRCA1 gene "as 'beautiful' and 'lovely' and deserving of all the praise it might win," and named Myriad's approach "the winne[r] of the day." JA485, 501-02. A competitor with respect to BRCA2 similarly failed because one of its tools was missing critical aspects of the gene's structure. JA507.

Myriad disclosed its inventions to the public in a series of patents. Contrary to Ostrer's mischaracterizations of the patents' effects, Pet. Br. 7-9, 43-45, since the patents issued, over 18,000 researchers have conducted studies on BRCA1/2 genes, published over 8,000 papers, and conducted over 130 clinical trials. JA336-37, 455-56. Indeed, one named plaintiff conceded that she may "sequence the BRCA1 and BRCA2 genes for purely research purposes," and has been doing so without impediment. JA59-60. And multiple laboratories provide "second opinions" regarding BRAC*Analysis*® results. JA364-65.

5. Nine claims in three patents remain at issue. Claims 1, 2, 5, 6, and 7 of U.S. Patent No. 5,747,282 (the "'282 patent") and claim 1 of U.S. Patent No. 5,693,473 (the "'473 patent") relate to BRCA1. Claims 1, 6, and 7 of U.S. Patent No. 5,837,492 (the "'492 patent") relate to BRCA2.

Each of the nine claims expressly recites "[a]n isolated DNA" or "[a]n isolated DNA molecule." An "isolated" molecule is defined in the patents as a

molecule "which is substantially separated from other cellular components which naturally accompany a native human sequence or protein, e.g., ribosomes, polymerases, many other human genome sequences and proteins. The term embraces a nucleic acid sequence or protein removed from its naturally occurring environment, and includes recombinant or cloned DNA isolates and chemically synthesized analogs or analogs biologically synthesized by heterologous systems." *E.g.*, JA755 (19:8-19). Some of the claims (claims 2, 6, and 7 of the '282 patent and claim 7 of the '492 patent) are drawn even more narrowly and cover only cDNA molecules—"synthetic molecules built by scientists" in a laboratory. U.S. Br. 4.

Claims to isolated DNA molecules. Claim 1 of the '282 patent is representative of these claims: "An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO: 2." JA822. SEQ ID NO:2 depicts the amino-acid sequence of the BRCA1 protein (the expression product of BRCA1 DNA). JA785-90. Claim 1 of the '492 patent is similar, but is directed to isolated BRCA2 DNA molecules. JA1028.

Claim 5 of the '282 patent is directed to portions of the isolated BRCA1 DNA molecules recited in claim 1: "An isolated DNA having at least 15 nucleotides of the DNA of claim 1." JA822.

Claim 6 of the '492 patent is directed to an "isolated DNA molecule" of the kind claimed in claim 1 of that patent, but having a mutation of the BRCA2 polypeptide "associated with susceptibility to cancer." JA1028.

Finally, claim 1 of the '473 patent is directed to specific, identified alterations of isolated BRCA1 DNA molecules. JA930.

Claims limited to cDNA molecules. The "isolated DNA" claims encompass cDNA molecules as well as other isolated molecules. A second group of claims, however, is limited to cDNA molecules. In addition to being "isolated," cDNA molecules differ from native DNA because, *inter alia*, they are synthesized in laboratories and exclude certain regulatory and other non-protein-coding sequences (introns) found in native DNA and include only protein-coding DNA (exons). JA779-85.

Claim 2 of the '282 patent is exemplary: "The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1." JA822. The "wherein" clause limits the claim to particular cDNA molecules—*i.e.*, the nucleotide sequence of just the coding regions, omitting introns, depicted in SEQ ID NO: 1. JA779 ("Molecule Type: cDNA"). Far from being "solely illustrative," Pet. Br. 14, the sequence in SEQ ID NO: 1 defines the structure of the claimed molecules by requiring that they have the recited cDNA sequence.

Claim 6 of the '282 patent is directed to limited portions of the molecules of claim 2: "An isolated DNA having at least 15 nucleotides of the DNA of claim 2." JA822.

The other two claims deal with cDNA molecules having genetic mutations. Claim 7 of the '282 patent is directed to specific, identified alterations of isolated BRCA1 cDNA molecules. JA822. Claim 7 of the '492 patent is directed to mutations of a BRCA2 cDNA composition. JA1028.

6. This declaratory-judgment action began when the American Civil Liberties Union Foundation ("ACLU") and the Public Patent Foundation ("PubPat") recruited 20 plaintiffs to, in ACLU counsel's words, "sue somebody." Joe Palazzolo, *Law Blog Fireside: Chris Hansen, the ACLU's Longest-Serving Attorney*, Wall Street Journal Law Blog (Nov. 9, 2012), http://blogs.wsj.com/law/2012/11/09/law-blog-fireside-chris-hansen-the-aclus-longest-serving-attorney (last visited Mar. 6, 2013) ("WSJ Law Blog"). The complaint alleged, *inter alia*, that a few selected claims of seven patents-in-suit are not patent-eligible under 35 U.S.C. § 101 and unconstitutional under Article I, § 8, cl. 8 of, and the First and Fourteenth Amendments to, the Constitution. JA54. In statutory terms, the entire lawsuit concerned only the narrow issue of § 101 patent-eligibility—there are no patentability challenges under §§ 102 (novelty), 103 (non-obviousness), or 112 (disclosure).

Myriad moved to dismiss for lack of a real and immediate case or controversy between Myriad and any of the plaintiffs. Pet. App. 25a. Although the district court sustained jurisdiction as to all plaintiffs, *id.* at 406a, the Court of Appeals subsequently held that only one, Ostrer, had a live controversy with Myriad, *id.* at 41a. In their certiorari petition, the other 19 plaintiffs unsuccessfully tried to obtain review of this ruling. Pet. i; JA21. Ostrer is thus the sole petitioner before the Court.

7. On summary judgment, after conducting only limited claim construction, the district court held all of the challenged claims patent-ineligible because

"none of the structural and functional differences cited by Myriad" constitute a marked difference between native DNA and the claimed isolated DNA molecules. Pet. App. 336a. (The district court declined to address plaintiffs' constitutional claims. *Id.* at 355a n.61.) The Federal Circuit reversed. *Id.* at 179a. After this Court decided *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012), it granted plaintiffs' first certiorari petition, vacated the Federal Circuit's judgment, and remanded for further consideration in light of *Mayo*, Pet. App. 1a.

On remand, the Federal Circuit reexamined the challenged claims to isolated DNA molecules in light of *Mayo* and again held them patent-eligible. Each member of the panel noted that the fundamental inquiry remained the *Chakrabarty* test understood in light of *Mayo*, evaluating whether the compositions were the product of human ingenuity.

Judge Lourie's lead opinion focused on the variety of differences between the claimed compositions and native DNA caused by human intervention, *e.g.*, isolated DNA molecules are "free-standing," are "synthesized" or have "chemically severed" backbones, and have significantly fewer nucleotides than native DNA. *Id.* at 49a, 51a (internal quotations and brackets omitted). Concurring, Judge Moore further explained that these structural changes to these molecules imparted new utilities. *Id.* at 80a-86a. Both judges underscored that the patent-eligibility of these claims is confirmed by the decades-long practice of granting patents on isolated DNA molecules, and the investing and inventing

communities' settled expectations based on that practice. *Id.* at 61a-62a, 87a-94a.

Dissenting in part, Judge Bryson agreed that cDNA claims are patent-eligible. *Id.* at 113a-14a; *accord* 47a, 54a, 80a-81a. For the other claims, he agreed that isolating DNA molecules causes a "material change made to those genes from their natural state," but he downplayed the significance of the change as "necessarily incidental to the extraction of the genes from the environment in which they are found." *Id.* at 102a.

SUMMARY OF ARGUMENT

I. The Federal Circuit distorted fundamental Article III principles to find that one of 20 declaratory-judgment plaintiffs, recruited by their counsel to bring this test case, presented a live case or controversy. A declaratory-judgment plaintiff must have a "real and substantial" dispute with the defendant, "of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118, 127 (2007) (internal quotations and citations omitted). This threat must exist "at the commencement of the litigation," *Davis v. FEC*, 554 U.S. 724, 732 (2008), and "subsis[t] through all stages" of proceedings thereafter, *Lewis v. Continental Bank Corp.*, 494 U.S. 472, 477-78 (1990).

Here, the alleged controversy was neither "real" nor "immediate," but manufactured and stale, when the complaint was filed in 2009. The Federal Circuit nonetheless concluded that Ostrer had a justiciable dispute with Myriad because he suspended BRCA testing in 1998 after NYU, his then-employer, received but did not accept a license offer from

Myriad. Even if that single communication had been sufficient to support jurisdiction in 1998, there were no further communications between Myriad, Ostrer, and NYU, and Ostrer's subjective conclusion that the 1998 license offer chilled his commercial activity when he filed suit in 2009 does not present a real or immediate dispute to support declaratory-judgment jurisdiction.

Further, Ostrer mooted any conceivable controversy when he left NYU in 2011 and moved to a different institution with *no* past history or communications with Myriad. In short, this is a lawyer-driven case with no concrete interest to support a declaratory-judgment action.

