Read after *Chakrabarty*

THE ASSOCIATION OF MOLECULAR PATHOLOGY V. U.S PATENT & TRADEMARK OFFICE AND MYRIAD GENETICS, INC.

653 F.3d 1329 (Fed. Cir. 2011)

LOURIE, Circuit Judge.

Myriad Genetics, Inc. and the Directors of the University of Utah Research Foundation (collectively, "Myriad") appeal … from the district court's decision granting summary judgment that all of the challenged claims are drawn to nonpatentable subject matter under 35 U.S.C. § 101. We affirm in part and reverse in part.

…. On the merits, we reverse the district court's decision that Myriad's composition claims to "isolated" DNA molecules cover patent-ineligible products of nature under § 101 since the molecules as claimed do not exist in nature. We also reverse the district court's decision that Myriad's method claim to screening potential cancer therapeutics via changes in cell growth rates is directed to a patent-ineligible scientific principle. We, however, affirm the court's decision that Myriad's method claims directed to "comparing" or "analyzing" DNA sequences are patent ineligible; such claims include no transformative steps and cover only patent ineligible abstract, mental steps.

BACKGROUND

Plaintiffs brought suit against Myriad, challenging the patentability of certain composition and method claims relating to human genetics. Specifically, Plaintiffs sought a declaration that fifteen claims from seven patents assigned to Myriad are drawn to patent-ineligible subject matter under 35 U.S.C. § 101: claims 1, 2, 5, 6, 7, and 20 of U.S. Patent 5,747,282 ("the '282 patent"); claims 1, 6, and 7 of U.S. Patent 5,837,492 ("the '492 patent"); claim 1 of U.S. Patent 5,693,473 ("the '473 patent"); claim 1 of U.S. Patent 5,709,999 ("the '999 patent"); claim 1 of U.S. Patent 5,710,001 ("the '001 patent"); claim 1 of U.S. Patent 5,753,441 ("the '441 patent"); and claims 1 and 2 of U.S. Patent 6,033,857 ("the '857 patent").

The challenged composition claims cover two "isolated" human genes, *BRCA1* and *BRCA2* (collectively, "*BRCA1/2* " or "*BRCA* "), and certain alterations, or mutations, in these genes associated with a predisposition to breast and ovarian cancers. Representative composition claims include claims 1, 2, and 5 of the '282 patent:

> 1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.
>
> 2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO: 1.

5. An isolated DNA having at least 15 nucleotides of the DNA of claim 1.

SEQ ID NO:2 depicts the amino acid sequence of the BRCA1 protein, and SEQ ID NO: 1 depicts the nucleotide sequence of the *BRCA1* DNA coding region. '282 patent col.19 ll.48–50.

All but one of the challenged method claims cover methods of "analyzing" or "comparing" a patient's *BRCA* sequence with the normal, or wild-type, sequence to identify the presence of cancer-predisposing mutations. Representative method claims include claim 1 of the '999 and '001 patents:

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

'999 patent claim 1 (emphases added).

1. A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises [ ] *comparing* a first sequence selected from the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample.

'001 patent claim 1 (emphasis added).

The final method claim challenged by Plaintiffs is directed to a method of screening potential cancer therapeutics. Specifically, claim 20 of the ' 282 patent reads as follows:

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

The challenged claims thus relate to isolated gene sequences and diagnostic methods of

identifying mutations in these sequences. To place this suit in context, we take a step back to provide background on the science involved, including the identification of the *BRCA* genes, and the Plaintiffs' connections to the invention and to Myriad.

I.

Human genetics is the study of heredity in human beings. The human genome, the entirety of human genetic information, contains approximately 25,000 genes, which form the basis of human inheritance. The majority of genes act by specifying polypeptide chains that form proteins. Proteins in turn make up living matter and catalyze all cellular processes.

Chemically, the human genome is composed of deoxyribonucleic acid ("DNA"). Each DNA molecule is made up of repeating units of four nucleotide bases—adenine ("A"), thymine ("T"), cytosine ("C"), and guanine ("G")—which are covalently linked, or bonded, together via a sugarphosphate, or phosphodiester, backbone. DNA generally exists as two DNA strands intertwined as a double helix in which each base on a strand pairs, or hybridizes, with a complementary base on the other strand: A pairs with T, and C with G. Figure 1 below depicts the structure of a DNA double helix and the complementary pairing of the four nucleotide bases, represented by A, T, C, and G.

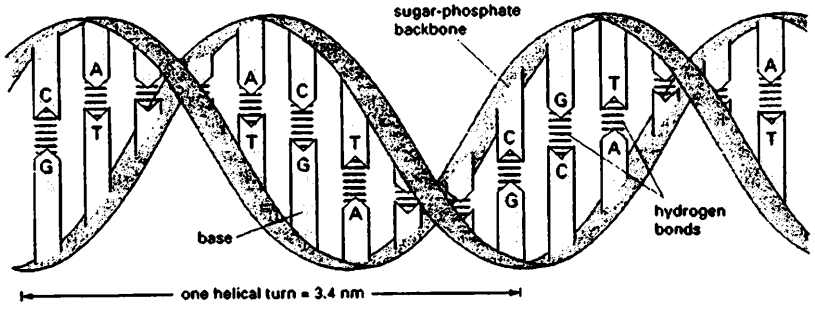

Figure 1

The linear order of nucleotide bases in a DNA molecule is referred to as its "sequence." The sequence of a gene is thus denoted by a linear sequence of As, Ts, Gs, and Cs. "DNA sequencing" or "gene sequencing" refers to the process by which the precise linear order of nucleotides in a DNA segment or gene is determined. A gene's nucleotide sequence in turn encodes for a linear sequence of amino acids that comprise the protein encoded by the gene, *e.g.*, the *BRCA1* gene encodes for the BRCA1 protein. Most genes have both "exon" and "intron" sequences. Exons are DNA segments that are necessary for the creation of a protein, *i.e* ., that code for a protein. Introns are segments of DNA interspersed between the exons that, unlike exons, do not code for a protein.

The creation of a protein from a gene comprises two steps: transcription and translation. First, the gene sequence is "transcribed" into a different nucleic acid called ribonucleic acid ("RNA"). RNA has a chemically different sugar-phosphate backbone than DNA, and it utilizes

the nucleotide base uracil (“U”) in place of thymine (“T”). For transcription, the DNA double helix is unwound and each nucleotide on the non-coding, or template, DNA strand is used to make a complementary RNA molecule of the coding DNA strand, *i.e.*, adenine on the template DNA strand results in uracil in the RNA molecule, thymine results in adenine, guanine in cytosine, and cytosine in guanine. The resulting “pre-RNA,” like the DNA from which it was generated, contains both exon and intron sequences. Next, the introns are physically excised from the pre-RNA molecule, in a process called “splicing,” to produce a messenger RNA (“mRNA”). Figure 2 below shows the steps of transcribing a gene that contains three exons (exon 1–3) and two introns (intron 1 and 2) into a pre-RNA, followed by RNA splicing of the introns to produce an mRNA containing just the exon sequences.

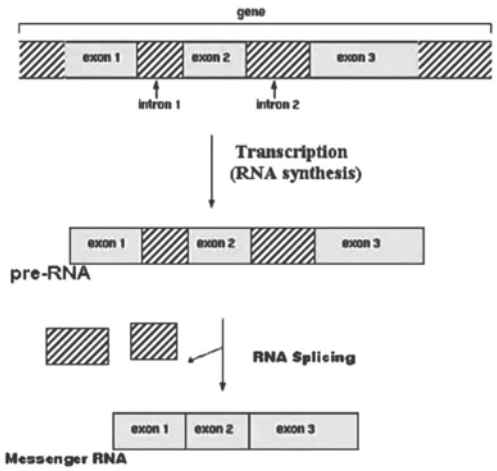

Figure 2

Following transcription, the resulting mRNA is “translated” into the encoded protein. Genes, and their corresponding mRNAs, encode proteins via threenucleotide combinations called codons. Each codon corresponds to one of the twenty amino acids that make up all proteins or a “stop” signal that terminates protein translation. For example, the codon adenine-thymine-guanine (ATG, or UTG in the corresponding mRNA), encodes the amino acid methionine. The relationship between the sixty-four possible codon sequences and their corresponding amino acids is known as the genetic code. Figure 3 below represents an mRNA molecule that translates into a protein of six amino acids (Codon 1, AUG, methionine; Codon 2, ACG, threonine; Codon 3, GAG, glutamic acid; Codon 4, CUU, leucine; Codon 5, CGG, arginine; Codon 6, AGC, serine), and ends with one of the three stop codons, UAG.

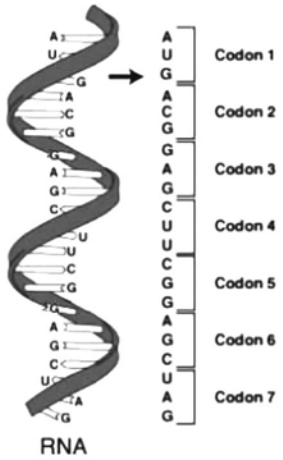

Figure 3

Changes, or mutations, in the sequence of a human gene can alter the structure as well as the function of the resulting protein. Small-scale changes include point mutations in which a change to a single nucleotide alters a single amino acid in the encoded protein. For example, a base change in the codon *G* CU to *C* GU changes an alanine in the encoded protein to an arginine. Larger scale variations include the deletion, rearrangement, or duplication of larger DNA segments, ranging from several hundreds to over a million nucleotides, and result in the elimination, misplacement, or duplication of an entire gene or genes. While some mutations have little or no effect on the body's processes, others result in disease, or an increased risk of developing a particular disease. DNA sequencing is used in clinical diagnostic testing to determine whether a gene contains mutations associated with a particular disease or risk of a particular disease.

