No. 12-398

In The
Supreme Court of the United States

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 AMICI CURIAE GILEAD SCIENCES, INC., ELAN PHARMACEUTICALS, INC. CONFLUENCE LIFE SCIENCES, INC., EUCLISES PHARMACEUTICALS, INC. & BIOGENERATOR, IN SUPPORT OF RESPONDENTS

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INTERESTS OF AMICI CURIAE

Each Amicus Party, named herein, is an organization that relies on chemical and biotechnology patents; each has a strong interest in ensuring the stability of the patent system as it relates to chemical and biotechnology inventions.[1]

Gilead Sciences, Inc. is a biopharmaceutical company that discovers, develops and commercializes innovative medicines in areas of unmet need.

Elan Pharmaceuticals, Inc. is a biopharmaceutical company that discovers, develops and commercializes innovative medicines in areas of unmet need.

Confluence Life Sciences, Inc. is a biopharmaceutical company engaged in research and development to commercialize innovative medicines in the fields of inflammation and oncology.

Euclises Pharmaceuticals, Inc. is a biopharmaceutical company engaged in research and development to commercialize innovative medicines in the fields of inflammation and oncology.

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[1] No counsel representing Petitioners or Respondents authored this Brief, in whole or in part, and no counsel or party-in-suit made any monetary contribution to preparation or submission of this Brief. Written consent from Counsel of Petitioners is on file with the Court, and consent from Counsel of Respondents will be filed with this Brief.

BioGenerator is a privately funded, non-profit §501(c)(3) organization that facilitates formation of successful, sustainable bioscience companies.

FACTUAL BACKGROUND

After years of intensive investigation and engineering, Myriad researchers synthesized a new and useful DNA chemical compound having a sequence of nucleotides, as recited in Myriad U.S. Patent No. 5,747,282 Claim 2 ("U.S.'282 Claim 2 Synthetic DNA").

U.S.'282 Claim 2 Synthetic DNA does not exist in nature. This is a fact not disputed on the record.

This Myriad Synthetic DNA is useful as an effective and highly-efficient probe in prediction or diagnosis of genetic pre-disposition to ovarian and breast cancers caused by genetic defects in the BRCA1 gene.[2]

I. See Appendix Figure 1 showing Myriad's Discovery Process Resulting in Myriad Synthetic DNA.

[2] "BRCA1 gene" is a designation assigned by earlier researchers to identify a locus in the human genome that may contain genetic mutations associated with a propensity for development of ovarian and breast cancers.

II. Myriad Natural Product Genomic Screening

As outlined in Figure 1, multipoint linkage analysis was used to localize and refine from Chromosome 17 (~81 million bp) a chromosomal region (6-10 million bp)[3] embracing the BRCAl gene locus (1.5 million bp),[4] which was subsequently mapped using positional cloning.[5] Candidate cDNA clones for the BRCAl genetic locus were identified, and detailed maps of transcripts for the target chromosomal region (600,000 bp) were constructed to provide 65 candidate expressed-sequences (selected by hybridization, direct screening of cDNA library, and random sequencing of subclones).[6] Candidate sequences were then screened within the target chromosomal region, and 21 of the screened sequences were found to constitute key fragments (100,000 bp) of the original BRCAl gene locus including introns and exons (the "BRCA1 segment").[7]

III. Myriad Chemical Transformative Steps

Key fragments of the BRCA1 segment were then transcribed to produce a molecule of pre-mRNA. During this transcription step, the BRCA1 segment was further chemically cleaved, breaking covalent bonds at sites between nucleotide sequences constituting introns and nucleotide sequences

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[3] U.S.'282 at col. 9, lines 29-32 and col. 46, lines 34-38.
[4] U.S.'282 at col. 9, lines 34-37 and col. 46, lines 45-46.
[5] Shattuck Decl., ¶ 4.; U.S.'282 at col. 46-49.
[6] U.S.'282 at col. 49-52.
[7] U.S.'282 at col. 53, lines 22-24 and FIGS 10A-H.

constituting exons, to make a newly-formed mRNA molecule. In the course of more than 20 splicing events, the remaining exon segments of the mRNA were joined forming new covalent bonds. These transformative steps produced mRNA in which the introns were excised from the molecule and the 23 coding exons[8] were covalently linked. The mRNA was then reverse transcribed to produce a full length, intron-free complementary DNA (cDNA) construct, which is a 5,914 bp sequence described in U.S.'282 as SEQ ID No. l (and recited in U.S.'282 Claim 2).[9]

SUMMARY OF ARGUMENT[10]

Question certified by the Court in Grant of Writ of Certiorari is:

"Are human genes patentable?"