II. Were the Court to reach the merits, it should affirm. Section 101 broadly covers "anything under the sun that is made by man." *Chakrabarty*, 447 U.S. at 309. The claimed isolated DNA molecules are physical, chemical compositions squarely within the plain language of § 101. The claims also clearly fall on the inventive side of the line drawn by this Court's precedent and exemplified in the USPTO's *Guidelines*. With no intervening dissent from Congress, continuing this approach respects the longstanding rule that isolated DNA molecules such as those claimed here warrant patent-eligibility—a judgment on which industry, inventors, and investors alike have relied in researching, developing, and bringing new and useful medical products to the world. *See J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124 (1996).

Ostrer instead offers an ambiguous, three-part test that obscures the language of the statute and the "product of human ingenuity" principle established

by precedent and long applied by the USPTO. He asks whether a "product of nature" has "markedly different" characteristics and improperly "preempts" research. These formulations possess neither the crispness nor the legal accuracy required to determine whether a composition is the product of human ingenuity. Ostrer further confuses the issue before the Court by misstating the claim language, the record, and scientific facts, and by conflating the conditions for ultimate patentability with the sole question presented concerning patent-eligibility. The claims, all compositions made by man, satisfy § 101. The judgment should be affirmed.

ARGUMENT

I. OSTRER HAD—AND NOW HAS—NO "REAL AND IMMEDIATE" DISPUTE WITH MYRIAD TO SUPPORT HIS DECLARATORY-JUDGMENT COMPLAINT

The Federal Circuit found that 19 plaintiffs had no real dispute with Myriad, but it strained to find a case or controversy as to one, Dr. Ostrer. The court's ruling was contrary to this Court's precedent and fundamental Article III principles that ensure resort to the federal courts only for real, live controversies. Ostrer had no real and immediate dispute with Myriad when this lawsuit was filed in 2009, and by his own unilateral conduct has none now.

A. Ostrer Never Had A "Real And Immediate" Dispute With Myriad

The Federal Circuit reasoned that Ostrer had presented a justiciable declaratory-judgment action because he averred that he "will immediately begin such [BRCA] testing" if Myriad's patents were

invalidated. Pet. App. 35a-36a. The court distinguished Ostrer's averments from those of two other plaintiffs, Drs. Ganguly and Kazazian, who only said they would "consider" resuming testing in that event. *Id.*

The reality and immediacy of the claimed dispute should not have been evaluated in such a unilateral fashion. Myriad's contribution to the supposed controversy was a single 1998 communication to NYU's Molecular Genetics Laboratory, nominally addressed to Ostrer because he was the lab's director at the time. Pet. App. 33a-36a; JA94-110. NYU did not sign the proposed license agreement enclosed with Myriad's letter, and there was no further communication until Ostrer and his co-plaintiffs filed this action in 2009. JA110. Radio silence for eleven years.

Under no plausible definition of "immediate" can an eleven-year-old, never-responded-to licensing offer to an employer serve to establish an Article III case or controversy with an employee. The Federal Circuit disagreed, reasoning that "the relevant circumstances remain unchanged" since 1998, describing Ostrer as somehow "laboring under Myriad's threat of infringement liability" since receiving the license offer. Pet. App. 37a.

But it was Ostrer's unilateral decision to suspend genetic testing, based entirely on his speculations about what Myriad might have done had Ostrer continued testing, that caused his claimed injury. That is not enough. *See Clapper v. Amnesty Int'l USA*, No. 11-1025, 2013 WL 673253, at *10 (U.S. Feb. 26, 2013) (expressing the Court's "usual reluctance to endorse standing theories that rest on speculation

about the decisions of independent actors"). In *Laird v. Tatum*, 408 U.S. 1, 2 (1972), this Court dismissed a declaratory-judgment action where plaintiffs alleged that the Army's "surveillance of lawful and peaceful civilian political activity" chilled their First Amendment speech rights. Plaintiffs' "[a]llegations of a subjective 'chill' [we]re not an adequate substitute for a claim of specific present objective harm or a threat of specific future harm." *Id.* at 13-14; *see also Clapper*, 2013 WL 673253, at *12. Just as the *Laird* plaintiffs' allegation that they spoke less in light of the surveillance program was inadequate, Ostrer cannot demonstrate standing by averring that, after serving as a conduit for Myriad's licensing offer to NYU, he ceased certain testing activities in 1998 (a fact he never communicated to Myriad), and continued that cessation on his own accord, again without any further communication from Myriad, until the 2009 complaint. Neither in *Laird*, nor in *Clapper*, nor here, was there a "certainly impending" injury traceable to Myriad. *Whitmore v. Arkansas*, 495 U.S. 149, 158 (1990); *Clapper*, 2013 WL 673253, at *7. The harm created by Ostrer's eleven-year-long cessation of testing is not a "real and immediate" bilateral dispute between parties, but unilateral, self-inflicted injury.

The filing of this suit in 2009 had nothing to do with Myriad or the existence of any real dispute, and everything to do with Ostrer's counsel's manufacturing of this cause. The ACLU's strategy was "let's sue somebody" (WSJ Law Blog, *supra*), and PubPat's stated intent was to "rend[er] invalid patents on many other genes . . . . We just had to pick one case as our case." C.A. App. 7387-88.

Neither "the intensity of [Ostrer's or his counsel's] interest [n]or the fervor of his advocacy" substitutes for the constitutional requirement of a real and immediate controversy. *Valley Forge Christian Coll. v. Ams. United for Separation of Church & State, Inc.*, 454 U.S. 464, 486 (1982). The eleven-year-old licensing offer to NYU—alone or in combination with Ostrer's unilateral cessation of testing—did not create a "real and immediate" controversy when this case was filed in 2009.

B. Even If Myriad's 1998 Licensing Offer To NYU Could Serve As A Basis For This Declaratory-Judgment Action, Ostrer's 2011 Departure From NYU Mooted This Case

If a controversy ceases to exist during any stage of a case, it is properly dismissed as moot. *Preiser v. Newkirk*, 422 U.S. 395, 401-03 (1975). On August 29, 2011, while this case was pending on appeal, Ostrer ended his employment at NYU and moved to the Albert Einstein College of Medicine and Montefiore Medical Center (collectively, "Montefiore"). JA721. Ostrer thereby extinguished any conceivable controversy that might have existed before.

Myriad and Montefiore have never communicated about the patents-in-suit; thus, Myriad never could have "chilled" any Montefiore scientist's testing. JA724-25. Ostrer's current claim to standing therefore reduces to a gripe that a licensing offer made to NYU in 1998 continues to "chill" his activities at an entirely different institution in 2013.

Ostrer has tried to avoid mootness by asserting that at Montefiore he retains the same readiness to perform genetic testing that he had while at NYU. JA722-23. But this makes the causal link to Myriad

even more speculative than the hypothetical Myriad-NYU connection. Even if Ostrer was "once bitten" when he was at NYU, he is not entitled to claim that he is "twice shy" at Montefiore. *Already, LLC v. Nike, Inc.*, 133 S. Ct. 721, 730 (2013). Ostrer's assertion that Myriad's license offer to NYU somehow traveled with him to Montefiore because it was addressed to him individually (JA723) is incorrect. The letter was addressed to Ostrer solely as the NYU laboratory director, not in his personal capacity. JA94-95 (offering license to "NYU Medical Center"). The enclosure was a proposed license between Myriad and NYU, not with Ostrer personally. JA96, 98-99 (NYU is specified throughout; Ostrer, not once), 110 (signature blank for "NYU Medical Center," not Ostrer). Had NYU accepted the license offer, Ostrer could not have taken its rights with him when he left. Yet, by upholding Ostrer's standing, the Federal Circuit's ruling exposes patentees (and similar rights holders) to lawsuits by current or former employees of a license offeree, for the lifetime of the holder's right.

The Federal Circuit never addressed this, instead summarily denying Myriad's suggestion of mootness without any analysis. Pet. App. 25a n.6. The § 101 claim pressed by Ostrer assuredly holds some abstract, academic interest. But a court without jurisdiction must "put aside the natural urge to proceed directly to the merits." *Raines v. Byrd*, 521 U.S. 811, 819-20 (1997); *Already*, 133 S. Ct. at 726 ("courts have 'no business' deciding legal disputes or expounding on law in the absence of" a case or controversy).

The proper scope of § 101 as applied to isolated molecules should be addressed in a concrete controversy, not in an abstract policy vehicle of public-interest law firms. The vitality of companies and industries that this Court's judgment could affect should not depend on such a one-sided dispute. Accordingly, even were this Court to find that Ostrer presented a "real and immediate" controversy in 2009, such a controversy no longer exists, and this action should be dismissed as moot.[5]

II. THE COURT OF APPEALS CORRECTLY DETERMINED THAT MYRIAD'S CLAIMS ARE PATENT-ELIGIBLE

Applying the proper legal framework, as reflected in the USPTO's longstanding practice and even longer-standing case law, the Federal Circuit correctly determined that Myriad's claims are drawn to patent-eligible compositions of matter.

A. The Challenged Claims Are Chemical "Compositions Of Matter" Squarely Within § 101

Section 101 of the Patent Act, enacted in 1952, is a "threshold" provision, setting forth categories of patent-eligible subject matter. *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010). Section 101 has a broad

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[5] If the Court vacates any prior decisions, it should include the district court's decision, because mootness resulted from the unilateral actions of Ostrer, who prevailed at the district court. *See U.S. Bancorp Mortgage Co. v. Bonner Mall P'ship*, 513 U.S. 18, 23 (1994).

scope, covering "anything under the sun that is made by man." *Chakrabarty*, 447 U.S. at 309. The statute provides in full:

> 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.