Nearly every cell in the human body contains an individual's entire genome. DNA in the cell, called “native” or “genomic” DNA, is packaged into twenty-three pairs of chromosomes. Chromosomes are complex structures of a single DNA molecule wrapped around proteins called histones, as shown in Figure 4 below.

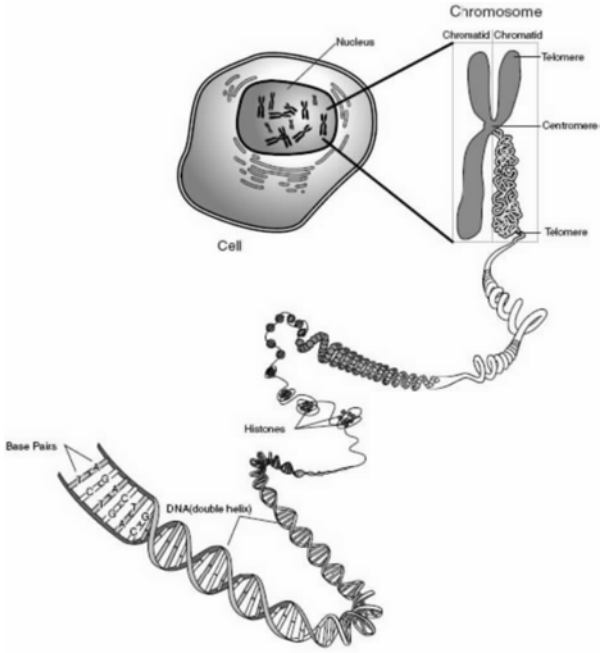

Figure 4

Humans have twenty-two pairs of autosomal chromosomes, numbered one to twenty-two according to size from largest to smallest, and one pair of sex chromosomes, two X chromosomes in females and one X and one Y chromosome in males.

Genomic DNA can be extracted from its cellular environment using a number of well-established laboratory techniques. A particular segment of DNA, such as a gene, can then be excised or amplified from the DNA to obtain the isolated DNA segment of interest. DNA molecules can also be synthesized in the laboratory. One type of synthetic DNA molecule is complementary DNA ("cDNA"). cDNA is synthesized from mRNA using complementary base pairing in a manner analogous to RNA transcription. The process results in a double-stranded DNA molecule with a sequence corresponding to the sequence of an mRNA produced by the body. Because it is synthesized from mRNA, cDNA contains only the exon sequences, and thus none of the intron sequences, from a native gene sequence.

II.

Mutations in the *BRCA* genes correlate with an increased risk of breast and ovarian cancer. The average woman in the United States has around a twelve to thirteen percent risk of developing breast cancer in her lifetime. Women with *BRCA* mutations, in contrast, face a cumulative risk of between fifty to eighty percent of developing breast cancer and a cumulative risk of ovarian cancer of between twenty to fifty percent. Diagnostic genetic testing for the existence of *BRCA* mutations is therefore an important consideration in the provision of clinical care for breast or ovarian cancer. This testing provides a patient with information on her risk for hereditary breast and ovarian cancers, and thus aids in the difficult decision regarding whether to un-

dertake preventive options, including prophylactic surgery. Diagnostic results can also be an important factor in structuring an appropriate course of cancer treatment, since certain forms of chemotherapy are more effective in treating cancers related to *BRCA* mutations.

The inventors of the patents in suit identified the genetic basis of *BRCA1* and *BRCA2*-related cancers using an analysis called positional cloning. Relying on a large set of DNA samples from families with inherited breast and ovarian cancers, the inventors correlated the occurrence of cancer in individual family members with the inheritance of certain marker DNA sequences. This allowed the inventors to identify, or "map," the physical location of the *BRCA* genes within the human genome and to isolate the *BRCA* genes and determine their exact nucleotide sequences. This in turn allowed Myriad to provide *BRCA* diagnostic testing services to women.

Myriad filed the first patent application leading to the patents in suit covering isolated *BRCA1* DNA and associated diagnostic methods in August 1994. The first patent, the '473 patent, issued on December 2, 1997. Myriad filed the first application leading to the patents in suit covering isolated *BRCA2* DNA and associated diagnostic methods in December 1995, and the first patent, the '492 patent, issued on November 17, 1998.

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IV.

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The district court held … that isolated DNA molecules fall within the judicially created "products of nature" exception to § 101 because such isolated DNAs are not "markedly different" from native DNAs. (quoting *Diamond v. Chakrabarty,* 447 U.S. 303 (1980)). The court relied on the fact that, unlike other biological molecules, DNAs are the "physical embodiment of information," and that this information is not only preserved in the claimed isolated DNA molecules, but also essential to their utility as molecular tools.

Turning to the method claims, the court held them patent ineligible under this court's then definitive machine-or-transformation test. (Citing *In re Bilski,* 545 F.3d 943 (Fed.Cir.2008), *affirmed on other grounds by Bilski v. Kappos,* 130 S.Ct. 3218, 3225 (2010)). The court held that the claims covered "analyzing" or "comparing" DNA sequences by any method, and thus covered mental processes independent of any physical transformations. In so holding, the court distinguished Myriad's claims from those at issue in *Prometheus* based on the "determining" step in the latter being construed to include the extraction and measurement of metabolite levels from a patient sample. (Citing *Prometheus Labs., Inc. v. Mayo Collaborative Servs.,* 628 F.3d 1347, 1350 (Fed.Cir.2010), *cert. granted* 2011 WL 973139 (June 20, 2011)). Alternatively, the court continued, even if the claims could be read to include the transformations associated with isolating and sequencing human DNA, these transformations would constitute no more than preparatory data-gathering steps. (Citing *In re Grams,* 888 F.2d 835, 840 (Fed.Cir.1989)). Finally, the

court held that the one method claim to "comparing" the growth rate of cells claimed a basic scientific principle and that the transformative steps amounted to only preparatory data gathering. *Id.* at 237.

Myriad appealed. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

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II. Patentable Subject Matter

Under the Patent Act, "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. The Supreme Court has consistently construed § 101 broadly, explaining that "[i]n choosing such expansive terms ... modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope." *Bilski v. Kappos*, 130 S.Ct. 3218, 3225 (2010) (quoting *Chakrabarty*, 447 U.S. at 308).

The Supreme Court, however, has also consistently held that § 101, although broad, is not unlimited. *Id.* The Court's precedents provide three judicially created exceptions to § 101's broad patent-eligibility principles: "laws of nature, physical phenomena, and abstract ideas." *Id.* (quoting *Chakrabarty*, 447 U.S. at 309). The Court has also referred to these exceptions as precluding the patenting of phenomena of nature, mental processes, *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972), and products of nature, *Chakrabarty*, 447 U.S. at 313 ("[T]he relevant distinction for purposes of § 101 is ... between products of nature ... and human-made inventions."). The Court has explained that, although not required by the statutory text, "[t] he concepts covered by these exceptions are 'part of the storehouse of knowledge of all men ... free to all men and reserved exclusively to none.' " *Bilski*, 130 S.Ct. at 3225 (quoting *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948))

Plaintiffs challenge under § 101 Myriad's composition claims directed to "isolated" DNA molecules and method claims directed to "analyzing" or "comparing" DNA sequences. We address each in turn.

A. Composition Claims: Isolated DNA Molecules

i.

Myriad argues that its challenged composition claims to "isolated" DNAs cover patent-eligible compositions of matter within the meaning of § 101. According to Myriad, the district court came to a contrary conclusion by (1) misreading Supreme Court precedent as excluding from patent eligibility all "products of nature" unless "markedly different" from naturally occur-

ring ones; and (2) incorrectly focusing not on the differences between isolated and native DNAs, but on one similarity: their informational content. Rather, Myriad argues, an isolated DNA molecule is patent eligible because it is, as claimed, "a nonnaturally occurring composition of matter" with "a distinctive name, character, and use." (Quoting *Chakrabarty*, 447 U.S. at 309–10). According to Myriad, isolated DNA does not exist in nature, and isolated DNAs, unlike native DNAs, can be used as primers and probes for diagnosing cancer. Moreover, Myriad asserts that a categorical "products of nature" exception not only would be unworkable, as every composition of matter is, at some level, composed of natural materials, but also would be contrary to this court's precedents, the PTO's 2001 *Utility Examination Guidelines*, and Congress's role in enacting the patent laws.

Plaintiffs respond that claims to isolated DNA molecules fail to satisfy § 101 because such claims cover natural phenomena and products of nature. According to Plaintiffs, Supreme Court precedent establishes that a product of nature is not patent eligible even if, as claimed, it has undergone some highly useful change from its natural form. Rather, Plaintiffs assert, to be patent eligible a composition of matter must also have a distinctive name, character, and use, making it "markedly different" from the natural product. In this case, Plaintiffs conclude that because isolated DNAs retain the same nucleotide sequence as native DNAs, they do not have any "markedly different" characteristics. Furthermore, according to Plaintiffs, the isolated DNA claims also have a preemptive effect, excluding anyone from working with the *BRCA* genes.

The government as amicus curiae does not defend the PTO's longstanding position that isolated DNA molecules are patent eligible, arguing instead for a middle ground. Specifically, the government argues that DNA molecules engineered by man, including cDNAs, are patent-eligible compositions of matter because, with rare exceptions, they do not occur in nature, either in isolation or as contiguous sequences within a chromosome. In contrast, the government asserts, isolated and unmodified genomic DNAs are *not* patent eligible, but rather patent-ineligible products of nature, since their nucleotide sequences exist because of evolution, not man.