Subordinate to this broad Question, as stated, is key question of patent-eligibility under 35 USC §101 of DNA sequences, especially new and useful synthetic DNA constructs.

This is not simply a "gene patenting" case. This case inquires into the scope of eligible

[8] U.S.'282 at col. 53, lines 22-24 and FIG. 6

[9] U.S.'282 at col. 53

[10] This Brief was significantly improved by the technical and legal contributions of HDP Attorney Gregory S. DeLassus and HDP Law Intern Nicholas W. Smith, Ph.D.

substances, specifically synthetic DNA nucleotide sequences, under 35 USC §101 (as "composition of matter," or article of "manufacture," or both).

Thus, a central issue is whether a synthetic, man-made sequence of nucleotides forming a "new and useful" molecule is §101-eligible.

In holding Myriad Synthetic DNA unpatentable,[11] the District Court of Southern District of New York ("SDNY") erred, in two respects:

1) As a matter of Patent Law, the SDNY District Court failed to apply the "made-by-man" fundamental standard for determining §101-eligible subject-matter.

2) As factual error, the SDNY District Court misapplied the "markedly different" test in its analysis of structural and functional characteristics of Myriad Synthetic DNA.

Argument in this Brief specifically targets §101-eligibility of new and useful synthetic, man-made DNA constructs, such as those recited in U.S. '282 Claim 2.[12]

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[11] *Assoc. for Molecular Pathology v. USPTO*, 702 F.Supp.2d 181 (SDNY 2010).

[12] As used throughout this Brief, the following terms are intended to be interchangeable when referring to U.S.'282 Claim 2 SEQ. ID No.1: DNA Sequence, molecule, compound, construct, substance and chemical entity.

ARGUMENT

I. Myriad Synthetic DNA of Claim 2 of U.S. 5,747,282 is Patent-Eligible Subject-Matter under 35 USC §101

A. CAFC Properly Recognized "Made-By-Man" As Fundamental Standard In Subject-Matter Inquiry Under §101

1. Broad Statutory Threshold of 35 USC §101

The threshold of patent-eligibility is defined in 35 USC §101:

> 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.[13]

Enacted in 1952, 35 USC §101 "embodied Jefferson's philosophy that 'ingenuity should receive a liberal encouragement'," and "Congress intended statutory subject matter to 'include anything under the sun that is made by man'."[14] The 1952 Act codifies prior case law. In 1980, *Diamond v.*

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[13] 35 USC §101.

[14] *Diamond v. Chakrabarty*, 447 U.S. 303, 308-309 (1980).

Chakrabarty, as well as subsequent cases, firmly established that patent-eligibility under §101 should have broad scope. Respondent Myriad Genetics, Inc. ("Myriad") invented a synthetic sequence of nucleotides (a chemical compound) which had never existed in nature. This new molecule is a "made-by-man" chemical compound useful as a probe in life-saving diagnosis of human genetic predisposition to ovarian and breast cancers to a high degree of certainty.[15]

This "new and useful" chemical compound is recited in Claim 2 of Myriad U.S. Patent No. 5,747,282 ("U.S.'282") as a DNA sequence defined as SEQ ID NO:1 ("Myriad Synthetic DNA").[16]

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[15] Myriad Synthetic cDNA is useful as a chemical probe to identify cancer-inducing gene-mutations. A woman who tests positive has, on average, an 82% lifetime risk of developing breast cancer and a 44% risk of developing ovarian cancer. These pre-symptomatic individuals, employing appropriate preventive therapies, can reduce their risk of developing breast cancer by approximately 50% (as reported in Journal of the National Cancer Institute), and can lower their risk of developing ovarian cancer by approximately 60% (as reported in New England Journal of Medicine). See: Hall MJ, Reid JE, Burbidge LA *et. al. BRCA1 and BRCA2 mutations in women of different ethnicities undergoing testing for hereditary breast-ovarian cancer*. Cancer. 2009; 115(1):2222-2233.doi: 10.1002/cncr/24200.; *See also* Swisher Decl. ¶¶ 11-13 of SDNY record.