35 U.S.C. § 101.

Myriad's claims are statutorily patent-eligible. Each claim is, on its face, to a chemical "composition of matter," or a "new and useful improvement thereof." Petitioners have never disputed this. C.A. App. 6911. Each claim recites "isolated DNA"—a physical, chemical compound (an acid) made up of nucleotides connected by a phosphodiester backbone. Pet. App. 14a. The molecules thus fall within the literal language of the statute.

B. The "Implicit Exception" To § 101 Excludes Only Things That Lack Human Invention

This Court has ruled that § 101 contains an "implicit exception[:] '[L]aws of nature, natural phenomena, and abstract ideas' are not patentable." *Mayo*, 132 S. Ct. at 1293. The touchstone of this implicit exception is the absence of human "invention."

This principle explains *Chakrabarty*, *Funk Brothers*, and *Mayo.* In *Chakrabarty*, the Court upheld the patent-eligibility of bacteria whose starting materials were in nature. The Court explained that the "relevant distinction" is whether the claims are directed to "human-made inventions."

447 U.S. at 313. Accordingly, *Chakrabarty* framed the § 101 question as whether the claimed composition is "a product of human ingenuity 'having a distinctive name, character and use'" from naturally-occurring starting materials. *Id.* at 309-10.

Chakrabarty distinguished the claims before it from those at issue in *Funk Brothers*, but it is clear that both cases turned on the presence (in *Chakrabarty*) or absence (in *Funk Brothers*) of human invention. As the Court of Appeals held (Pet. App. 49a-50a), *Funk Brothers*—which was decided when there was a single statutory provision governing both patent-eligibility and patentability (R.S. § 4886, codified at 35 U.S.C. § 31)—was a case involving the then-implicit requirement of "invention."[6] *Funk Bros.*, 333 U.S. at 131-32 ("a product must be more than new and useful to be patented; it must also satisfy the requirements of invention or discovery" (citing *Cuno Eng'g Corp. v. Automatic Devices Corp.*, 314 U.S. 84, 90, 91 (1941))). That requirement is now codified in § 103, with Congress "emphasiz[ing] 'nonobviousness' as the operative test of the section, rather than the less definite 'invention' language of *Hotchkiss [v.*

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[6] Whereas former R.S. § 4886 combined them, the 1952 Patent Act divided into separate statutory sections the requirements for patent-eligibility (§ 101) and patentability (§ 102 for novelty, § 103 for nonobviousness, § 112 for disclosure, etc.). Ostrer is thus wrong to describe *Funk Brothers* as a case involving "Section 101" (Pet. Br. 28), for § 101 did not exist in 1948. The United States makes the same error. U.S. Br. 14-15.

Greenwood, 52 U.S. (11 How.) 248 (1851)] that Congress thought had led to 'a large variety' of expressions in decisions and writings," including *Cuno*'s "controversial phrase 'flash of creative genius.'" *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 15 (1966).

Applying the then-implicit invention principle, *Funk Brothers* pronounced that the claimed combination of bacteria, which maintained the same attributes as the preexisting bacteria in their uncombined form (the claim required the cultures to be "*unaffected by each other* in respect to their ability to fix nitrogen"), "d[id] not disclose an invention or discovery." 333 U.S. at 128 n.1, 132 (emphasis added). Instead, by attempting to claim only the combination of the natural properties of the bacteria, without "improv[ing] in any way their natural functioning" or enlarging "the range of their utility," *id.* at 131, the patentee in *Funk Brothers* "had discovered 'only some of the handiwork of nature,'" *Chakrabarty*, 447 U.S. at 310 (quoting *Funk Bros.*, 333 U.S. at 131). Dr. Chakrabarty's claim, by contrast, was "not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter" with "significant utility"—his "discovery [wa]s not nature's handiwork, but his own." *Id.* at 309-10. That constituted an invention under § 101.[7] *Id.* at 310.

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[7] *Chakrabarty*'s discussion of the 1930 Plant Patent Act illuminates the meaning of invention under § 101. Prior to 1930, it was "belie[ved] that plants, even those artificially bred, were

Mayo similarly focused on invention. The Court concluded that patent claims covering methods of determining the proper dose of thiopurine drugs did not involve any human invention because "the claims inform a relevant audience about certain laws of nature," and further supplied only "well-understood, routine, conventional activity already engaged in by the scientific community . . . add[ing] nothing significant beyond the sum of their parts taken separately." 132 S. Ct. at 1298. Thus, there was no "invention." Indeed, the Court distinguished *Diamond v. Diehr*, 450 U.S. 175 (1980), by noting no evidence there that the method steps, "or at least the combination of those steps, were in context *obvious*, already in use, or purely conventional." 132 S. Ct. at 1299 (emphasis added).

In short, what § 101 requires, beyond the statutorily enumerated categories of eligible subject matter, is a modicum of "invention"—the "human ingenuity" referred to in *Chakrabarty* and the

(continued…)

products of nature for purposes of the patent law." 447 U.S. at 311. By enacting the PPA, Congress "explained at length its belief that the work of the plant breeder 'in aid of nature' was [a] patentable invention." *Id.* at 312. The PPA's congressional reports stated that "a plant discovery resulting from cultivation is unique, isolated, and is not repeated by nature, nor can it be reproduced by nature unaided by man." *Id.* at 313. So, too, with the Myriad inventions—they are the work of the inventors in addition to nature, and their inventive compositions cannot be reproduced in nature unaided by man.

"inventive concept" in *Mayo.* Even then, the requirement must not be applied too rigorously, lest it swallow entirely the requirements of § 103 or run afoul of Congress's intent to bring more certainty to the longstanding but "less definite" "invention" requirement by codifying it as "nonobviousness." *Graham*, 383 U.S. at 14-15 (in § 103, Congress intended to abolish the "large variety of ways" courts had used to assess "invention"). The § 103 inquiry is more nuanced; it requires that "invention" be measured against prior art defined by § 102, looking to the level of skill in the art at the time of the claimed invention, the differences between the claimed invention and the prior art, and an important set of "secondary considerations" or "subtests of nonobviousness," to determine the nonobviousness *vel non* of a claimed invention. *Id.* at 17-18. Under § 103, the challenged molecules unquestionably represent a patentable invention in view of the differences between the newly created molecules and native DNA, the level of skill and knowledge in genetics in 1994, and the secondary considerations such as commercial success, upsetting the conventional wisdom, long-felt need, failure by others, and tribute from competitors. *See* pp. 2-10, *supra*.

The "invention" analysis of § 101, by contrast, parallels the eligibility threshold of copyright law, which requires authorial "originality"—defined as a "minimal level of creativity." *Feist Pub., Inc. v. Rural Tel. Serv. Co.*, 499 U.S. 340, 358-59 (1991) (calling this requirement "not particularly stringent"). Copyright, of course, shares an "historic kinship" and constitutional roots with patent law. *Sony Corp. of*

Am. v. Universal City Studios, Inc., 464 U.S. 417, 439 (1984). In copyright as with patent law, "facts and ideas" generally belong to the public, while original expressions "that display the stamp of the author's originality," like inventions demonstrating human ingenuity, are protectable. *See Harper & Row, Pub., Inc. v. Nation Enters.*, 471 U.S. 539, 547 (1985). Unlike copyright, however, patent law contains numerous other hurdles that an invention must surmount before a patent will issue.

C. The Identification, Definition, And Isolation Of A Particular Molecule With A Substantial Real-World Utility Is An "Invention" Under § 101

For over 30 years, the USPTO has applied § 101 and this Court's precedent to conclude that claims to isolated DNA molecules are "inventive" and therefore patent-eligible. This is an independent reason to uphold the patent-eligibility of Myriad's claims.

In 1982, less than two years after *Chakrabarty*, the USPTO granted the first human DNA-related patents. The issuance of these patents reflected an application of *Chakrabarty*, and a continuation of the more than 100-year-old practice of issuing patents on isolated forms of natural products. *See* pp. 2-5, *supra*. Patenting of DNA-related inventions has continued ever since, with the USPTO granting over 40,000 patents drawn to genetic material, almost 3,000 of which are directed to particular isolated DNA molecules. *See* Rogers, *supra*, at 19, 40; Pet. App. 61a-62a, 87a-88a, JA527-28.

One such patent was directed to "purified and isolated" forms of DNA encoding human erythropoietin ("EPO"), which are used to increase

patients' red-blood-cell levels. Over 20 years ago, the Federal Circuit upheld the patent, distinguishing the claimed composition from what exists in nature: "It is important to recognize that neither Fritsch nor Lin invented EPO or the EPO gene. The subject matter of claim 2 was the novel *purified and isolated* sequence which codes for EPO . . . ." *Amgen*, 927 F.2d at 1206 (emphasis in original); *see also Amgen, Inc. v. Chugai Pharm. Co.*, No. 87-2617-Y, 1989 U.S. Dist. LEXIS 16110, at *89 (D. Mass. Dec. 11, 1989). This decision followed longstanding precedent by the Federal Circuit, its predecessor court (the C.C.P.A.), and courts evaluating patents prior to its creation, which have held that compositions that are isolated or extracted from natural products are patent-eligible (and patentable). *See* pp. 4-5, *supra*.