At oral argument, the government illustrated its argument by way of a "magic microscope" test. According to the government's test, if an imaginary microscope could focus in on the claimed DNA molecule as it exists in the human body, the claim covers unpatentable subject matter. The government thus argues that because such a microscope could focus in on the claimed isolated *BRCA1* or *BRCA2* sequences as they exist in the human body, the claims covering those sequences are not patent eligible. In contrast, the government contends, because an imaginary microscope could not focus *in vivo* on a cDNA sequence, which is engineered by man to splice together non-contiguous coding sequences (*i.e.*, exons), claims covering cDNAs are patent eligible.

In sum, although the parties and the government appear to agree that isolated DNAs are compositions of matter, they disagree on whether and to what degree such molecules fall within the exception for products of nature. As set forth below, we conclude that the challenged claims

to isolated DNAs, whether limited to cDNAs or not, are directed to patent-eligible subject matter under § 101.

ii.

The Supreme Court's decisions in *Chakrabarty* and *Funk Brothers* set out the framework for deciding the patent eligibility of isolated DNA molecules.

In *Chakrabarty,* the Court addressed the question whether a man-made, living microorganism is a patentable manufacture or composition of matter within the meaning of § 101. The microorganisms were bacteria genetically engineered with four naturally occurring DNA plasmids, each of which enabled the breakdown of a different component of crude oil. The bacteria, as a result, could break down multiple components of crude oil, a trait possessed by no single naturally occurring bacterium and of significant use in more efficiently treating oil spills. The Court held that the bacteria qualified as patentable subject matter because the "claim is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use.' " *Id.* at 309–10 (quoting *Hartranft v. Wiegmann*, 121 U.S. 609, 615 (1887)).

To underscore the point, the Court compared Chakrabarty's engineered bacteria with bacteria inoculants found unpatentable in *Funk Brothers,* again casting this case decided on obviousness in terms of § 101. In *Funk Brothers,* the patentee discovered that certain strains of nitrogen-fixing bacteria associated with leguminous plants do not mutually inhibit each other. Based on this discovery, the patentee produced (and claimed) mixed cultures of nitrogen-fixing species capable of inoculating a broader range of leguminous plants than single-species cultures. The Court held that the bacteria's qualities of non-inhibition were, "like the heat of the sun, electricity, or the qualities of metals," the "work of nature," and thus not patentable. The Court also held that application of the newly discovered bacterial trait of non-inhibition to create a mixed bacterial culture was not a patentable advance because no species acquired a different property or use. The *Chakrabarty* Court thus concluded that what distinguished Chakrabarty's bacteria from those claimed in *Funk Brothers,* and made the former patent eligible, was that Chakrabarty's bacteria had "markedly different characteristics from any [bacterium] found in nature" based on the efforts of the patentee. *Chakrabarty,* 447 U.S. at 310.

The distinction, therefore, between a product of nature and a human-made invention for purposes of § 101 turns on a change in the claimed composition's identity compared with what exists in nature. Specifically, the Supreme Court has drawn a line between compositions that, even if combined or altered in a manner not found in nature, have similar characteristics as in nature, and compositions that human intervention has given "markedly different," or "distinctive," characteristics. *Id. Hartranft,* 121 U.S. at 615; *see also Am. Fruit Growers v. Brogdex Co.,* 283 U.S. 1, 11 (1931). Applying this test to the isolated DNAs in this case, we conclude that the challenged claims are drawn to patentable subject matter because the claims cover molecules that are

markedly different—have a distinctive chemical identity and nature—from molecules that exist in nature.

It is undisputed that Myriad's claimed isolated DNAs exist in a distinctive chemical form-as distinctive chemical molecules—from DNAs in the human body, *i.e.*, native DNA. Native DNA exists in the body as one of forty-six large, contiguous DNA molecules. Each DNA molecule is itself an integral part of a larger structural complex, a chromosome. In each chromosome, the DNA molecule is packaged around histone proteins into a structure called chromatin, which in turn is packaged into the chromosomal structure. *See supra*, Figure 3.

Isolated DNA, in contrast, is a free-standing portion of a native DNA molecule, frequently a single gene. Isolated DNA has been cleaved (*i.e.*, had covalent bonds in its backbone chemically severed) or synthesized to consist of just a fraction of a naturally occurring DNA molecule. For example, the *BRCA1* gene in its native state resides on chromosome 17, a DNA molecule of around eighty million nucleotides. Similarly, *BRCA2* in its native state is located on chromosome 13, a DNA of approximately 114 million nucleotides. In contrast, isolated *BRCA1* and *BRCA2*, with introns, each consists of just 80,000 or so nucleotides. And without introns, *BRCA2* shrinks to just 10,200 or so nucleotides and *BRCA1* to just around 5,500 nucleotides. Furthermore, claims 5 and 6 of the '282 patent cover isolated DNAs having as few as fifteen nucleotides of a *BRCA* sequence. Accordingly, *BRCA1* and *BRCA2* in their isolated state are not the same molecules as DNA as it exists in the body; human intervention in cleaving or synthesizing a portion of a native chromosomal DNA imparts on that isolated DNA a distinctive chemical identity from that possessed by native DNA.

As the above description indicates, isolated DNA is not purified DNA. Purification makes pure what was the same material, but was previously impure. Although isolated DNA must be removed from its native cellular and chromosomal environment, it has also been manipulated chemically so as to produce a molecule that is markedly different from that which exists in the body. It has not been purified by being isolated. Accordingly, this is not a situation, as in *Parke–Davis & Co. v. H.K. Mulford Co.*, in which purification of adrenaline resulted in the *identical* molecule being "for every practical purpose a new thing commercially and therapeutically." 189 F. 95, 103 (C.C.N.Y.1911). Although, we note, Judge Learned Hand held the claimed purified "Adrenalin" to be patentable subject matter. *Id.* The *In re Marden* cases are similarly inapposite, directed as they are to the patent ineligibility of purified natural elements—ductile uranium, 47 F.2d 957 (CCPA 1931), and vanadium, 47 F.2d 958 (CCPA 1931)—that are inherently ductile in purified form. *Parke–Davis* and *Marden* address a situation in which claimed compound A is purified from a physical mixture that contains compound A. In this case, the claimed isolated DNA molecules do not exist as in nature within a physical mixture to be purified. They have to be chemically cleaved from their chemical combination with other genetic materials. In other words, in nature, isolated DNAs are covalently bonded to such other materials. Thus, when cleaved, an isolated DNA molecule is not a purified form of a natural material, but a distinct chemical entity. In fact, some forms of isolated DNA require no purification at all, because

DNAs can be chemically synthesized directly as isolated molecules….

Plaintiffs argue that because the claimed isolated DNAs retain the same nucleotide sequence as native DNAs, they do not have any "markedly different" characteristics. This approach, however, looks not at whether isolated DNAs are markedly different—have a distinctive characteristic—from naturally occurring DNAs, as the Supreme Court has directed, but at one similarity: the information content contained in isolated and native DNAs' nucleotide sequence. Adopting this approach, the district court disparaged the patent eligibility of isolated DNA molecules because their genetic function is to transmit information. We disagree, as it is the distinctive nature of DNA molecules as isolated compositions of matter that determines their patent eligibility rather than their physiological use or benefit. Uses of chemical substances may be relevant to the non-obviousness of these substances or to method claims embodying those uses, but the patent eligibility of an isolated DNA is not negated because it has similar informational properties to a different, more complex natural material that embodies it. The claimed isolated DNA molecules are distinct from their natural existence as portions of larger entities, and their informational content is irrelevant to that fact. We recognize that biologists may think of molecules in terms of their uses, but genes are in fact materials having a chemical nature and, as such, are best described in patents by their structures rather than their functions.

The district court in effect created a categorical rule excluding isolated genes from patent eligibility. But the Supreme Court has "more than once cautioned that courts 'should not read into the patent laws limitations and conditions which the legislature has not expressed,' " *Bilski,* 130 S.Ct. at 3226 (quoting *Diamond v. Diehr,* 450 U.S. 175, 182 (1981)), and has repeatedly rejected new categorical exclusions from § 101's scope, *see id.* at 3227–28 (rejecting the argument that business method patents should be categorically excluded from § 101); *Chakrabarty,* 447 U.S. at 314–17 (same for living organisms). We therefore reject the district court's unwarranted categorical exclusion of isolated DNA molecules.

Because isolated DNAs, not just cDNAs, have a markedly different chemical structure compared to native DNAs, we reject the government's proposed "magic microscope" test, as it misunderstands the difference between science and invention and fails to take into account the existence of molecules as separate chemical entities. The ability to visualize a DNA molecule through a microscope, or by any other means, when it is bonded to other genetic material, is worlds apart from possessing an isolated DNA molecule that is in hand and usable. It is the difference between knowledge of nature and reducing a portion of nature to concrete form, the latter activity being what the patent laws seek to encourage and protect. The government's microscope could focus in on a claimed portion of any complex molecule, rendering that claimed portion patent ineligible, even though that portion never exists as a separate molecule in the body or anywhere else in nature, and may have an entirely different utility. That would discourage innovation. One cannot visualize a portion of a complex molecule, including a DNA containing a particular gene, and will it into isolation as a unique entity. Visualization does not cleave and isolate the particular DNA; that is the act of human invention.