[16] DNA claims at issue in lower courts include: Claims 1, 2, 5, 6 and 7 of U.S. Patent No. 5,747,282 ("U.S.'282"); Claim 1 of U.S. Patent No. 5,693,473 ("U.S. '473"); and Claims 1, 6 and 7 of U.S. Patent No. 5,837,492 ("U.S. '492"). This Brief, however, shall address U.S.'282 Claim 2, only, reciting DNA sequence of SEQ. ID No 1.

Because the SDNY District Court erred in questions of both law and fact, in a manner contrary to statutory intent and meaning of §101,as well as all applicable case law, the Court of Appeals Federal Circuit ("CAFC") properly reversed holdings of the SDNY District Court's adverse ruling on §101-eligibility.[17] Following grant of Petition for Writ of Certiorari, from the earlier CAFC decision, the U.S. Supreme Court remanded this case to the CAFC for disposition in view of rulings in the Supreme Court decision in the *Mayo* case.[18] In a second review of facts and law of the SDNY decision on U.S. '282 Claim 2 §101-eligiblity, the CAFC re-affirmed that Myriad Synthetic DNA:

1) Is §101-eligible; and

2) *Mayo* has no bearing on the issue of DNA patent eligibility.

Diamond v. *Chakrabarty* held that genetically engineered microorganisms are patent-eligible under 35 USC §101.[19] Interpreting 35 USC §101, *Chakrabarty* explained that, "[i]n choosing such

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[17] The patentability of process claims at issue is not discussed herein. Only patent eligibility under §101 of U.S.'282 Claim 2 DNA sequence is discussed herein. This Amicus Brief does not discuss novelty, obviousness, and other patentability issues under 35 USC §102, §103, and §112.

[18] *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S.Ct. 1289 (2012).

[19] *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

expansive terms as 'manufacture' and 'composition of matter,' (modified by the comprehensive 'any'), Congress plainly contemplated that the patent laws would be given wide scope."[20] The *Chakrabarty* Court reviewed the legislative history since the Patent Act of 1793, including the Committee Reports accompanying the 1952 Act, and concluded that "Congress intended statutory subject matter to 'include anything under the sun that is made-by-man'."[21] Thus, the current statutory design sets a broad, welcoming threshold to "embod[y] Jefferson's philosophy that 'ingenuity should receive a liberal encouragement'."[22]

Of course, such a broad construction does not mean that §101 is without limit. §101 qualifies specified categories of patentable subject matter by the phrase "new and useful". The *Chakrabarty* Court reiterated that laws of nature, physical phenomena, and abstract concepts are not patentable,[23] and emphasized that "Congress thus recognized that the relevant distinction was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions."[24] Thus, under *Chakrabarty*, the fundamental question, beside utility and subject matter category inquiries, should be whether the invention is truly "made-by-man", i.e., whether the

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[20] *Chakrabarty*, at 308.
[21] *Id.* at 309 (citation omitted).
[22] *Id.* at 308-309.
[23] *Id.* at 309.
[24] *Id.* at 313 (emphasis added).

invention is "the result of human ingenuity and research."[25]

2. CAFC Properly Found Myriad DNA of U.S.'282 Claim 2 as Meeting "Markedly Different" Test and to Be §101-Eligible

To the extent that the Supreme Court in *Chakrabarty* interpreted §101 to require "markedly different characteristics", Myriad U.S.'282 Claim 2 fully satisfies such standard.

Under *Chakrabarty*, "natural product" or "natural phenomena" are exclusions to the broad scope of §101."[26] Under *Chakrabarty's* interpretation of the "new and useful" requirements in §101, an invention is patent-eligible if:

(a) It belongs to a statutory category of subject matter (process, machine, manufacture, or composition of matter);

(b) It is "made-by-man" (i.e., non-naturally occurring substance); and

(c) It has practical utility.

Myriad U.S.'282 Claim 2 Synthetic DNA molecule meets all three requirements.