For its part, the USPTO drew on its unique knowledge of and familiarity with each of the roads at the intersection of science, technology, and patent law to reinforce the existing rule. Indeed, at several junctures, culminating in its 2001 *Utility Guidelines*, the USPTO evaluated its practice in light of relevant precedents, but never determined that isolated DNA molecules should be ineligible for patenting. *See* 66 Fed. Reg. at 1092. And even before the 2001 *Guidelines*, the USPTO had long issued patents on isolated natural products. *See id.* at 1093 ("Patenting compositions or compounds isolated from nature follow well-established principles, and is not a new practice"); Pet. App. 87a (the 2001 *Guidelines* were "simply a continuation of a longstanding and consistent policy of allowing patents for isolated natural products"); pp. 2-4, *supra*.

This Court has emphasized that a consistent and longstanding USPTO practice is entitled to substantial weight in interpreting and applying § 101. In *J.E.M.*, the Court observed that the USPTO applies "specific expertise in issues of patent law." 534 U.S. at 145; *see also Microsoft Corp. v. i4i Ltd.*, 131 S. Ct. 2238, 2242 (2011); *Dickinson v. Zurko*, 527 U.S. 150, 160 (1999). And in *Mayo*, this Court emphasized that it should "hesitate before departing from established general legal rules," and allow Congress to "craf[t] more finely tailored rules when necessary." 132 S. Ct. at 1305.

Respecting that role, and reiterating that § 101 has "broad scope and applicability," the Court in *J.E.M.* refused to deny patent protection to sexually reproduced plants where the USPTO had issued "some 1,800 utility patents" for approximately 16 years, with no "indication from either Congress or agencies with expertise that such coverage is inconsistent with [the governing statutes]." 534 U.S. at 144-45.

The case for continuing the established practice is even more compelling here than in *J.E.M.* The USPTO has issued almost *3,000* patents on isolated DNA molecules over the last *30* years, and, more broadly, over 40,000 DNA-related patents. Throughout, Congress has not altered the landscape or given any indication that the USPTO's practice should change. Rather, despite repeated attempts to change that longstanding practice, and fully aware of

the debate being initiated by petitioners, their counsel, and others, Congress has declined to intervene. *See* Pet. App. 61a-62a, 92a-93a.[8]

Indeed, Congress has modified the Patent Act since the 2001 *Utility Guidelines*, including the recent America Invents Act, hailed as "the most significant reform of the Patent Act since 1952." Press Release, White House, President Obama Signs America Invents Act, Overhauling the Patent System to Stimulate Economic Growth, and Announces New Steps to Help Entrepreneurs Create Jobs (Sept. 16, 2011), www.whitehouse.gov/the-press-office/2011/09/16/president-obama-signs-america-invents-act-overhauling-patent-system-stim (last visited Mar. 6,

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[8] "For example, Congress included, as part of the Patent Office's appropriations, language affirming the Patent Office's interpretation of § 101 to prohibit patents on human organisms. Consolidated Appropriations Act, 2004, Pub. L. No. 108-199, § 634, 118 Stat. 3, 101. Although Congress was aware 'that there are many institutions . . . that have extensive patents on human genes,' 149 Cong. Rec. H7248, H7274, it explicitly declined to implement legislation to 'affect any of those current existing patents.' 149 Cong. Rec. E2417-01. To the contrary, it made clear that the language related to 'human organisms' was not intended to change the Patent Office's policy with respect to claims to genes, stem cells, or other similar inventions. Far from oblivious to the patenting of genes, Congress introduced and declined to pass several bills which would put a moratorium on gene patents, authorize funding for the study of whether genes ought to be patentable, and exempt from patent infringement anyone who uses patented genes for non-commercial research purposes or medical practitioners who use genetic diagnostic tests." Pet. App. 92a-93a (Moore, J., concurring-in-part).

2013). Yet Congress made no modifications to § 101 that would affect the established legal rule, or the USPTO's conforming practice with respect to isolated DNA molecules.

In this way, this case presents the mirror image of *Mayo*. There, under the "established general legal rules," natural laws coupled with insignificant steps were not patent-eligible method claims. *Mayo*, 132 S. Ct. at 1305. Here, however, the established rule for over 100 years has been that isolates or extracts from natural materials that reflect human invention *are* eligible for patents, and the USPTO and courts have concluded for over 30 years that particular claimed isolated DNA molecules reflect patent-eligible human ingenuity. That, plus the interests in reliance and certainty engendered by the established rule, confirm that the Court should not disturb longstanding practice. *See J.E.M.*, 534 U.S. at 144-45.

Additionally, this established rule harmonizes with that of every other industrialized nation. Europe and Japan, for example, have officially pronounced their adherence to this rule. *See* EU Directive 98/44/EC, Art. 5(2), *available at* http://eur-lex.europa.eu/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=en&numdoc=31998L0044&model=guichett; Japanese Patent Office Examination Guidelines for Inventions in Specific Fields, Ch. 2, § 2.2.1(1), *available at* http://www.jpo.go.jp/tetuzuki_e/t_tokkyo_e/Guidelines/7_2.pdf; *see also* WTO Agreement on Trade-related Aspects of Intellectual Property Rights, Art. 27(1), *available at* http://www.wto.org/english/docs_e/legal_e/27-trips.pdf; JA567-68; Brief of *Amicus Curiae* The Institute of Professional Representatives

before the European Patent Office (EPI) in Support of Neither Party (endorsing declaration at JA565-70).

The Federal Court of Australia, too, has endorsed this rule in rejecting an identical attack on Myriad's Australian patents. *See Cancer Voices Australia v. Myriad Genetics Inc.*, [2013] FCA 65 ¶ 108 (Austl.), *appeal docketed*, No. NSD35912013 (F.C.R. Mar. 4, 2013) ("[I]n the absence of *human intervention*, naturally occurring nucleic acid does not exist outside the cell, and 'isolated' nucleic acid does not exist inside the cell." (emphasis added)). Reversing the rule exemplified in the USPTO's *Guidelines* would set back the United States in an industry born and raised here, and often funded by the United States government. JA451-52.

Also, the longstanding rule reflected in the *Guidelines* makes sense. "[A]ll inventions at some level embody, use, reflect, rest upon or apply laws of nature, natural phenomena, or abstract ideas"; "too broad an interpretation of th[e] exclusionary principle could eviscerate patent law." *Mayo*, 132 S. Ct. at 1293. It is more judicious to determine patent-eligibility based on the presence of human ingenuity, rather than focus myopically on whether a natural law or product was somewhere involved. "'While a scientific truth . . . is not a patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be.'" *Id.* at 1294 (quoting *Mackay*, 306 U.S. at 94).

As Judge Lourie explained, although isolated DNA molecules "are prepared from products of nature, so is every other composition of matter." Pet. App. 44a; Gunnar Samuelson & Lars Bohlin, DRUGS OF NATURAL ORIGIN: A TEXTBOOK OF PHARMACOGNOSY 19

(6th ed. 2009) ("[A]mong the modern drugs in use today about 40% are of natural origin," including "[a]pproximately 60% of anticancer remedies and 75% of drugs for infectious diseases"; "[m]any of the natural compounds are isolated from the producing organisms."). These products "are different from natural materials, even if they are ultimately derived from them." Pet. App. 45a. So, too, isolated DNA molecules differ from native DNA based on the contributions of human inventors.

D. Myriad's Claims Are Patent-Eligible

Adhering to the "established general legal rule," the Federal Circuit correctly concluded that Myriad's claims are patent-eligible.

1. Myriad's claimed molecules are human-made.

Myriad's claims are drawn to man-made compositions of matter (or at least man-made improvements thereof). Only by human intervention have the claimed molecules come about. For over a dozen years, Myriad's scientists and researchers engaged in intense effort, marked by novel scientific method and inquiry, to identify and define what came to be known as the BRCA1 and BRCA2 genes. Where others failed, Myriad identified the BRCA genes, and then, using information it had collected and discerned from studying the genes, characterized, defined, and isolated these particular molecules. The creation of new molecules never before available to the public is invention.

2. Myriad made new molecules with great and valuable utility.

These new molecules have "significant utility" not present in native DNA, but conferred precisely because of the Myriad inventors' ingenuity. *See Chakrabarty*, 447 U.S. at 310. Although the molecules were derived from natural materials, those materials in a state of nature provided none of the benefits of the claimed molecules. Only the isolated molecules can be used as, *e.g.*, probes and primers, allowing physicians and molecular biologists to determine a patient's predisposition to breast and ovarian cancers. These new attributes are the result of human ingenuity—the quintessential mark of patent-eligible subject matter. *See id.*; *see also* Dan L. Burk, *Anticipating Patentable Subject Matter*, 65 STAN. L. REV. ONLINE 109, 114 (2013) ("we want to reward inventors who provide access to molecules that were previously giving us no benefit"); Dan L. Burk & Mark A. Lemley, *Inherency*, 47 WM. & MARY L. REV. 371, 407 (2005) (similar). Without Myriad's work, there is no indication whether these particular molecules, and the valuable uses to which they have been put, would ever have come about.