The parties and amici have provided many thought-provoking hypotheticals, each of which raises a complicated issue of patent eligibility not before the court. Accordingly, we address them only briefly; courts decide cases, they do not draft legal treatises. It is suggested that holding isolated DNAs patent eligible opens the door to claims covering isolated chemical elements, like lithium; minerals found in the earth, like diamonds; atomic particles, like electrons; and even organs, like a kidney, and a leaf from a tree. None of these examples, however, as far as we can discern, presents the case of a claim to a composition having a distinctive chemical identity from that of the native element, molecule, or structure. Elemental lithium is the same element whether it is in the earth or isolated; the diamond is the same lattice of carbon molecules, just with the earth removed; the kidney is the same kidney, the leaf the same leaf. Some may have a changed form, quality, or use when prepared in isolated or purified form, but we cannot tell on this record whether the changes are sufficiently distinctive to make the composition markedly different from the one that exists in nature. In contrast, a portion of a native DNA molecule—an isolated DNA—has a markedly different chemical nature from the native DNA. It is, therefore, patentable subject matter.

The dissent indicates that we "acknowledge[ ] that elemental lithium (like other elements) would not be patentable subject matter because it 'is the same element whether it is in earth or isolated.' " Again, these facts are not before us, so we do not attempt to evaluate the patentability of one form of lithium over another. Suffice it to say, however, that if lithium is found in the earth as other than elemental lithium, such as "in molecular form" "because it reacts with air and water," it is not the same material as elemental lithium.

It is also important to dispute the dissent's analogy to snapping a leaf from a tree. With respect, no one could contemplate that snapping a leaf from a tree would be worthy of a patent, whereas isolating genes to provide useful diagnostic tools and medicines is surely what the patent laws are intended to encourage and protect. Snapping a leaf from a tree is a physical separation, not one creating a new chemical entity.

The dissent also mentions several times in its opinion the breadth of certain claims as grounds for objecting to their patentability. However, we do not have here any rejection or invalidation on the various grounds relating to breadth, such as in 35 U.S.C. § 112. The issue before us is patent eligibility, not the adequacy of the patents' disclosure to support particular claims.

Finally, our decision that isolated DNA molecules are patent eligible comports with the longstanding practice of the PTO. The Supreme Court has repeatedly stated that changes to longstanding practice should come from Congress, not the courts. In *J.E.M. Ag Supply, Inc. v. Pioneer Hi–Bred International, Inc.*, the Court rejected the argument that plants did not fall within the scope of § 101, relying in part on the fact that "the PTO has assigned utility patents for plants for at least 16 years and there has been no indication from either Congress or agencies with expertise that such coverage is inconsistent with [federal law]." 534 U.S. 124, 144–45 (2001).

In this case, the PTO has issued patents directed to DNA molecules for almost thirty years. In the early 1980s, the Office granted the first human gene patents. It is estimated that the PTO has issued 2,645 patents claiming "isolated DNA" over the past twenty-nine years, and that by 2005, had granted 40,000 DNA-related patents covering, in non-native form, twenty percent of the genes in the human genome. In 2001, the PTO issued *Utility Examination Guidelines*, which re-affirmed the agency's position that isolated DNA molecules are patent eligible, 66 Fed.Reg. 1092–94 (Jan. 5, 2001) [A copy of these guidelines are available on the casebook website under Chapter 3 – see http://law.case.edu/lawofpatents/], and Congress has not indicated that the PTO's position is inconsistent with § 101. If the law is to be changed, and DNA inventions excluded from the broad scope of § 101 contrary to the settled expectation of the inventing community, the decision must come not from the courts, but from Congress.

II. Method Claims

We turn next to Myriad's challenged method claims. The district court's decision predated the Supreme Court's decision in *Bilski*, which rejected this court's machine-or-transformation test as the exclusive test for determining whether an invention is a patent-eligible process under § 101, although the test remains "a useful and important clue." 130 S.Ct. at 3227. Both parties, however, had the opportunity to address the Court's decision in briefing and at oral arguments. Accordingly, we proceed to the merits, and we conclude that all but one of Myriad's method claims are directed to patent-ineligible, abstract mental processes, and fail the machine-or-transformation test.

A. Methods of "Comparing" or "Analyzing" Sequences

Myriad argues that its claims to methods of "comparing" or "analyzing" *BRCA* sequences satisfy the machine-or-transformation test as applied by this court in *Prometheus* because each requires a transformation-extracting and sequencing DNA molecules from a human sample—before the sequences can be compared or analyzed. According to Myriad, the district court failed to recognize the transformative nature of the claims by (1) misconstruing the claim term "sequence" as just information, rather than a physical molecule; and (2) erroneously concluding, in the alternative, that Myriad's proposed transformations were mere data-gathering steps, rather than central to the purpose of the claims.

Plaintiffs respond that these method claims are drawn to the abstract idea of comparing one sequence to a reference sequence and preempt a phenomenon of nature-the correlation of genetic mutations with a predisposition to cancer. And, according to the Plaintiffs, limiting the claims' application to a specific technological field, *i.e.*, *BRCA* gene sequences, is insufficient to render the claims patent eligible. Plaintiffs also assert that the claims do not meet the machine-or-transformation test because the claims' plain language includes just the one step of "comparing" or "analyzing" two gene sequences.

We conclude that Myriad's claims to "comparing" or "analyzing" two gene sequences fall

outside the scope of § 101 because they claim only abstract mental processes. *See Benson,* 409 U.S. at 67 ("Phenomena of nature, ... mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work."). The claims recite, for example, a "method for screening a tumor sample," by "comparing" a first *BRCA1* sequence from a tumor sample and a second *BRCA1* sequence from a non-tumor sample, wherein a difference in sequence indicates an alteration in the tumor sample. This claim thus recites nothing more than the abstract mental steps necessary to compare two different nucleotide sequences: look at the first position in a first sequence; determine the nucleotide sequence at that first position; look at the first position in a second sequence; determine the nucleotide sequence at that first position; determine if the nucleotide at the first position in the first sequence and the first position in the second sequence are the same or different, wherein the latter indicates an alternation; and repeat for the next position.

Limiting the comparison to just the *BRCA* genes or, as in the case of claim 1 of the '999 patent, to just the identification of particular alterations, fails to render the claimed process patent eligible. As the Supreme Court has held, "the prohibition against patenting abstract ideas 'cannot be circumvented by attempting to limit the use of the formula to a particular technological environment.'" *Bilski,* 130 S.Ct. at 3230 (quoting *Diehr,* 450 U.S. at 191–92); *see also id.* at 3231 ("*Flook* established that limiting an abstract idea to one field of use ... did not make the concept patentable."). Although the *application* of a formula or abstract idea in a process may describe patentable subject matter, *id.* at 3230, Myriad's claims do not apply the step of comparing two nucleotide sequences in a process. Rather, the step of comparing two DNA sequences is the entire process claimed.

To escape this result, Myriad attempts to read into its method claims additional, transformative steps. As described above, Myriad reads into its claims the steps of (1) extracting DNA from a human sample, and (2) sequencing the *BRCA* DNA molecule, arguing that both steps necessarily precede the step of comparing nucleotide sequences. The claims themselves, however, do not include either of these steps. The claims do not specify any action prior to the step of "comparing" or "analyzing" two sequences; the claims recite just the one step of "comparing" or "analyzing." Moreover, those terms' plain meaning does not include Myriad's proposed sample-processing steps; neither comparing nor analyzing means or implies "extracting" or "sequencing" DNA or otherwise "processing" a human sample.

Myriad claims that "comparing" and "analyzing" take on this meaning when read in light of the patent specifications. Specifically, Myriad argues that the specifications show that the claim term "sequence" refers not to information, but rather to a physical DNA molecule, whose sequence must be determined before it can be compared. We disagree. The patent specifications make clear that "sequence" does not exclusively specify a DNA molecule, but refers more broadly to the linear sequence of nucleotide bases of a DNA molecule. For example, Figure 10A–10H is described as showing the "genomic sequence of BRCA1." '473 patent col.5 l.66. Figure 10 does not show a physical DNA molecule; the figure lists a series of letters (Gs, As, Ts, and Cs)

corresponding to the nucleotides guanine, adenine, thymine, and cytosine of a DNA molecule. Similarly, the patent specifications state that "[t]he nucleotide sequence for BRCA1 exon 4 is shown in SEQ ID NO: 11." *Id.* col.53 ll.50–53. SEQ ID NO: 11 again lists a series of Gs, As, Ts, and Cs corresponding to the nucleotide sequence of *BRCA1* exon 4.

Accordingly, Myriad's challenged method claims are distinguishable from the claims upheld under § 101 in *Prometheus.* In *Prometheus,* the patents claimed methods for optimizing the dosage of thiopurine drugs administered to patients with gastrointestinal disorders. 628 F.3d at 1350. As written, the claimed methods included the steps of (a) "administering" a thiopurine drug to a subject, and/or (b) "determining" the drug's metabolites levels in the subject, wherein the measured metabolite levels are compared with predetermined levels to optimize drug dosage. *Id.* In holding that the claims satisfied § 101, this court concluded that, in addition to the "administering" step being transformative, the "determining" step was both transformative and central to the purpose of the claims. *Id.* at 1357. Specifically, the court held that because the metabolite levels could not be determined by mere inspection, the determining step necessarily required a transformation: "Some form of manipulation ... is necessary to extract the metabolites from a bodily sample and determine their concentration." *Id.* Moreover, we concluded that this transformation was not just insignificant extra-solution activity or necessary data-gathering steps, but was central to the claims, because determining the metabolite levels was what enabled the optimization of drug dosage. *Id.*

Myriad's claims, in contrast, do not include the step of "determining" the sequence of *BRCA* genes by, *e.g.,* isolating the genes from a blood sample and sequencing them, or any other necessarily transformative step. Rather, the comparison between the two sequences can be accomplished by mere inspection alone. Accordingly, Myriad's claimed methods of comparing or analyzing nucleotide sequences fail to satisfy the machine-or-transformation test, and are instead directed to the abstract mental process of comparing two nucleotide sequences. The claims thus fail to claim a patent-eligible process under § 101.