Firstly, DNA molecules are chemical entities that consist essentially of carbon, hydrogen, oxygen,

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[25] *Id.*

[26] *Chakrabarty*, at 309.

nitrogen and phosphorous elements. There is no fundamental difference between DNA and other chemicals for purposes of patent law; they are all compositions of matter eligible for §101 inclusion.[27]

Secondly, Myriad Synthetic DNA is a made-by-man substance. For claims covering a synthetic substance, the human intervention is making or transforming (*i.e.*, to chemically modify, synthesize and characterize) a compound from building blocks (which, in turn, can be basic chemicals such as nucleotides). Myriad Synthetic DNA molecule is a biochemically-synthesized DNA sequence of nucleotides resulting from a series of transformative steps outlined in Figure 1 (Appendix). Such DNA sequence does not exist in nature. Unlike Myriad Synthetic DNA molecule, the naturally-occurring DNA of human Chromosome 17 has fragments of the BRCA-gene coding sequence (in the form of exons and introns) scattered across an 81 million base-pair

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[27] Some historical perspective is beneficial here. John J. Doll, former Acting Undersecretary of the USPTO, observes that Plaintiffs' arguments, in many ways, resemble those voiced 30 to 40 years ago when polymer chemistry was an emerging technology. The concerns raised in the current case are similar to those raised when polymers were first patented:

> "At the time, it was argued that patents on the building blocks of basic polymers would devastate the industry. In fact, no such disaster occurred. For example, the issuance in 1965 of a basic patent broadly claiming… ethylene-propylene-diene monomer ("EPDM") rubber… did not preclude the later issuing of patents to different inventors for several copolymers of this type." Doll Decl. ¶ 25.

DNA sequence."[28] Myriad did not purify or extract U.S.'282 Claim 2 Synthetic DNA from natural sources (such as Chromosome 17). Rather, Myriad synthesized U.S.'282 Claim 2 DNA sequence *de novo* from basic nucleotide components, which are themselves artificially synthesized compounds (e.g., oligonucleotide primers). Figure 1 (Appendix) shows the key transformative steps (*i.e.*, chemical manipulations) used to identify and synthesize U.S.'282 Claim 2 DNA.[29] Each of these steps represents the application of careful, intensive and creative efforts by Myriad researchers over a decade.

Thus, but for Myriad's transformative synthetic activity, Myriad Synthetic DNA would not exist as a chemical entity. In short, after laborious effort to identify the BRCA1 gene coding sequence, believed critical for cancer diagnosis, Myriad "human intervention" transformed nucleotide building blocks into a non-natural composition of matter, thus rendering Myriad Synthetic DNA the result of human ingenuity, and not the handiwork of nature.

Thirdly, Myriad Synthetic DNA is a proven-useful diagnostic tool, as evidenced by Myriad's medical and economic success employing Myriad

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[28] Myriad Synthetic DNA is not a natural gene. Genes are "integrated into the chromosome and are not broken or detached from the chromosome." Kay Decl. ¶ 27. Myriad Synthetic DNA has ~0.005% of natural human Chromosomal DNA and does not have the same ordering of nucleotides as the native BRCA1/2 genetic sequence.

[29] See Factual Background, *supra*.

Synthetic DNA compound to predict genetic predisposition to breast and ovarian cancers.[30]

Therefore, under *Chakrabarty* three-fold criteria, Myriad Synthetic DNA is patent-eligible subject-matter under §101.

3. Case Law Is Unanimous That New DNA Molecules Synthesized By Biochemical Transformative Steps Are §101-Eligible

Consistent with the broad interpretation as set forth in *Chakrabarty,* U.S. Courts have upheld §101-eligibility of synthetic compounds including DNA constructs.[31] There is no reported case law in the

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[30] See description of BRCA*Analysis*™, Crichtfield Decl. ¶¶ 26-30; Skolnick Decl. ¶¶ 19-23.

[31] Case law finding synthetic compounds and materials as §101-eligible include:

(a) *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) (genetically engineered bacteria held to be patentable);

(b) *In re Bergy*, 596 F.2d 952, 960 (C.C.P.A. 1979) (microbe having synthetic DNA plasmid is statutory);

(c) *In re Folkers*, 344 F.2d 970 (C.C.P.A. 1965) (Quinones having electron-transport property are useful);

(d) *Amgen v. Chugai*, 927 F.2d 1200 (Fed. Cir. 1991) (DNA encoding for natural-EPO is patentable);

(e) *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993) (isolated DNA is patentable);

(f) *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Intern., Inc.*, 534 U.S. 124 (2001) (new hybrid corn seed is statutory);

(g) *Plant Genetic Sys. v. DeKalb Genetics Corp.*, 175 F.Supp.2d 246 (D.Conn. 2001) (genetically-modified seeds are statutory);

past 60 years (since the discovery of natural DNA) declaring that a synthetic DNA compound is excludable from §101.