E. The United States' Position Does Not Respect The Established Legal Rule Or Longstanding USPTO Practice

In its brief, the United States asserts that the eligibility line should be drawn between cDNA (eligible) and other isolated DNA molecules (not). *See* U.S. Br. 9. Over 30 years of precedent and practice have already drawn the line elsewhere—where human ingenuity causes a newly created, newly available composition to be isolated from

natural, genomic material. This "established general legal rule"—not to mention the enormous reliance interests and property rights arising from that practice—is far more worthy of respect than the arbitrary line now being offered as a mere litigating position by the United States. *Cf. Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 212 (1988). The Federal Circuit unanimously upheld the patent-eligibility of cDNA claims, and the United States and other *amici* concur—but there is no defensible line to exclude other isolated DNA claims, for both came about through human intervention.

The United States is correct to conclude that claims drawn to cDNA molecules are patent-eligible. cDNA is a wholly synthetic molecule with a sequence nowhere found in native DNA. U.S. Br. 6, 18-19; Pet. App. 113a-14a; JA430-31. Indeed, the '282 patent specification makes clear that Myriad created SEQ ID NO:1 (*e.g.*, the isolated molecules of claim 2) as an artificial composite of fragmentary sequences isolated from various patient samples; it did not originate in a single human sample. JA772 (53:4-7 (describing "construction of a composite")). Fragments of this artificial composite (*e.g.*, the isolated molecules of claim 6) were then created and used by the Myriad inventors in further studies. JA772 (53:23-26); *see also* Pet. App. 81a-85a. Thus, because SEQ ID NO:1 in the '282 patent recites a particular man-made cDNA sequence, its claims 2, 6, and 7 are clearly patent-eligible. Likewise, because SEQ ID NO:1 in the '492 patent recites a particular cDNA sequence, its claim 7 is clearly patent-eligible. JA974-85, 1028.

There is, however, no basis for the United States' appellate lawyers to substitute their judgment for

that of the USPTO, the agency with relevant expertise, in excluding other isolated DNA molecules from patent-eligibility. Even though the United States acknowledges that this Court's decision "will significantly affect the work of the [USPTO]," the agency "responsible for issuing patents" (U.S. Br. 1), the USPTO has not signed the brief (it did not sign the United States' briefs filed in the Federal Circuit, either). This is unprecedented in patent cases before this Court.[9] And the USPTO has not deviated from the *Utility Guidelines* in response to this litigating position. *See* Peter Loftus, *US Patent Office Keeps Status Quo Amid Gene-Patent Fight*, DOW JONES NEWS SERVICE, Nov. 2, 2010.

The Court should prefer the *Guidelines*' longstanding eligibility rule under which the isolation of a molecule with new utility represents sufficient human intervention to constitute patent-eligible subject matter.

First, isolated DNA molecules—including cDNA molecules—are "compositions of matter" within the language of the statute. *See* 66 Fed. Reg. at 1094 ("A purified DNA *molecule* isolated from its natural environment . . . is a chemical compound" (emphasis in original)).

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[9] At least since the Federal Circuit's 1982 creation, the USPTO has always joined the United States' brief in a patent case reviewed by this Court. *See, e.g.*, the United States' briefs in *Bowman v. Monsanto*, No. 11-796; *Mayo v. Prometheus*, No. 10-1150; and *J.E.M. Ag Supply v. Pioneer Hi-Bred International*, No. 99-1996.

Second, the USPTO's approach—but not the United States'—adheres to this Court's decisions, particularly *Chakrabarty*, and the legislative history indicating that "anything under the sun that is made by man" is eligible for a patent. In its *Guidelines*, the USPTO explains that, whether as "an excised gene" or "synthetic DNA preparations," isolated DNA molecules are patent-eligible because they "d[o] not occur in that isolated form in nature" and are "different from the naturally occurring compound." 66 Fed. Reg. at 1093. By their identification, definition, and excision, or by their synthetic preparation, the claimed compositions are man-made and inventive. The analysis that compels the patent-eligibility of cDNA compels the same conclusion as to other isolated DNA molecules.

Third, the USPTO's approach is consistent with longstanding interpretations of § 101. *See J.E.M.*, 534 U.S. at 145; *see also, e.g.*, *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993) (considering patentability of DNA-related claims and preemption concerns under § 112); *Amgen*, 927 F.2d at 1206. For more than 30 years, parties have relied on the USPTO's practice as reflected in the *Guidelines*. It is remarkable that no court, other than the district court here, has ruled a claimed composition patent-ineligible since § 101's 1952 enactment. Meanwhile, the USPTO's longstanding practice has seen no contrary action or indication by Congress.

Fourth, continuing to follow the established legal rule, set out in the USPTO's *Guidelines*, would avoid the *post hoc* scuttling of thousands of patents, and the property rights and reliance interests of inventors, investors, and industry that have allowed the United

States' biotechnology sector to grow and flourish. The stability and certainty of these interests has contributed to the public good in numerous ways—it has made new, life-saving products and environmental and consumer advancements available to the public; it has yielded a robust industry that contributes greatly to the national economy; and it has created countless jobs.

F. Ostrer's Approach Is Misguided

Although Ostrer gives a nod to whether a composition has an inventive concept (Pet. Br. 35-39; *Mayo*, 132 S. Ct. at 1294), he also proposes two other "ways" of determining patent-eligibility that misread the statute and this Court's precedent, ignore the USPTO's longstanding judgment, and diminish the clarity of the § 101 threshold. *E.g.*, Pet. Br. 23-24 (applying "inventive concept," "markedly different," and "preemption" tests). And in applying his cumbersome three-part test, he ignores and misrepresents the claim language and the science.

1. Ostrer misreads Chakrabarty and elides the differences that human ingenuity has imparted to isolated DNA molecules.

Ostrer makes much of the phrase "markedly different" from *Chakrabarty*. He catalogs certain similarities between the Myriad inventions and the native genetic starting materials, concluding that these similarities demonstrate that the isolated molecules are not "markedly different" from their starting materials. Pet. Br. 28-35; *accord* Brief for

Amicus Curiae Eric S. Lander in Support of Neither Party at 10-12 ("Lander Br.").[10] As an initial matter, the legal rule announced in *Chakrabarty* asks whether a claimed composition is "a product of human ingenuity 'having a distinctive name, character and use'" from a natural product. 447 U.S. at 309-10 (drawing from precedent). *Chakrabarty*'s use of "markedly different characteristics" reflected not the legal rule, but the Court's factual description of *how different* Chakrabarty's bacterium was from bacteria in the wild.

Regardless, the proper inquiry focuses on the differences, not similarities. Because every patent-eligible composition of matter has its origins in nature, there will always be similarities to a natural substance. A patent-eligible baseball bat, though shaped and formed by human hands, will share the characteristics of the wood embedded in the tree from

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[10] A word about Ostrer's terminology. When Ostrer speaks of a "product of nature," he includes within its scope products, like isolated molecules and cDNA molecules, whose starting materials originated in nature but have been manipulated into existence by humans. As Justice Frankfurter presciently observed, however, "[i]t only confuses" matters "to introduce such terms as 'the work of nature' and the 'laws of nature,'" because these are "vague and malleable terms infected with too much ambiguity and equivocation." *Funk Bros.*, 333 U.S. at 134-35 (Frankfurter, J., concurring). Ostrer's fluid use of the term "product of nature" to include such human-created compositions of matter seeks to capitalize on this ambiguity. *See id.* ("Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every patent.").

which the bat was formed. But the fact that the bat shares the properties of natural wood does not make the resulting, human-made product ineligible for patenting.

Yet Ostrer utilizes the vagaries of his proposed tests by making essentially the same argument about isolated DNA molecules. Instead of acknowledging the differences—including the different utilities—that human inventors brought to the patented molecules, he improperly focuses on similarities between native DNA and isolated BRCA DNA molecules. But it is the differences that make a difference.

For instance, Ostrer repeatedly emphasizes that the "information content" of isolated DNA remains the same as native DNA, because "the gene sequence, the information it includes, and the laws it embodies are the same whether in or out of the body." Pet. Br. 9; *see also id.* at 30, 33, 35 (applying his fluid "markedly different" test). But nowhere does Ostrer acknowledge the differences that human intervention worked upon that molecule. A baseball bat can be used to hit a baseball because of the combination of the inherent qualities of the natural wood and the shape and size imparted to the bat by the inventor. Similarly, an isolated DNA molecule can be used as a cancer-mutation-detecting probe or primer because of natural qualities (their ordering of nucleotides, which in some cases other than cDNA molecules follows the ordering of native nucleotides) *in combination with* the inventors' scientific work and ingenuity in characterizing and defining the molecule's starting and end points, the severing of covalent bonds, and the removal of the specific defined molecule from

other materials in its native environment to create new functionality as a probe or primer. Only because of the addition of human invention do these molecules exist to help patients chart their own course of medical treatments.[11] Even accepting the United States' argument that a patent should not be granted for discovering "useful properties of something that already exists in nature" (U.S. Br. 16-17), the useful properties of Myriad's isolated DNA molecules (as in *Chakrabarty*, but unlike in *Funk Brothers*) were not pre-existing. They exist only because of their characterization and isolation by human inventors.[12]

Ostrer thus mischaracterizes the Federal Circuit's opinion as "privileging the breaking of covalent bonds over all else." Pet. Br. 33. Not so. The court acknowledged that the claimed molecules exist in a "distinctive" form "from DNAs in the human body." Pet. App. 51a. As it explained, isolated DNA "consist[s] of just a fraction of a naturally occurring

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[11] Ostrer contends that isolated DNA nearing a gene's full length is not useful as a primer. Pet. Br. 34. This is irrelevant. Long strands of isolated DNA molecules are useful as probes and PCR templates. *See* pp. 7-8, *supra*.