B. Method of Screening Potential Cancer Therapeutics

Lastly, we turn to Myriad's method claim directed to a method for screening potential cancer therapeutics via changes in cell growth rates. '282 patent claim 20. Plaintiffs challenge this claim as directed to the abstract idea of comparing the growth rates of two cell populations and as preempting a basic scientific principle—that a slower growth rate in the presence of a potential therapeutic compound suggests that the compound is a cancer therapeutic. We disagree.

Starting with the machine-or-transformation test, we conclude that the claim includes transformative steps, an "important clue" that it is drawn to a patent-eligible process. Specifically, the claim recites a method that comprises the steps of (1) "growing" host cells transformed with an altered *BRCA1* gene in the presence or absence of a potential cancer therapeutic, (2) "determining" the growth rate of the host cells with or without the potential therapeutic, and (3) "compar-

ing" the growth rate of the host cells. The claim thus includes more than the abstract mental step of looking at two numbers and "comparing" two host cells' growth rates. The claim includes the steps of "growing" transformed cells in the presence or absence of a potential cancer therapeutic, an inherently transformative step involving the manipulation of the cells and their growth medium. The claim also includes the step of "determining" the cells' growth rates, a step that also necessarily involves physical manipulation of the cells. Furthermore, these steps are central to the purpose of the claimed process. *See Prometheus,* 628 F.3d at 1356–57, 1358 (quoting *In re Bilski,* 545 F.3d at 962). The goal of the claim is to assess a compound's potential as a cancer therapeutic, and growing the cells and determining their growth rate is what achieves that goal.

Furthermore, the claim is not so "manifestly abstract" as to claim only a scientific principle, and not a patent-eligible process. *See Research Corp. Techs., Inc. v. Microsoft Corp.,* 627 F.3d 859, 869 (Fed.Cir.2010). The claim does not cover all cells, all compounds, or all methods of determining the therapeutic effect of a compound. Rather, it is tied to specific host cells transformed with specific genes and grown in the presence or absence of a specific type of therapeutic. Moreover, the claim is tied to measuring a therapeutic effect on the cells solely by changes in the cells' growth rate. The claim thus presents "functional and palpable applications" in the field of biotechnology. *Id.* at 868; *see also Prometheus,* 628 F.3d at 1355 ("[T]he claims do not preempt all uses of the natural correlations; they utilize them in a series of specific steps."). Accordingly, we hold that claim 20 of the ' 282 patent claims patentable subject matter under § 101.

CONCLUSION

For the foregoing reasons, … we reverse the district court's grant of summary judgment with regard to Myriad's composition claims to isolated DNAs, we affirm the district court's grant of summary judgment with regard to Myriad's method claims to comparing or analyzing gene sequences, and we reverse the district court's grant of summary judgment with regard to Myriad's method claim to screening potential cancer therapeutics via changes in cell growth rates.

***

BRYSON, Circuit Judge, concurring in part and dissenting in part:

I concur with the portions of this court's judgment that are directed to … the patentability of the cDNA claims, and the patentability of the method claims. I respectfully dissent, however, from the court's holding that Myriad's BRCA gene claims and its claims to gene fragments are patent-eligible. In my view, those claims are not directed to patentable subject matter, and if sustained the court's decision will likely have broad consequences, such as preempting methods for whole-genome sequencing, even though Myriad's contribution to the field is not remotely consonant with such effects.

In its simplest form, the question in this case is whether an individual can obtain patent rights to a human gene. From a common-sense point of view, most observers would answer, "Of course

not. Patents are for inventions. A human gene is not an invention." The essence of Myriad's argument in this case is to say that it has not patented a human gene, but something quite different—an *isolated* human gene, which differs from a native gene because the process of extracting it results in changes in its molecular structure (although not in its genetic code). We are therefore required to decide whether the process of isolating genetic material from a human DNA molecule makes the isolated genetic material a patentable invention. The court concludes that it does; I conclude that it does not.

At the outset, it is important to identify the inventive contribution underlying Myriad's patents. Myriad was not the first to map a BRCA gene to its chromosomal location. That discovery was made by a team of researchers led by Dr. Mary–Claire King. *See* Jeff M. Hall et al., *Linkage of Early–Onset Familial Breast Cancer to Chromosome 17q21*, 250 Science 1684 (1990). And Myriad did not invent a new method of nucleotide sequencing. Instead, it applied known sequencing techniques to identify the nucleotide order of the BRCA genes. Myriad's discovery of those sequences entailed difficult work, and the identified sequences have had important applications in the fight against breast cancer. But the discovery of the sequences is an unprotectable fact, just like Dr. King's discovery of the chromosomal location of the BRCA1 gene.

Of course, Myriad is free to patent applications of its discovery. As the first party with knowledge of the sequences, Myriad was in an excellent position to claim applications of that knowledge. Many of its unchallenged claims are limited to such applications. *See, e.g.*, '441 patent, claim 21; '492 patent, claim 22; '282 patent, claim 9. Yet some of Myriad's challenged composition claims effectively preempt any attempt to sequence the BRCA genes, including whole-genome sequencing. In my view, those claims encompass unpatentable subject matter, and a contrary ruling is likely to have substantial adverse effects on research and treatment in this important field.

I

As the majority and concurring opinions explain, the claims at issue in this case fall into three categories: claims that cover the isolated BRCA genes (claim 1 of the '282 patent, claim 1 of the '473 patent, and claims 1 and 6 of the '492 patent); claims that cover only the BRCA cDNA (claims 2 and 7 of the '282 patent and claim 7 of the '492 patent); and claims that cover portions of the BRCA genes and cDNA as small as 15 nucleotides long (claims 5 and 6 of the '282 patent). I first address the claims to the BRCA genes.

A

In the seminal case of *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), the Supreme Court held that an artificial life form could be patented. In the course of its opinion, and critically for purposes of its reasoning, the Court stated that not all living things or other items found in nature were subject to patenting. The Court explained that although the language of section 101 of the Patent Act is broad, it is not the case that it "has no limits or that it embraces every discovery."

Id. at 309. The Court then set forth the general proposition that "laws of nature, physical phenomena, and abstract ideas have been held not patentable." *Id.* As examples, the Court noted that "a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter." Thus, even though a mineral or a plant is a "composition of matter," and could be viewed as falling within a broad construction of section 101, the Court explained that those "manifestations of ... nature" are not patentable subject matter, but are "free to all men and reserved exclusively to none." *Id.*, quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948); *see also Bilski v. Kappos*,130 S.Ct. 3218, 3225 (2010).

The Court in *Chakrabarty* held the artificial life form at issue in that case to be patentable because the claim was "not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use.'" *Id.* at 309–10, quoting *Hartranft v. Wiegmann*, 121 U.S. 609, 615 (1887). In distinguishing between naturally occurring substances and nonnaturally occurring manufactures, the Court relied heavily on its earlier decision in *Funk Brothers*, in which the inventor discovered that certain useful bacterial strains did not exert an inhibitive effect on each other. Based on that discovery, the inventor obtained a patent on a mixed culture of those non-inhibitive strains. The Supreme Court held the product unpatentable, however, because the bacteria remained structurally and functionally the same as in their natural state. *Funk Bros.*, 333 U.S. at 131. By contrast, because Chakrabarty had produced "a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility," the Court held Chakrabarty's invention to be patentable. *Chakrabarty*, 447 U.S. at 310.

B

Myriad's claims to the isolated BRCA genes seem to me to fall clearly on the "unpatentable" side of the line the Court drew in *Chakrabarty*. Myriad is claiming the genes themselves, which appear in nature on the chromosomes of living human beings. The only material change made to those genes from their natural state is the change that is necessarily incidental to the extraction of the genes from the environment in which they are found in nature. While the process of extraction is no doubt difficult, and may itself be patentable, the isolated genes are not materially different from the native genes. In this respect, the genes are analogous to the "new mineral discovered in the earth," or the "new plant found in the wild" that the Supreme Court referred to in *Chakrabarty*. It may be very difficult to extract the newly found mineral or to find, extract, and propagate the newly discovered plant. But that does not make those naturally occurring items the products of invention.

The same is true for human genes. Like some minerals, they are hard to extract from their natural setting. Also like minerals, they can be used for purposes that would be infeasible if they remained in their natural setting. And the process of extracting minerals, or taking cuttings from wild plants, like the process of isolating genetic material, can result in some physical or chemical changes to the natural substance. But such changes do not make extracted minerals or plant cut-

tings patentable, and they should not have that effect for isolated genes. In each case, merely isolating the products of nature by extracting them from their natural location and making those alterations attendant to their extraction does not give the extractor the right to patent the products themselves.

The majority characterizes the isolated genes as "new molecules" and considers them different substances from the corresponding native DNA. Because the native BRCA genes are chemically bonded to other genes and histone proteins, the majority concludes that cleaving those bonds to isolate the BRCA genes turns the isolated genes into "different materials." Yet there is no magic to a chemical bond that requires us to recognize a new product when a chemical bond is created or broken, but not when other atomic or molecular forces are altered.[3] A chemical bond is merely a force between two atoms or groups of atoms strong enough "to make it convenient for the chemist to consider [the aggregate] as an independent molecular species." Linus Pauling, *The Nature of the Chemical Bond* 6 (3d ed.1960). Weaker interatomic forces will be broken when, for example, a dirty diamond is cleaned with water or another solvent, but that does not make the clean diamond a human-made invention. *See Am. Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 12 (1931) (cleaning a shell by acid and then grinding off a layer with an emery wheel did not convert it into a different product). Nor should it make a difference for purposes of patentability if the portion of a wild plant that is collected for purposes of later regeneration is separated from the original plant by chemical means or by scissors.