All prior case law, bearing on new and useful synthetic compounds, has consistently given §101 broad interpretation to conform to the legislative intent of the 1952 Patent Act that any new and useful compound (*i.e.*, Myriad U.S.'282 Claim 2 synthetic DNA construct) "made-by-man", or involving transformative steps, or intervention by man, satisfies the statutory requirement of §101. Up to the present SDNY decision, in every case where a court has explicitly or implicitly evaluated §101-eligibility of a synthetic DNA molecule, the court has ruled for inclusion.[32]

(h) *Chiron v. Genentech*, 268 F.Supp.2d 1148 (E.D.Cal. 2002) (monoclonal antibody binding to breast-cancer antigen is statutory);

(i) *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2005) (recombinant DNA characterized as "non-natural");

(j) *Monsanto v. Good*, 2004 WL 1664013 (D.N.J. 2003) (soybean chimeric gene is statutory);

(k) *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331 (Fed. Cir. 2005) (PHC hemihydrate is synthetic man-made compound as "manufacture" or "composition-of-matter");

(l) *Genentech v. Insmed*, 436 F.Supp.2d 1080 (N.D.Cal. 2006) (insulin-like human growth factor is statutory even without utility).

[32] See case cited at Footnote 31, *infra.*

B. Myriad Synthetic DNA §101-Eligibility Does Not Disturb Any Case Precedent.

In finding for Myriad U.S.'282 Claim 2 synthetic DNA §101-eligibility, the Court need not rely upon any precedent directed to §101-eligibility of a chemical substance based upon case law rulings on purification or isolation of such substance, for two reasons:

(1) Myriad U.S.'282 Claim 2 DNA is a Man-Made synthetic construct.

(2) Case precedent on purification or isolation for determination of §101-eligibility is a fact-driven, but variable and unpredictable, outcome.[33,34]

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[33] Case law finding purified compounds as "new structures" being §101-eligible include:

(a) *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F.95 103 (S.D.N.Y. 1911) (adrenaline composition purified from gland tissue was not "for a degree of purity, and therefore not for a new 'composition of matter.'… it does not include a salt, and no one had ever isolated a substance which was not in salt form, and which was anything like [Patentee's]… [t]hat was a distinction *not in degree, but in kind.* The adrenaline was a new thing "commercially and therapeutically.");

(b) *Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958) (naturally occurring vitamin B12 in purified form is patentable);

(c) *Kuehmsted v. Farbenfabriken of Elberfeld Co.* 179 F. 701 (7th Cir. 1910) (purified aspirin is new, useful & patent-eligible);

(d) *In re Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970) (purified prostaglandin compounds are new);

(e) *In re Kratz*, 592 F.2d 1169 (C.C.P.A. 1979) (purified 2-methyl-2-pentenoic acid, a chemical compound naturally responsible for the flavor of strawberries, was held to be patentable);

(f) *Schering Corp. v. Amgen, Inc.*, 18 F.Supp.2d 372 (D. Del. 1998) (the substantially pure DNA encoding recombinant human interferon-like peptide as substantially-pure DNA sequence is statutory subject matter), affirmed 222 F.3d 1347 (Fed. Cir. 2000).

[34] All cases (since 1874) failing to find new structures, or purified or isolated compounds and materials, as basis for §101-eligible subject matter, as cited by Petitioners or the SDNY District Court, are listed below:

(a) *American Fruit Growers, Inc. v. Brogdex*, 283 U.S. 1 (1931) (combination of a natural fruit and a boric compound carried by the rind or skin of an Orange was not an "article of manufacture," and "does not produce from the raw material an article for use which possesses a new or distinctive form, quality, or property.");

(b) *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884) (naturally-occurring alizarine is not patent-eligible subject matter because it is not a "new composition of matter.");

(c) *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 129, 130 (1948) (a mixed culture of naturally occurring bacteria was not a patentable advance because no species acquired a *different property or use* - the composition was simply a mixture of bacteria.);

(d) *Gen. Elec. Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d Cir. 1928) (post-filing discovery that patentee's substantially pure tungsten was naturally occurring tungsten, with identical properties as the claimed invention, rendered patentee's invention not a "new metal.");