[12] Ostrer further argues that isolated DNA "reinserted into the cell . . . functions as it did previously." Pet. Br. 9. This is both inaccurate and irrelevant. The likelihood of a reinserted DNA molecule landing in exactly the right spot and necessarily functioning exactly as it did in its native environment is minuscule and hypothetical. Regardless, a reinserted DNA molecule cannot diagnose cancer risk—the principal utility of the claimed isolated molecules.

DNA molecule," and the definition, isolation, and utility of the particular claimed molecule "results from human intervention." Pet. App. 51a-52a. Just as *Chakrabarty*'s "markedly different" observation was a factual conclusion rather than a pronouncement of the § 101 legal inquiry, Judge Lourie's discussion of covalent bonds merely reflects the importance in his overall analysis of those structural differences between native and isolated DNA molecules. While he spoke forcefully in chemical terms, he understood the human manipulation required to create the claimed molecules. And Judge Moore's concurring opinion complemented Judge Lourie's by centering its attention on the different *utilities* imparted by such human invention. Pet. App. 80a-86a.

Under Ostrer's myopic focus on similarities to the exclusion of differences, *Chakrabarty* would have come out the opposite way. The bacterium in *Chakrabarty* was identical to the native one, P. aeruginosa, in innumerable ways. P. aeruginosa has one of the largest bacterial genomes of those sequenced to date. U.S. Patent No. 4,259,444; C.K. Stover et al., *Complete Genome Sequence of Pseudomonas Aeruginosa PA01, An Opportunistic Pathogen*, 406 NATURE 959 (2000). The size and complexity of P. aeruginosa's genome underlies its ability to thrive in a multitude of environments and its resistance to many drugs. Stover, *supra*, at 959. Chakrabarty's inventive act did not alter any of the preexisting 6.3 million base pairs of DNA in P. aeruginosa, or any of the bacterium's inherent capabilities.

Instead, by adding only two plasmids to P. aeruginosa's already-massive genetic content, Chakrabarty created a new bacterium. *Chakrabarty*, 447 U.S. at 310. That was so despite the fact that the two added plasmids contributed only a tiny fraction of the overall genetic content and capabilities of the modified bacterium. Thus, this Court's conclusion that the new bacterium had "markedly different characteristics" could not have been based solely on tallying the number of similar physical characteristics. The similarities *vastly* outnumbered the differences. The modified bacterium retained all of its original functions and properties and simply aggregated naturally-existing functionalities from other organisms. *See id.* But this Court correctly affirmed that even modest changes introduced by man may confer "significant" utilities that make a composition patent-eligible.

The claimed compositions here go even further beyond nature than Chakrabarty's invention did, by not just aggregating naturally-existing properties from several bacteria into one, but instead creating new utilities *where none existed before*. If the modest structural changes in Chakrabarty's bacterium so altered its utility as to give it a "distinctive name, character and use" and make the resulting product patent-eligible, 447 U.S. at 309-10, then surely Myriad's inventors' transformation of undifferentiated genomic material into DNA molecules that exist outside of the body with a different structure, and having additional, significant new utilities, is patent-eligible. And while extraction of random DNA may have been "well-understood, routine, conventional activity" in 1994, that is *not*

what Myriad did or claimed. Instead, Myriad identified, characterized, and isolated *specific* molecular structures, never before known, used, or available.

When Ostrer does consider the differences, he concedes that isolated DNA has significant utilities that native DNA does not. Pet. Br. 2 (asserting that "it is not possible to study or use the genes unless they are isolated"); *id.* at 9, 41 (similar). Even though Ostrer is wrong to contend that one cannot study or look at genes without isolation (whole-genome sequencing does not involve isolation), he appropriately (if inadvertently) acknowledges that the different, human-imparted characteristics of isolated DNA molecules make them extremely useful in ways that genes in the body cannot possibly be.

Accordingly, Ostrer cannot analogize this case to *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1 (1931), which involved not the "implicit exception" to § 101, but the statutory definition of "manufacture" (not relevant here). There, the small amount of borax added to the rind of a fresh orange did not constitute a "manufacture" because it did not change "the name, appearance, or general character of the fruit." *Id.* at 12. It "remain[ed] a fresh orange fit only for the same beneficial uses as theretofore." *Id.* Here, by contrast, new structures and new "beneficial uses" arose from the addition of human ingenuity.

2. Ostrer's reliance on "preemption" is factually and legally unsound.

Ostrer's proposed test also relies on "preemption," but he uses that concept in such a heavy-handed way that it would destroy wide swaths of valid patents drawn to all kinds of inventions. Pet. Br. 40-48.

First, "preemption" is not a test for patent-eligibility. If it were, no patent could exist, for all patents are by their nature preemptive—they give their owners the right to exclude others. 35 U.S.C. § 154(a)(1). At most, preemption is an after-the-fact confirmation that a claimed invention is not patent-eligible because it would preempt use of noninventive ideas, laws, or phenomena. In *Mayo*, the Court's concern with preemption reflected the patent-ineligibility conclusion it had already drawn for a claim that added only well-understood, routine, conventional steps that doctors were already engaged in—a conclusion that does not apply here, where BRCA molecules had never before been known, used, or available. *See* 132 S. Ct. at 1301. Too much emphasis on preemption as even an alternative test could too broadly interpret the exclusionary principle, in violation of congressional intent to accord § 101 substantial scope. *Id.* at 1293.

Second, while Ostrer makes provocative assertions about the preemptive scope of Myriad's patent claims (*e.g.*, gene therapy, DNA-based computers), he has not based these assertions on fact. Any intelligent application of Ostrer's preemption test would require rigorous claim construction and a detailed infringement analysis comparing the claims to a specific device or activity, neither of which has occurred here. Because of the abstract, hypothetical nature of this lawyer-engineered "test case," there are no infringement claims or counterclaims to evaluate. Thus, Ostrer, unlike a party having real and immediate plans to engage in infringing activity (who would have an interest in construing the claims narrowly lest they cover that activity), freely urges

that Myriad's claims are broad, expansive, and would cover every kind of genetic research. This goes beyond any reasonable reading of the patents. *See* pp. 50-55, *infra*.

Third, it is clear that the claims—properly understood—do not preempt ineligible subject-matter or other, competitive technologies. One example of something Ostrer contends is preempted (Pet. Br. 14-15, 31, 44), but which is clearly not, is whole-genome sequencing. In 2001, seven years after Myriad's inventions, the human genome project used random sequencing—without "isolation" of particular DNA molecules—to determine and publish the entire human genome sequence. In 2007, the entire genetic makeup of Dr. James Watson, an *amicus* supporting Ostrer, was characterized using whole-genome sequencing without isolation; Watson himself was found to harbor a BRCA mutation. *See* BIO-IT WORLD, *Project Jim: Watson's Personal Genome Goes Public*, www.bio-itworld.com/newsitems/2007/may/05-31-07-watson-genome (last visited Mar. 6, 2013). A host of other technologies—gene expression profiles, untargeted single-molecule sequencing, and protein-truncation testing—sequence DNA or detect genetic mutations without isolation.[13] Ostrer's contrary

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[13] *See, e.g.*, http://www.nanoporetech.com/technology/analytes-and-applications-dna-rna-proteins/dna-sequencing-applications; http://www.nanoporetech.com/technology/analytes-and-applications-dna-rna-proteins/dna-an-introduction-to-nanopore-sequencing; http://pacificbiosciences.com; http://www.ncbi.nlm.nih.gov/pubmed/10425032; http://www.ncbi.nlm.nih.gov/pubmed/19668243 (all last visited Mar. 5, 2013);

assertion (Pet. Br. 9) cites only the district court's observations, which were unsupported by any evidence. *See, e.g.*, Pet. App. 342a (incorrectly positing that "a time may come when the use of DNA for molecular and diagnostic purposes may not require" isolation; as demonstrated, that time has long since come).

Nor have Myriad's patents inhibited research, denied patients access to their genetic material or information, engaged in monopolistic pricing, prevented other laboratories from providing second opinions or conducting BRCA clinical tests, created a faulty test, or caused any of the other "chilling effects" Ostrer alleges. Pet. Br. 2-3, 7-9, 43-48. The claims do not preempt, preclude, or prohibit others from researching BRCA genes or creating and offering new and improved tests, and Myriad's extensive patient services and "gold standard" BRAC*Analysis*® have significantly furthered, not limited, patient care. *See* pp. 8-10, *supra*.

(continued…)

Christopher M. Holman, *Will Gene Patents Derail the Next Generation of Genetic Technologies?: A Reassessment of the Evidence Suggests Not*, 80 UMKC L. REV. 563, 579 (2012); Int'l Patent Application No. PCT/US2008/080358, Publication No. WO/2009/052417 (published Apr. 23, 2009) (Wendy S. Rubinstein, applicant).