Although the majority insists that the changes in the DNA molecule that occur as part of the process of isolation render the gene claims patentable, the majority does not appear to take a similar position with respect to chemical elements. The government as amicus curiae argues that patenting the BRCA genes would be like patenting the element lithium. Isolated lithium does not occur naturally because it reacts with air and water and thus is found in nature only as part of a chemical compound, ionically bound to other elements. Robert E. Krebs, *The History and Use of Our Earth's Chemical Elements* 48 (2d ed.2006). Once isolated, lithium has many industrial applications, and in order to isolate lithium, it is necessary to break ionic bonds in the lithium compounds that are found in nature. But the majority acknowledges that elemental lithium (like other elements) would not be patentable subject matter because it "is the same element whether it is in the earth or isolated."

The principles underlying that analysis apply to genetic material as well. In order to isolate the BRCA gene, it is necessary to break chemical bonds that hold the gene in its place in the

[3] The majority characterizes the question in this case as turning on the breaking of covalent bonds linking the BRCA genes to the rest of the DNA in chromosomes 13 and 17, but its analysis appears to place patentable weight on the breaking of other chemical bonds, such as the hydrogen bonds that are broken when separating DNA from histones or—in an example unrelated to this case—the ionic bonds that are broken when lithium is derived from a salt. It is difficult to see why differences between types of chemical bonds should matter for patentability purposes, and I see little support for such a distinction in the governing precedents.

body, but the genetic coding sequence that is the subject of each of the BRCA gene claims remains the same whether the gene is in the body or isolated. The majority, however, does not agree that the cases are analogous, and indeed appears to have adopted the following rule: Isolated atoms are not patent eligible, but isolated molecules are.

Apart from the arbitrariness of such a rule, if we are to apply the conventional nomenclature of any field to determine whether Myriad's isolated DNA claims are "new," it would seem to make more sense to look to genetics, which provides the language of the claims, than to chemistry. Aside from Myriad's cDNA claims, its composition claims are not defined by any particular chemical formula. For example, claim 1 of the '282 patent covers all isolated DNAs coding for the BRCA1 protein, with the protein being defined by the amino acid sequence encoded by the naturally occurring BRCA1 gene. From a molecular perspective, that claim covers a truly immense range of substances from the cDNA that is 5,914 nucleotides long to the isolated gene that contains more than 120,000 nucleotides. And the patent does not define the upper end of that range because the patent does not identify a unique nucleotide sequence for the 120,000–nucleotide–long isolated BRCA1 gene. Instead, the patent contains a sequence that is just 24,000 nucleotides long with numerous gaps denoted "vvvvvvvvvvvvv." '282 patent, fig. 10. An almost incalculably large number of new molecules could be created by filling in those gaps with almost any nucleotide sequence, and all of those molecules would fall within the scope of claim 1. Included in that set are many important molecular variations to the BRCA1 gene that Myriad had not yet discovered and could not have chemically described. Yet those molecules would share only one unifying characteristic: each codes for the same protein as the naturally occurring BRCA1 gene.

From a genetic perspective, that claim covers one "composition of matter"—the BRCA1 gene. The isolated BRCA genes are identical to the BRCA genes found on chromosomes 13 and 17. They have the same sequence, they code for the same proteins, and they represent the same units of heredity. During the transcription phase of protein synthesis, the BRCA genes are separated from chromosomal proteins. The transcription process then proceeds from a starting point called the promoter to a stopping point often called the terminator. James D. Watson et al., *Molecular Biology of the Gene* 382, 394–96 (6th ed.2008). The only difference between the naturally occurring BRCA genes during transcription and the claimed isolated DNA is that the claimed genes have been isolated according to nature's predefined boundaries, i.e., at points that preserve the ability of the gene to express the protein for which it is coded.

In that respect, extracting a gene is akin to snapping a leaf from a tree. Like a gene, a leaf has a natural starting and stopping point. It buds during spring from the same place that it breaks off and falls during autumn. Yet prematurely plucking the leaf would not turn it into a human-made invention. *See Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1295 (Fed.Cir.2010) (Dyk, J., concurring in part and dissenting in part). That would remain true if there were minor differences between the plucked leaf and the fallen autumn leaf, unless those differences imparted "markedly different characteristics" to the plucked leaf. *Chakrabarty*, 447 U.S. at 310.

Both the majority and the concurring opinions attach significant weight to the fact that the claimed coding portions of the native BRCA genes are part of a much larger molecule and that the isolated BRCA genes, being smaller molecules extracted from the larger one, are therefore man-made inventions. But to argue that the isolated BRCA gene is patentable because in its native environment it is part of a much larger structure is no more persuasive than arguing that although an atom may not be patentable, a subatomic particle is patentable because it was previously part of a larger structure, or that while a tree is not patentable, a limb of the tree becomes a patentable invention when it is removed from the tree.

Of course, it is an over-simplification to say that something that can be characterized as "isolated" or "extracted" from its natural setting always remains a natural product and is not patentable. One could say, for example, that a baseball bat is "extracted" or "isolated" from an ash tree, but in that case the process of "extracting" the baseball bat necessarily changes the nature, form, and use of the ash tree and thus results in a manmade manufacture, not a naturally occurring product. In that setting, man has defined the parts that are to be retained and the parts that are to be discarded. The result of the process of selection is a product with a function that is entirely different from that of the raw material from which it was obtained. In the case of the BRCA genes, by contrast, nature has defined the genes as independent entities by virtue of their capacity for protein synthesis and, ultimately, trait inheritance. Biochemists extract the target genes along lines defined by nature so as to preserve the structure and function that the gene possessed in its natural environment. In such a case, the extraction of a product in a manner that retains the character and function of the product as found in nature does not result in the creation of a human invention.[4] That principle was captured by the Supreme Court's statement in *Chakrabarty* that the invention in that case was not to "a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter 'having a distinctive name, character [and] use.'" 447 U.S. at 309–10.

Cases involving the "purification" of a natural substance employ similar analysis. Our predecessor court recognized that merely purifying a naturally occurring substance does not render the substance patentable unless it results in a marked change in functionality. *In re Merz,* 97 F.2d 599, 601 (CCPA 1938) (holding that there was no right to a patent on a purer version of ultramarine, but recognizing that if a claimed article is "of such purity that it differs not only in degree but in kind it may be patentable"); *see also In re King,* 107 F.2d 618, 620 (CCPA 1939) (same, for purified vitamin C); *In re Marden,* 18 C.C.P.A. 1057, 47 F.2d 958, 959 (CCPA 1931) (same, for purified vanadium); *Gen. Elec. Co. v. DeForest Radio Co.,* 28 F.2d 641, 643 (3d Cir.1928) (same, for purified tungsten). On the other hand, the purified natural substance is patentable if the "purification" results in a product with such distinct characteristics that it becomes "for every

[4] By analogy, extracting a slab of marble from the earth does not give rise to protectable intellectual property rights, but "extracting" a piece of sculpture from that slab of marble does. In the case of the BRCA gene claims, what Myriad has claimed is more akin to the slab of marble found in the earth than to the sculpture carved from it after its extraction.

practical purpose a new thing commercially and therapeutically." *Parke–Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (C.C.S.D.N.Y.1911); *see also Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156, 161–64 (4th Cir.1958) (holding that a purified composition of vitamin B–12 was patentable because the purification process resulted in a product that was therapeutically effective, whereas the natural form was not).

In sum, the test employed by the Supreme Court in *Chakrabarty* requires us to focus on two things: (1) the similarity in structure between what is claimed and what is found in nature and (2) the similarity in utility between what is claimed and what is found in nature. What is claimed in the BRCA genes is the genetic coding material, and that material is the same, structurally and functionally, in both the native gene and the isolated form of the gene.

The structural differences between the claimed "isolated" genes and the corresponding portion of the native genes are irrelevant to the claim limitations, to the functioning of the genes, and to their utility in their isolated form. The use to which the genetic material can be put, i.e., determining its sequence in a clinical setting, is not a new use; it is only a consequence of possession. In order to sequence an isolated gene, each gene must function in the same manner in the laboratory as it does in the human body. Indeed, that identity of function in the isolated gene is the key to its value. Moreover, as Judge Moore's concurring opinion explains, Myriad has failed to credibly identify new uses for the isolated BRCA genes as probes or primers. The naturally occurring genetic material thus has not been altered in a way that would matter under the standard set forth in *Chakrabarty*. For that reason, the isolation of the naturally occurring genetic material does not make the claims to the isolated BRCA genes patent-eligible.

II

As noted, in addition to the BRCA gene claims discussed above, the claims at issue in this appeal include four claims to BRCA cDNA and two claims to portions of the BRCA genes and cDNA as small as 15 nucleotides long.

I agree with the court that the claims to BRCA cDNA are eligible for patenting. The cDNA cannot be isolated from nature, but instead must be created in the laboratory. Although that process occurs with natural machinery, the end product is a human-made invention with distinct structure because the introns that are found in the native gene are removed from the cDNA segment. Additionally, the cDNA has a utility not present in the naturally occurring BRCA DNA and mRNA because cDNA can be attached to a promoter and inserted into a non-human cell to drive protein expression.