1. Synthetic DNA of U.S.'282 Claim 2 Is a Man-Made Construct Not "Purified" From Nature.

The DNA of U.S.'282 Claim 2 is the product of a multistep synthesis that involves (1) transcribing the nucleotide segments identified from the BRCAI gene, (2) altering such nucleotide segments by chemically cleaving with 20 or more cleaving and splicing events at 24 splicing sites to form an exon-exclusive mRNA molecule, and (3) reverse transcription of the exon-exclusive molecule into the DNA of U.S.'282 Claim 2, which is a product that does not exist in nature. Furthermore, reverse transcription requires the use of an enzyme, reverse transcriptase, which is not present in a usable form

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(e) *Cf. Am. Wood Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874) (cellulose purified from wood and useful for making paper is patent ineligible);

(f) *Ex Parte Latimer*, 46 O.G. 1638; 1889 Dec. Comm'r Pat. 123 (1889). (The fiber "when it is made free, is in nowise changed or different from its natural construction. There is no chemical combination effected by the treatment which frees it by which the fiber becomes something new or different from the fiber in its natural state.");

(g) *In re Marden*, 47 F.2d 958 (C.C.P.A. 1931) (Rejecting patent on purified vanadium because "pure vanadium is not new in the inventive sense, and, it being a product of nature, no one is entitled to a monopoly of the same.");

(h) *In re Marden*, 47 F.2d 957 (C.C.P.A. 1931) (Purified uranium is patent ineligible);

(i) *In re Merz*, 97 F.2d 599 (C.C.P.A. 1936) (Purified ultramarine is patent ineligible).

in human cells. These transformative steps create the distinct chemical entity of U.S.'282 Claim 2 (not the result of "purification" or "isolation").

2. Patent-Eligibility of DNA of U.S.'282 Claim 2 Is Not Contravened By Any Case Cited By Petitioner.

Every case cited by Petitioner relates to purification or isolation of a known material or lacks a new structure.[35] Conversely, Myriad U.S.'282 Claim 2 synthetic DNA is a man-made, synthetic, and structurally-new and useful molecule. Thus, no case evaluating a known purified or isolated material supports exclusion of §101-eligibility for U.S.'282 Claim 2 DNA.

C. *Mayo* Does Not Compel Reversal of CAFC Decision on §101-Eligibility.

In its July 2011 decision, the CAFC properly reversed the SDNY District Court on matters of law and fact, as to §101-eligibility, of Myriad U.S.'282 Claim 2 DNA.

§101-eligibility of Myriad DNA is fundamentally consistent with the Supreme Court's holding in *Chakrabarty*, and fully supported by firmly established case law developed since enactment of the 1952 Patent Act.

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[35] See cases cited at Footnote 34, *infra.*

Nothing in *Mayo* directs the Supreme Court now to alter the CAFC's holding that U.S.'282 Claim 2 DNA sequence is §101-eligible, as decided by two CAFC reviews (29 July 2011 and 16 August 2012).

Mayo is factually distinguished on two grounds.

Firstly, *Mayo* concerned a diagnostic-method claim, lacking sufficient structural definition to distinguish over natural phenomena. By contrast, U.S.'282 Claim 2 is directed to a DNA composition of matter, namely to a biochemically-synthesized sequence of specific nucleotide content and size.

Secondly, a fundamental component of the *Mayo* Court's examination was whether the Prometheus patent "otherwise forecloses more future invention than the underlying discovery could reasonably justify." This consideration is viewed under the Constitutional requirement of promoting the useful arts, by disclosure of invention in exchange for a government-grant of a limited right to exclude others from using the invention. If the DNA of U.S.'282 Claim 2 were not patent eligible, the discovery would likely not have occurred in the first place. Petitioner's brief urges that researchers would continue BRCA research if Myriad synthetic DNA were held not patent-eligible.[36] However, this position fails to recognize that subsequent researchers would not have the opportunity to do BRCA research had patent protection not

[36] Pet. Br. 43.

incentivized Myriad to discover the DNA of U.S.'282 Claim 2. Perhaps the discovery would have been made by someone else at a later date, but this date may have been far into the future absent the incentive of patent protection.