3. Ostrer ignores J.E.M. and the Utility Guidelines.

Understandably, Ostrer prefers ambiguous tests like "product of nature," "markedly different," and "preemption" over the clear rule reflected in the *Utility Guidelines.* Indeed, he does not acknowledge the USPTO's longstanding practice as reflected in the *Guidelines* until the very end of his brief. And even there, he accuses the USPTO's exhaustive, expert, consistent, and coherent understanding of the law of being "remarkably free of any analysis." Pet. Br. 54. The *Guidelines* on their face belie this accusation—they address, in detail, the reasons for the USPTO's conclusions that particular isolated DNA molecules satisfy § 101, buttressed by legal citations and references to the Office's longstanding practice, dating back over 100 years. The Court should by now be familiar with Ostrer's counsel's pattern of directing rash (and unsupported) insults towards the USPTO and the work of its public servants.[14]

The USPTO's "specific expertise in issues of patent law," *J.E.M.*, 534 U.S. at 145, and its consistent and

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[14] Ostrer's counsel is fond of such rhetoric, calling patents today "nothing more than some overly worked patent examiner's decision to allow claims requested by an applicant," Br. of Public Patent Foundation as *Amicus Curiae* in Support of Petitioner at 2, *FTC v. Actavis, Inc.*, No. 12-416 (U.S. Jan. 29, 2013), and accusing the USPTO "of being a rubber stamp" and granting patents for financial, rather than legal, reasons, Br. of Public Patent Foundation as *Amicus Curiae* in Support of Petitioner at 6, *Already*, 133 S. Ct. 721 (No. 11-982).

longstanding practice of issuing patents to particular isolated DNA molecules, should lead this Court to respect the *Guidelines* as a proper application of § 101 and this Court's decisions, most notably *Chakrabarty*. Ostrer's blithe attempt to sweep away the *Guidelines* by contending that they are "not binding on this Court" (Pet. Br. 54) is unresponsive. The *Guidelines*' force does not depend on their "binding" nature, but upon the USPTO's expertise in this area, *J.E.M.*, 534 U.S. at 145, and the fact that this "highly visible decision has led to the issuance of [thousands of] utility patents for [isolated DNA molecules]. Moreover, the PTO, which administers § 101 . . . recognizes and regularly issues utility patents for [isolated DNA molecules]." *Id.*

There is more. In this case—as in *J.E.M.*—"Congress has not only failed to pass legislation indicating that it disagrees with the PTO's interpretation of § 101; it has even recognized the availability of utility patents" upon genetic material. *Id.* Judge Moore's opinion canvassed this Congressional recognition and approval. *See* p.31 n.8, *supra*. Lacking any "indication from either Congress or agencies with expertise that such coverage is inconsistent with [§ 101]," *J.E.M.*, 534 U.S. at 144-45, this Court should uphold the line drawn by the USPTO's *Guidelines* as a proper interpretation and application of the statute.

4. Ostrer relies on claim constructions never sought or made in the lower courts, and otherwise does violence to the claim language.

Ostrer's arguments rely, in substantial part, on efforts to have this Court ignore claim terms or

construe claim language for the first time. These arguments are not fairly included within the question presented, and they seek to do considerable violence to the claim language.

"Isolated." Ostrer calls this important term "clever draftsmanship" that has duped the USPTO. Pet. Br. 27; *accord id.* at 2; U.S. Br. 20 (addressing the claims "[a]bsent the 'isolated' limitation"). The most glaring example of his effort to ignore this claim term appears in his framing of the question presented—whether "human genes" can be patented. Pet. Br. 11. But, by their express terms, the claims cover "isolated" DNA molecules, not "human genes." *See also* 66 Fed. Reg. at 1093 ("A patent on a gene covers the isolated and purified gene but does not cover the gene as it occurs in nature"; "[p]atents do not confer ownership of genes.").

By avoiding the claim term "isolated," Ostrer fails to engage each claim "as a whole." *Diehr*, 450 U.S. at 192. More significantly, by minimizing this claim term as though it does not appear in the claims, Ostrer seeks to eliminate the very aspect of the claims that confirms the application of "human ingenuity," and that imparts the differences between the claimed isolated molecules and the naturally-existing, genomic DNA that is bound up in the body.

For instance, Ostrer and his *amici* contend that there are fragments of genetic material in the body with broken bonds that are "identical to the fragments created by Myriad when it isolates the gene." Pet. Br. 11; *see also id.* at 9-10, 32 (contending that "the gene separated from the chromatin can be found in the body" and that "gene fragments exist in the body," including in maternal plasma); Lander Br.

12-18 (similar). But fetal DNA floating within a mother's blood, or DNA floating within a person's own blood, is not "isolated" within any conceivable interpretation of the claims, because it remains in its natural environment. It has not been removed or "separated from other cellular components which naturally accompany" it, as the claims require. JA755 (19:8-19). Nor is there any record support that these fragments in the body have the same sequences specified in Myriad's claims.

Likewise, Ostrer contends that the claimed cDNA molecules of claim 2 of the '282 patent are patent-ineligible because they exist in the body as "pseudogenes." Pet. Br. 51. But such pseudogenes have significant structural differences from the molecules of claim 2 and are not "isolated," and thus do not make available to the public the diagnostic benefits of the claimed cDNA molecules.

"DNA." Ostrer also tries to expand the claims beyond the scope of § 101 by broadening the meaning of "DNA." According to Ostrer, "DNA" as used in the claims "is defined broadly," and thus the claims "are not limited to any particular molecular structure" and thus include all variations and mutations of the sequences recited in the claims. Pet. Br. 6, 13-14, 30-31; *accord, e.g.*, *Amicus Curiae* Brief for Academics in Law, Medicine, Health Policy and Clinical Genetics in Support of Neither Party at 33.

Ostrer never made this claim-construction argument before, so it is not properly before this Court. In any event, since there is no explicit definition of "DNA" in the patents, the term is properly defined by its plain and ordinary meaning to one of ordinary skill in the art: as the macromolecule

deoxyribonucleic acid. *See* JA755 (19:1-11); Pet. App. 308a. More importantly, the claims do not use "DNA" in a vacuum, but instead modify that word with additional terms that make absolutely clear how specific and focused these claims are—"isolated" molecules having the particular "SEQ IDs" that are claimed.

Ostrer's references to other defined terms in the specifications (terms not used in the claims),[15] and to passages in the specifications that generally describe the invention (*e.g.*, JA748, 755 (6:26-28, 19:51-53, 53-57)), cannot be imported into the claims. It is the claims that measure the metes and bounds of the inventors' invention and the patent grant. *See* 35 U.S.C. § 112; *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 29 (1997). Again seeking to shift the ground upon which this case has been litigated, Ostrer asserts a too-broad, never-before-argued claim interpretation.

"Coding for." Ostrer also contends that, by reciting DNA "coding for" the specific strings of A, T, C, and G nucleotides in the SEQ ID set forth in a claim, the claims cover mere genetic information—any person's genetic information with that sequence or as represented in a printout of a patient's DNA sequence. Pet. Br. 34-35. This does further violence to the claim language. The claims are not directed to

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[15] *E.g.*, "BRCA1 Locus" and other similar terms (JA755 (19:35-40, 20:34-35)); "substantial homology" (JA757 (24:62-63)); and "fragment," "portion," and "segment" (JA755, 758 (19:1-5, 20:63-65, 25:33-35)).

functions, information, or printouts. They claim precisely defined molecules—compositions of matter—having a specific, non-naturally-occurring structure. [16] Here, again, the *Utility Guidelines* answer Ostrer's charge: "Patents do not confer ownership of . . . genetic information, or sequences"; "descriptive sequence information alone is not patentable subject matter." 66 Fed. Reg. at 1093; *see also Cancer Voices Australia*, [2013] FCA 65 ¶ 109.

Use. Ostrer has never disputed that the claims have substantial utility unavailable before the invention. He nonetheless seeks to make something of the fact that the claims "are not limited to any particular use." Pet. Br. 17; *accord id.* 34 & n.9. There is a serious question whether the claims would cover the activities cited by Ostrer, and, in the important case of whole-genome sequencing, it is clear they would not. But that is irrelevant. A patent need only describe a single utility to support § 101's utility requirement. *See In re Ziegler*, 992 F.2d 1197, 1200 (Fed. Cir. 1993). Moreover, by statute, *see* 35 U.S.C. § 112(a) (formerly ¶ 1), an invention's use must be disclosed in the specification, not in the claims themselves. *See id.* A patentee is

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[16] The "coding for" limitation reflects structural, not functional, attributes. *See In re Deuel*, 51 F.3d 1552, 1555, 1557-58 (Fed. Cir. 1995) (claims reciting an isolated DNA sequence "encoding" a particular sequence claimed "new chemical entities in structural terms"). Similarly, the SEQ IDs represent the composition claimed. *See* 37 C.F.R. §§ 1.821-1.825; MPEP § 2420 *et seq.*

not required to specify an invention's use within the claim.[17]

5. Ostrer relies on distortions of the record and "facts" that are not consistent with science.

In numerous additional ways, Ostrer mischaracterizes and distorts the record and science, exacerbating his misunderstanding of the claims' patent-eligibility.

a. Ostrer makes various incorrect assertions about genes and native DNA and their supposed similarities to Myriad's molecules. He describes a gene as "a segment of chromosomal DNA," implying that native DNA is naturally broken up into discrete, individual genes, just like the claimed isolated compositions. Pet. Br. 4 & n.1. A gene, however, is a human-defined region(s) of a chromosome—not a single, self-contained "segment" ready for picking. JA228-29, 378, 418-19 468; *see also* p. 7, *supra*.

b. Ostrer's and his *amici*'s analogies to gold, kidneys, or leaves removed from their "natural environment" are factually inapt. Pet. Br. 34; U.S.