However, I disagree with the court as to the two claims to short segments of DNA having at least 15 nucleotides. Claim 6 of the '282 patent covers any sequence of the BRCA1 cDNA that is at least 15 nucleotides long. That claim encompasses each BRCA1 exon, even though each exon is naturally defined by transcription. Moreover, because small sequences of DNA are repeated throughout the three billion nucleotides of the human genome, the claim covers portions of the

cDNA of more than 4% of human genes. It also covers portions of the DNA of nearly all human genes. Accordingly, efforts to sequence almost any gene could infringe claim 6 even though Myriad's specification has contributed nothing to human understanding of other genes.

Myriad could easily have claimed more narrowly to achieve the utility it attaches to segments of cDNA. It contends that those segments can be used as probes and primers. DNA probes must be chemically altered or "tagged" before they can be so used, and Myriad could have claimed the tagged segments to achieve probe functionality. A claim to tagged segments would not encompass the BRCA1 exons. As to primer functionality, many of the cDNA segments will not work. Some will be too long. Some will be too short. Some will be palindromic and fold in on themselves. Myriad could have identified a subset of the segments that work as primers, and such a claim could be patentable if it were limited to species with "markedly different characteristics from any found in nature and ... having the potential for significant utility." *Chakrabarty,* 447 U.S. at 310. The problem with claim 6 is that it is so broad that it includes products of nature (the BRCA1 exons) and portions of other genes; its validity is not salvaged because it includes some species that are not natural. Accordingly, I would hold claim 6 unpatentable.

Myriad's last claim, claim 5 of the '282 patent, is breathtakingly broad. That claim covers any segment of the DNA defined by claim 1, provided that the segment is at least 15 nucleotides long. Claim 1, in turn, covers any isolated DNA that codes for the BRCA1 polypeptide. Thus, claim 5 would cover not only the isolated BRCA1 gene in each of its untold molecular variations, but also any sub-sequence of those molecules, including portions that fall in the undefined range of those molecules denoted "vvvvvvvvvvvv." Claim 5 would therefore be unpatentable for the same reasons as claim 1 and claim 6.

Of course, in light of its breadth, claim 5 of the '282 patent is likely to be invalid on other grounds, and thus a ruling as to patent-eligibility with respect to that claim may be superfluous. Nonetheless, it is important to consider the effects of such broad patent claims on the biotechnology industry. While Myriad has emphasized the biotechnology industry's need of patent protection to encourage and reward research in this difficult and important field, there is another side to the coin. Broad claims to genetic material present a significant obstacle to the next generation of innovation in genetic medicine—multiplex tests and whole-genome sequencing. New technologies are being developed to sequence many genes or even an entire human genome rapidly, but firms developing those technologies are encountering a thicket of patents. Secretary's Advisory Comm. on Genetics, Health, and Society, Dep't of Health & Human Servs., *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* 49–62 (2010). In order to sequence an entire genome, a firm would have to license thousands of patents from many different licensors. *See id.* at 50–51. Even if many of those patents include claims that are invalid for anticipation or obviousness, the costs involved in determining the scope of all of those patents could be prohibitive. *See id.* at 51–52; Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research,* 45 Hou. L.Rev. 1059, 1076–1080 (2008) (concluding that existing studies "have focused relatively little attention on

downstream product development" and that interviews accompanying those studies suggest that, though smaller than initially feared, the costs associated with the patent thicket are "quite real in the calculations of product-developing firms"). In light of these considerations, this may well be one of those instances in which "*too much* patent protection can impede rather than 'promote the Progress of Science and useful Arts.'" *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 126 (2006) (Breyer, J., dissenting from dismissal of writ as improvidently granted).

My colleagues assign significant weight to the fact that since 2001 the PTO has had guidelines in place that have allowed patents on entire human genes. They conclude that those guidelines, and the PTO's earlier practice, are entitled to deference from this court as to the question whether patents to isolated human genes constitute patent-eligible subject matter. I think the PTO's practice and guidelines are not entitled to significant weight, for several reasons.

First, as we have recognized, the PTO lacks substantive rulemaking authority as to issues such as patentability. *Animal Legal Def. Fund v. Quigg*, 932 F.2d 920, 930 (Fed.Cir.1991). In areas of patent scope, we owe deference only commensurate with the "the thoroughness of its consideration and the validity of its reasoning." *Merck & Co. v. Kessler*, 80 F.3d 1543, 1550 (Fed.Cir.1996). The comments that the PTO issued at the time of its 2001 guidelines in response to suggestions that isolated human genes were not patentable are, frankly, perfunctory. Because those comments, at least on their face, do not reflect thorough consideration and study of the issue, I do not regard them as worthy of much weight in the analysis of this complex question.

Second, whatever force the PTO's views on the issue of patent eligibility may have had in the past has, at the very least, been substantially undermined by the position the government has taken in this case. The Department of Justice filed a brief on behalf of the United States in this court taking the position that Myriad's gene claims (other than the cDNA claims) are not patent-eligible. Although the PTO did not "sign" the brief and we are left to guess about the status of any possible continuing interagency disagreements about the issue, the Department of Justice speaks for the Executive Branch, and the PTO is part of the Executive Branch, so it is fair to assume that the Executive Branch has modified its position from the one taken by the PTO in its 2001 guidelines and, informally, before that.

Finally, prior to the Supreme Court's decision in *Chakrabarty*, the PTO had determined that microorganisms were not subject to patenting, but the Supreme Court gave no indication that it regarded that view as entitled to deference. Moreover, the Court gave short shrift to the Commissioner's contention (which was made the lead argument in its brief) that the patentability of life-forms was an issue that should be left to Congress. Citing *Marbury v. Madison*, 5 U.S. (1 Cranch) 137 (1803), the Court explained that "Congress has performed its constitutional role in defining patentable subject matter in § 101; we perform ours in construing the language Congress has employed." *Chakrabarty*, 477 U.S. at 315. We have the same responsibility and should not shy away from deciding the issues of law that the parties have brought to us. Although my colleagues believe our analysis of the legal question in this case should be influenced by purport-

ed expectations of the invening community based on the PTO's past practice of issuing patents on human genes, that is in effect to give the PTO lawmaking authority that Congress has not accorded it.[6] There is no collective right of adverse possession to intellectual property, and we should not create such a right. Our role is to interpret the law that Congress has written in accordance with the governing precedents. I would do so and would affirm the district court's rulings as to the BRCA gene and BRCA gene segment claim.

Comments

Comments

3. ***DNA, Proteins, and Notions of Purity and Isolation*** **(Revised).** Recent studies have shown that about 20 percent of human genes are patented. See, e.g., Kyle Jensen & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, SCIENCE 14 October 2005, Vol. 310, pp. 239-40. There are approximately 25,000 genes, which make up about 2% of the human genome. *See Human Genome Project Information* at http://www.ornl.gov/sci/techresources/Human_Genome/project/info.shtml ("Genes comprise only about 2% of the human genome; the remainder consists of noncoding regions, whose functions may include providing chromosomal structural integrity and regulating where, when, and in what quantity proteins are made.")

If naturally occurring substances are not patentable, then how is it that firms obtain patents on DNA sequences (i.e., genes) and proteins? The legal answer is human intervention, which allows, for instance, one to claim an isolated gene that is markedly different from the naturally occurring gene; or claim the gene as part of a vector or transformed cell. In other words, a gene as it exist in the human body is not subject to patent protection, but a gene "isolated from its natural state" (i.e., isolated from other cellular components such as ribosomes) resulting in markedly different characteristics is eligible for patent protection under § 101. According to USPTO Guidelines, "an inventor's discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it." Thus, isolation and purification renders the gene eligible for patent protection, but utility (see section B, below) and the other patentability requirements must be satisfied. See USPTO.gov.

Historically, courts expressed skepticism that purified, naturally occurring substances were patentable. See, e.g., *American Wood Paper Co. v. Fiber Disintegrating Co.*, 90 U.S. 566 (1874) (responding to the assertion that the claimed subject matter (cellulose) was purified, the Court wrote: "There are many things well known and valuable in medicine or in the arts which

[6] Because the asserted reliance interest is based on PTO practice and not on prior judicial decisions, this case is not analogous to *Warner Jenkinson Co. v. Hilton Davis Chemical Co.*, 520 U.S. 17 (1997), or *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722 (2002), where the expectations of the inventing community were based on longstanding Supreme Court precedent.

may be extracted from diverse substances. But extract is the same, no matter from what it has been taken…. Whether a slight difference in the degree of purity of an article produced by several processes justifies denominating the products different manufactures, so that different patents may be obtained for each, may well be doubted, and it is not necessary to decide").

In the early part of the twentieth century, however, arguments based on human intervention and purification in the context of chemical and biological inventions were received more generously by the courts. One of the most important cases in this regard was *Parke-Davis & Co. v. H.K. Mulford & Co.*, 189 F.95 (S.D.N.Y. 1911), a case that provided the doctrinal foundation for the patenting of purified DNA sequences and proteins. The subject matter at issue in Parke-Davis was an adrenalin compound derived from the suprarenal glands of various animals. But the patentee's (Takamine) claimed compound was a purified version, which was an important factor for Judge Learned Hand:

> [E]ven if it were merely an extracted product without change, there is no rule that such products are not patentable. Takamine was the first to make it available for any use by removing it from the other gland-tissue in which it was found, and, while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically…. Everyone, not already saturated with scholastic distinctions, would recognize that Takamine's crystals were not merely the old dried glands in a purer state, nor would his opinion change if he learned that the crystals were obtained from the glands by a process of eliminating the inactive organic substances. The line between different substances and degrees of the same substance is to be drawn rather from the common usages of men than from nice considerations of dialectic.