Upholding §101-eligibility of Myriad U.S.'282 Claim 2 will not preempt an entire field of research because Claim 2 embraces a single nucleotide sequence. Indeed, a broad application of patent ineligibility, however, may, in fact, disrupt the expectations of many chemical and biotechnology patent holders and researchers. These researchers depend on the patent system to secure valuable patent rights, allowing them to attract outside investment.

D. *Bilski* and *Morse* Do Not Support Notion of Myriad Patent Pre-emption

The Court in *Bilski v. Kappos* held that a risk-hedging patent method that would pre-empt use of the approach *in all fields* is not patent-eligible.[37] By contrast, U.S.'282 Claim 2 does not encompass a large number of DNA sequences. Instead, the DNA of U.S.'282 Claim 2 comprises a specific DNA sequence for diagnostic testing of certain pathologies. U.S.'282 Claim 2 does not dominate or encompass all diagnostic testing for genetic mutations. The DNA, therefore, does not pre-empt use of DNA "in all fields."

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[37] *Bilski v. Kappos*, 130 S. Ct. 3218 (2010).

The 1853 case of *O'Reilly v. Morse*[38] is also distinguishable from the facts of the Myriad invention. *Morse* involved a claim on any machinery or process using electromagnetism that would be invented, now or in the future, regardless of the machinery used to perform it.[39] In *Morse*, the use of electrical current was preempted because new ways of using the naturally occurring electrical current, however invented, would infringe the claim. Unlike electromagnetism, Myriad DNA is not naturally occurring. Moreover, U.S.'282 Claim 2 recites no "law of nature" element. The DNA of U.S.'282 Claim 2 is not preempting research because U.S.'282 Claim 2 does not comprise DNA sequences yet to be discovered.

Upholding §101-eligibility of Myriad U.S.'282 Claim 2 will not preempt an entire field of research. However, holding synthetic DNA as patent ineligible would severely hinder research in the biotechnology industry.

This Court has "more than once cautioned that courts 'should not read into the patent laws limitations and conditions which the legislature has not expressed."[40] Rendering DNA patent-ineligible as a whole is the province of the legislature.

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[38] *O'Reilly v. Morse*, 56 U.S. 62 (1853).

[39] *Id.* at 112.

[40] *Bilski* , 450 U.S. at 182). *Diehr* at 3226 (quoting

II. Leahy-Smith America Invents Act ("AIA") re-confirms Myriad Synthetic DNA §101-Eligibility.

The Leahy-Smith America Invents Act (AIA)[41] adopts and recodifies the content of 35 USC §101 verbatim, and further qualifies §101 by this provision:

> "Notwithstanding any other provision of law, no patent may issue on a claim directed to or encompassing a *human organism*." (Emphasis added.)

The AIA legislative history sheds light on the meaning of this provision: "[T]he U.S. Patent Office has already issued patents on genes, stem cells, animals with human genes, and a host of non-biologic products used by humans, but it has not issued patents on claims directed to human organisms, including human embryos and fetuses. My amendment would not affect the former, but would simply affirm the latter."[42] Thus, AIA §33(a) codifies existing USPTO policy that new and useful synthetic DNA constructs are §101-eligible, while

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[41] Public Law 112-29, § 33(a), 125 Stat. 284

[42] 157 Cong. Rec. E1177-04 (testimony of Representative Dave Weldon previously presented in connection with the Consolidated Appropriations Act, 2004, Pub. L. No. 108-199, '634, 118 Stat. 3, 101, and later resubmitted with regard to the AIA; see 149 Cong. Rec. E2417-01).

human organisms are not patent-eligible subject matter.[43]

The Weldon testimony shows that §33(a) applies only to humans as a whole, not to components that make up the human, and avoids applying the patent prohibition on components such as synthetic cells and DNA. Therefore, because a cell is comprised of molecular components such as DNA and other molecules of the cell, these molecules, like cells, should not be included in the "organism" genus of AIA §33(a). Therefore, DNA of Myriad U.S.'282 Claim 2 is not included in the prohibition of "organism."

Lastly, under the AIA, the statutory language for §101 is unchanged from that of the 1952 Act. If Congress intended for a different statutory meaning, Congress would have altered the statutory language accordingly. Thus, DNA should continue to be patent-eligible subject-matter post-AIA.

[43] Manual of Patent Examining Procedure, section 2105.