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[17] Ostrer also asserts that claim 2 of the '282 patent is "useless to Myriad" without covering any mutations or variations of that sequence. Pet. Br. 14-15. That is incorrect. Claim 2 is a "consensus sequence," synthetically created by Myriad after studying a large number of individuals to identify a sequence that ordinarily does not have mutations. *See* JA771-74. Thus, when the coding regions of an individual's DNA differ from the consensus sequence of claim 2, a predisposition to cancer is likely—making the claim a very valuable contribution.

Br. 22. After removal, the gold remains gold, the kidney remains a kidney, and the leaf remains a leaf. As the Court of Appeals explained, "[a] kidney is an organ, not a well defined composition of matter or an article of manufacture specified by § 101." Pet. App. 60a. Here, by contrast, the DNA is not merely removed from the body but is "isolated"—*i.e.*, human manipulation created specific chemical compositions that differ structurally from what exists in nature, providing the molecules with new properties that permit them to operate differently than their starting materials. While the United States minimizes this transformation as "snipped" ends having "no functional consequences" (U.S. Br. 22), such dismissive rhetoric severely understates the inventive activity. The isolated DNA molecules are designed by humans to "zero-in" on the BRCA DNA in the patient sample, so that their "snipped" reactive ends direct the amplification of the target DNA. This was the product of creative, human ingenuity.

c. Ostrer greatly distorts the factual record of Myriad's inventions, giving only lip service to "Myriad's work." Pet. Br. 41 n.10. Contrary to that characterization, Myriad's inventions were universally hailed. The European Patent Office called Myriad's inventions "a major breakthrough which was not obvious to the skilled person." Board of Appeal of the European Patent Office, No. T 1213/05 at 69-70 (2007), *available at* www.epo.org/law-practice/case-law-appeals/pdf/t051213eu1.pdf; *see also* JA490 (Myriad's invention was "a scientific accomplishment that required many inventive steps, not the least of which was to contradict the scientific dogma of the time"); *accord*

JA478-90, 746-47, 851-52, 945-46. Even Myriad's competitors acknowledged its breakthrough. JA485, 501-02.

6. Ostrer conflates patentability with patent-eligibility.

This case is solely about patent-eligibility under § 101 (Pet. 19, JA54 (disclaiming reliance on any provision of the Patent Act other than § 101)), yet Ostrer repeatedly challenges the claims' "patentability"—the province of other sections of the Act. Pet. Br. i, 2, 20-21, 23, 25-29, 32, 34, 48, 51, 53-55. He even recasts his legal theory as broadly embracing whether "human genes" are "patentable." Pet. Br. i. Since the complaint was limited to § 101, the record is necessarily incomplete on any other issues. The Court should not mistake the many patentability arguments that appear in Ostrer's brief (and the faulty factual assertions presented in support) as relevant to eligibility.

For instance, Ostrer asserts that Myriad's claims have "extraordinary breadth" and "reac[h] a huge number of compositions." Pet. Br. 15, 31; *accord id.* at 14-15, 15-16, 37, 41. Claim breadth and clarity are patentability considerations evaluated under § 112, which demands that a claimed invention be "fully and particularly described" and "distinctly claimed." *Bilski*, 130 S. Ct. at 3225; *see also Festo Corp. v. Shoketsu Kinzoku Kagyo Kabushki Co.*, 535 U.S. 722, 736 (2002). Section 112 adequately protects against indefinite patents. *See, e.g.*, *Fiers*, 984 F.2d at 1171

("Claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement"). This is no concern of the § 101 threshold.[18]

Likewise, despite acknowledging that "cDNA is generally made in the laboratory," Pet. Br. 51, Ostrer insists that cDNA is not "patentable" because "cDNA is identical to DNA except the non-coding regions have been removed," *id.* at 49. This relates to the novelty requirement of § 102, not patent-eligibility under § 101's invention principle. *See Diehr*, 450 U.S. at 190 (novelty "is wholly apart from whether the invention falls into a category of statutory subject matter").

Similarly, whether the differences between man-made isolated DNA molecules (including cDNA molecules "made in the laboratory") and native DNA render the former ultimately patentable is most appropriately assessed under § 103's nonobviousness requirement. That inquiry requires a sensitive, fact-dependent analysis, *see* p. 27, *supra*, but plaintiffs developed none of those facts in the district court. The undisputed facts available to the Court all point in favor of nonobviousness, *id.*, particularly in light of

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[18] Ostrer also suggests that the claims are ineligible because they cover an entire class of mutations without a corresponding disclosure. Pet. Br. 14-15, 31, 37. That argument is irrelevant to § 101. Moreover, the rule under § 112 is that "disclosure of a species may be sufficient written description support" for a claim to a genus. *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1124 (Fed. Cir. 2004).

the fact that plaintiffs would have borne the burden of proof by clear-and-convincing evidence. 35 U.S.C. § 282; *i4i*, 131 S. Ct. at 2242; *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 417 (2007).[19]

Myriad is prepared to defend against any patentability challenges on an adequately-developed record. This case does not afford that opportunity. *See Diehr*, 450 U.S. at 191 (limiting inquiry where case presented "only the question of whether respondents' claims fall within the § 101 categories of possibly patentable subject matter").

* * * *

Patentability challenges, under §§ 102, 103, and 112, typically present legal issues based on an extensive evaluation of underlying facts. *See i4i*, 131 U.S. at 2253 (Breyer, J., concurring). It is easy to see how a § 101 determination could depend on resolving factual disputes, just as the similar question of "nonobviousness" presents underlying factual questions under § 103. (Certainly, the number of misstated facts relied upon by Ostrer suggests that factual questions could overwhelm a § 101 inquiry.) Accordingly, the Court should view § 101 challenges as ones where the challenger bears the burden of proof, and must establish any underlying facts by

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[19] Judge Bryson, dissenting as to the non-cDNA claims, cited to research by one of Myriad's principal competitors for BRCA1, who was "the first to map a BRCA gene to its chromosomal location [17p21]." Pet. App. 99a. This might be relevant to novelty and prior invention under § 102, and nonobviousness under § 103, but not eligibility under § 101.

clear and convincing evidence. That is unnecessary here, however. The undisputed material facts established on the summary-judgment record demonstrate that Myriad's patent claims to isolated DNA molecules are human-made compositions—the product of an "inventive concept," *see Mayo*, 132 S. Ct. at 1294.

G. The Court Should Not Undo The "Established General Legal Rule"

Given long-established practice and precedent, this Court's guidance in *Mayo* applies with full force: Courts should not "depar[t] from established general legal rules lest a new protective rule that seems to suit the needs of one field produce unforeseen results in another." 132 S. Ct. at 1304-05. Yet Ostrer and his *amici*, many of whom have an interest in competing with Myriad by using Myriad's own inventions, ask the Court to unravel over 30 years of reliance—in the form of investment and advance across multiple industries benefiting millions of patients and consumers, as the purpose of the Patent Act contemplates. The Act accomplished that here, incentivizing and protecting Myriad's inventions, and with Myriad using its inventions to develop life-saving tests to the benefit of the public.

Perhaps sensing the extent of the damage their theories would impose, Ostrer and others suggest that the Court could cabin the outcome to only isolated *human* DNA molecules. Pet. Br. i; *e.g.*, Lander Br. 5. There is no principled way to distinguish between isolated "human" DNA molecules and isolated plant and animal DNA molecules, which are themselves used for untold agricultural, livestock, consumer, and biofuel

products. For *all* of these industries, "the legitimate expectations of inventors in their property," and the consequent benefits to the public, would be destroyed if the established legal rule were changed. *Festo*, 535 U.S. at 739; *Warner-Jenkinson*, 520 U.S. at 32 n.6 (changing "the rules of the game now could very well subvert the various balances the PTO sought to strike when issuing the numerous patents which have not yet expired and which would be affected by [the Court's] decision").

In short, "[a]ny recalibration" of the longstanding rule should "remai[n] in [Congress's] hands." *i4i*, 131 S. Ct. at 2252; *see also Chakrabarty*, 447 U.S. at 317 (policy matters are "for resolution within the legislative process after the kind of investigation, examination, and study that legislative bodies can provide and courts cannot").

III. THE CLAIMS CONFORM WITH THE FIRST AMENDMENT

In barely two pages, Ostrer seeks to reinstate his First Amendment challenge. Pet. Br. 55-58. That argument is waived. Though plaintiffs' complaint included a First Amendment claim, their challenge to the composition claims here was limited to patent-eligibility. Pet. i. Even the body of their petition included only one paragraph and one general citation regarding the First Amendment (Pet. 30-31), and their reply in support of certiorari nowhere mentioned the First Amendment. That claim is not "fairly included" within the question presented—*see* this Court's Rule 14.

Besides, the claims do not violate the First Amendment for the same reason that Ostrer's § 101 challenge is incorrect. *See* pp. 39-60, *supra.* The

claims are to physical compositions, not abstract thoughts or information; thus the claims cannot "restrict access to information" or speech. Pet. Br. 56.

CONCLUSION

This case should be dismissed for lack of jurisdiction. If the Court were to reach the merits, the judgment of the Court of Appeals should be affirmed.

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