CONCLUSION

For the foregoing reasons, Amici herein named, respectfully request:

(1) On the specific question of §101-eligibility of Myriad U.S.'282 Claim 2 DNA, the Court should uphold the CAFC decision; and

(2) On the broader and vague question of patentability of genes, the Court should refer the question to Congress.

Respectfully submitted on 14 March 2013:

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APPENDIX

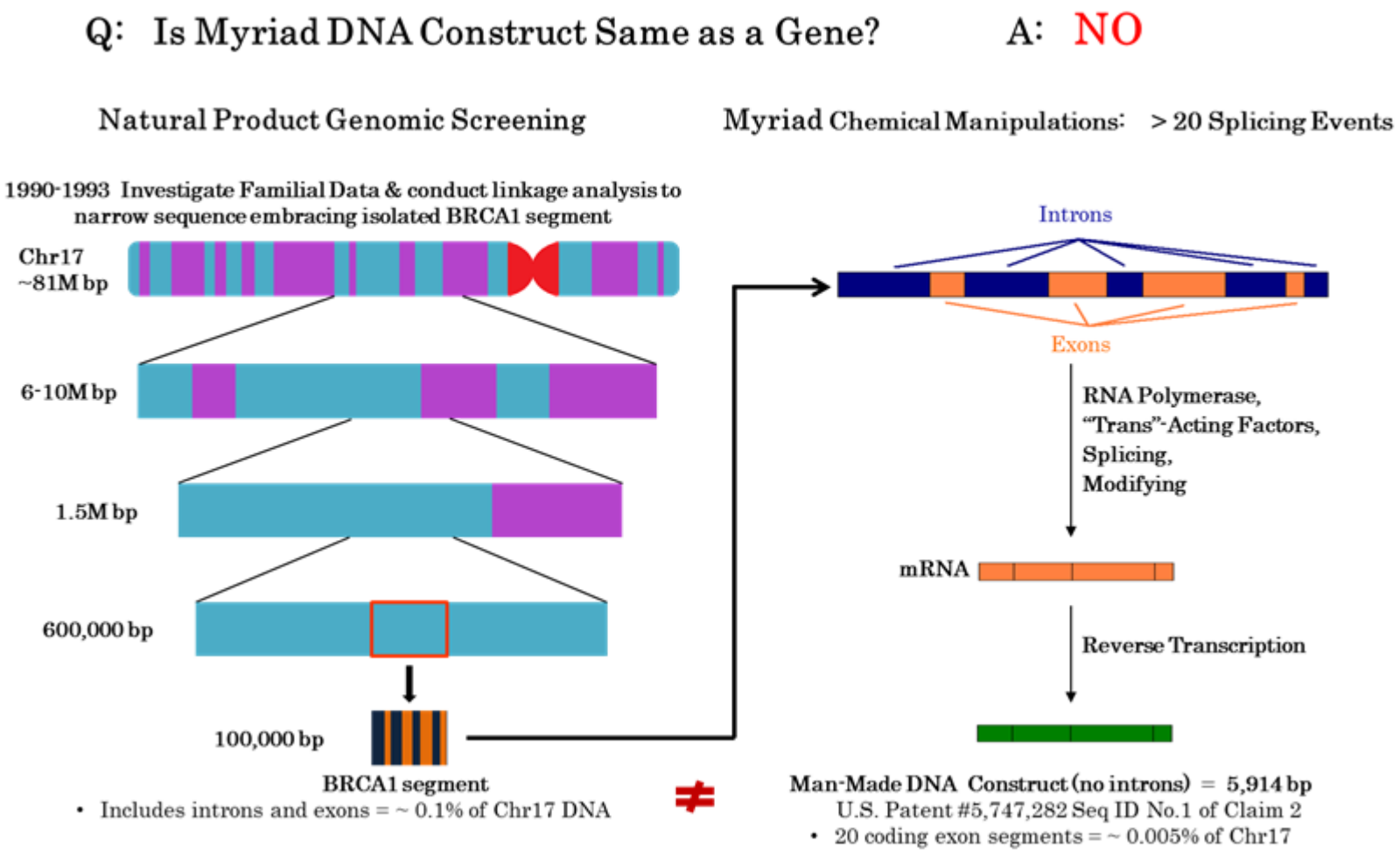

Figure 1:
Transformative-Steps to Make Myriad Synthetic DNA BRCA-Probe Recited in U.S.'282 Claim 2.