Id. at 103. See generally Linda H. Demaine & Aaron X. Fellmeth, Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent, 55 Stan. L. Rev. 303 (2002).

The "isolation/purification" principle was at issue in the high-profile and controversial *Myriad* case. The Federal Circuit, in *Myriad*, distinguished Judge Hand's opinion in *Parke-Davis*, noting that the isolated DNA is not purified DNA; rather, it is chemically manipulated "to produce a molecule that is markedly different from that which exists in the body." The majority's emphasis on "markedly different" characteristics — language from *Chakrabarty* — was fundamental to the court's analysis. To satisfy this test, the court relied heavily on the structural differences between the claimed DNA and native DNA, namely the cleaving of the covalent bonds. The fact that the information between the claimed and native DNA may be the same is "irrelevant" for the court. Rather, chemical entities such as DNA are "best describe in patents by their structures rather than their functions."

The dissent strongly challenged this characterization, stressing the majority's analysis would lead to the patenting of new minerals discovered in the earth or new plants found in the

wild. By relying so heavily on the structural differences between isolated and native DNA, the majority reveals the weakness of its argument and conveniently ignores the fact that both forms of DNA have "the same sequence, they code for the same proteins, and they represent the same units of heredity." Unlike the making of a baseball bat from an Ash tree, which leads to a distinct product in terms of nature, form, and use, the very purpose of isolating DNA is to preserve its function and use.

Faced with the dissent's logic, the majority seemed to also justify its holding by reference to patent law's objectives, which are designed to "reducing a portion of nature to concrete form." Isolating a gene that can provide important diagnostic tools and medicines is far more worthy of patent protection than snapping a leaf from a tree. In this regard, perhaps the majority was on more secure footing, particularly in the light of the fact that *Chakrabarty's* decision was based in part on Mr. Chakrabarty having invented something with the "potential for significant utility."

The Supreme Court denied certiorari, and isolated DNA molecules, for now, are eligible for patent protection. (How the *Prometheus* decision may affect *Myriad* remains to be seen — see Comment 3 following *Prometheus*, the next principal case.) Does this mean that if an individual undergoes a whole-genome sequence analysis that individual (or the company that performs the analysis) may be liable for patent infringement? Of course, the answer to this question depends on what is claimed in the gene patent. Would an entire-genome analysis infringe a claim to an *isolated* gene sequence? Recall that the Federal Circuit based its decision in large part on the structural dissimilarities between a native gene and an isolated gene. Nonetheless, gene patents could "have significant implications for the development of multigene (multiplex) genetic tests and the anticipated eventual development of whole-genome sequencing for clinical use." Secretary's Advisory Committee on Genetics, Health, and Society, *Public Consultation Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* 36 (2009). Thus, it would not be unreasonable for a company that provides whole-genome sequencing to seek a license.

Read after *Myriad*

MAYO COLLABORATIVE SERVICES V. PROMETHEUS LABORATORIES, INC.

132 S.Ct. 1289 (2012)

BREYER, J., delivered the opinion for a unanimous Court.

Section 101 of the Patent Act defines patentable subject matter. It says:

> 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.

The Court has long held that this provision contains an important implicit exception. "[L]aws of nature, natural phenomena, and abstract ideas" are not patentable. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). Thus, the Court has written that "a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of ... nature, free to all men and reserved exclusively to none.'" *Chakrabarty, supra,* at 309.

"Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972). And monopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it

The Court has recognized, however, that too broad an interpretation of this exclusionary principle could eviscerate patent law. For all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas. Thus, in *Diehr* the Court pointed out that "'a process is not unpatentable simply because it contains a law of nature or a mathematical algorithm.'" 450 U.S., at 187. It added that "an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection." *Diehr, supra,* at 187. And it emphasized Justice Stone's similar observation in *Mackay Radio & Telegraph Co. v. Radio Corp. of America*, 306 U.S. 86 (1939):

> While a scientific truth, or the mathematical expression of it, is not a patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be. 450 U.S., at 188 (quoting *Mackay Radio, supra,* at 94).

Still, as the Court has also made clear, to transform an unpatentable law of nature into a patent-eligible *application* of such a law, one must do more than simply state the law of nature while adding the words "apply it."

The case before us lies at the intersection of these basic principles. It concerns patent claims covering processes that help doctors who use thiopurine drugs to treat patients with autoimmune diseases determine whether a given dosage level is too low or too high. The claims purport to apply natural laws describing the relationships between the concentration in the blood of certain thiopurine metabolites and the likelihood that the drug dosage will be ineffective or induce harmful side-effects. We must determine whether the claimed processes have transformed these unpatentable natural laws into patent-eligible applications of those laws. We conclude that they have not done so and that therefore the processes are not patentable.

Our conclusion rests upon an examination of the particular claims before us in light of the Court's precedents. Those cases warn us against interpreting patent statutes in ways that make patent eligibility "depend simply on the draftsman's art" without reference to the "principles underlying the prohibition against patents for [natural laws]." *Parker v Flook,* 437 U.S. 584, 593 (1978). They warn us against upholding patents that claim processes that too broadly preempt the use of a natural law. And they insist that a process that focuses upon the use of a natural law also contain other elements or a combination of elements, sometimes referred to as an "inventive concept," sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself.

We find that the process claims at issue here do not satisfy these conditions. In particular, the steps in the claimed processes (apart from the natural laws themselves) involve well-understood, routine, conventional activity previously engaged in by researchers in the field. At the same time, upholding the patents would risk disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries.

I

A

The patents before us concern the use of thiopurine drugs in the treatment of autoimmune diseases, such as Crohn's disease and ulcerative colitis. When a patient ingests a thiopurine compound, his body metabolizes the drug, causing metabolites to form in his bloodstream. Because the way in which people metabolize thiopurine compounds varies, the same dose of a thiopurine drug affects different people differently, and it has been difficult for doctors to determine whether for a particular patient a given dose is too high, risking harmful side effects, or too low, and so

likely ineffective.

At the time the discoveries embodied in the patents were made, scientists already understood that the levels in a patient's blood of certain metabolites, including, in particular, 6–thioguanine and its nucleotides (6–TG) and 6–methyl–mercaptopurine (6–MMP), were correlated with the likelihood that a particular dosage of a thiopurine drug could cause harm or prove ineffective. But those in the field did not know the precise correlations between metabolite levels and likely harm or ineffectiveness. The patent claims at issue here set forth processes embodying researchers' findings that identified these correlations with some precision.

More specifically, the patents—U.S. Patent No. 6,355,623 ('623 patent) and U.S. Patent No. 6,680,302 ('302 patent)—embody findings that concentrations in a patient's blood of 6–TG or of 6–MMP metabolite beyond a certain level (400 and 7000 picomoles per $8x10^8$ red blood cells, respectively) indicate that the dosage is likely too high for the patient, while concentrations in the blood of 6–TG metabolite lower than a certain level (about 230 picomoles per $8x10^8$ red blood cells) indicate that the dosage is likely too low to be effective.

The patent claims seek to embody this research in a set of processes. Like the Federal Circuit we take as typical claim 1 of the '623 Patent, which describes one of the claimed processes as follows:

> A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6–thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6–thioguanine in said subject having said immune-mediated gastrointestinal disorder,
>
> wherein the level of 6–thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and
>
> wherein the level of 6–thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

'623 patent, col.20, ll.10–20, 2 App. 16.

B

Respondent, Prometheus Laboratories, Inc. (Prometheus), is the sole and exclusive licensee of the '623 and '302 patents. It sells diagnostic tests that embody the processes the patents describe. For some time petitioners, Mayo Clinic Rochester and Mayo Collaborative Services (collectively Mayo), bought and used those tests. But in 2004 Mayo announced that it intended to

begin using and selling its own test—a test using somewhat higher metabolite levels to determine toxicity (450 pmol per $8x10^{8}$ for 6–TG and 5700 pmol per $8x10^{8}$ for 6–MMP). Prometheus then brought this action claiming patent infringement….

[T]he Federal Circuit … pointed out that… the claimed processes specify the steps of (1) "administering a [thiopurine] drug" to a patient and (2) "determining the [resulting metabolite] level." These steps, it explained, involve the transformation of the human body or of blood taken from the body. Thus, the patents satisfied the Circuit's "machine or transformation test," which the court thought sufficient to "confine the patent monopoly within rather definite bounds," thereby bringing the claims into compliance with § 101.

We granted the petition, vacated the judgment, and remanded the case for reconsideration in light of *Bilski*, 130 S.Ct. 3218, 3234-3235 which clarified that the "machine or transformation test" is not a definitive test of patent eligibility, but only an important and useful clue. On remand the Federal Circuit reaffirmed its earlier conclusion. It thought that the "machine-or-transformation test," understood merely as an important and useful clue, nonetheless led to the "clear and compelling conclusion ... that the ... claims ... do not encompass laws of nature or preempt natural correlations." Mayo again filed a petition for certiorari, which we granted.

II

Prometheus' patents set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm. Claim 1, for example, states that *if* the levels of 6–TG in the blood (of a patient who has taken a dose of a thiopurine drug) exceed about 400 pmol per $8x10^{8}$ red blood cells, *then* the administered dose is likely to produce toxic side effects. While it takes a human action (the administration of a thiopurine drug) to trigger a manifestation of this relation in a particular person, the relation itself exists in principle apart from any human action. The relation is a consequence of the ways in which thiopurine compounds are metabolized by the body—entirely natural processes. And so a patent that simply describes that relation sets forth a natural law.

The question before us is whether the claims do significantly more than simply describe these natural relations. To put the matter more precisely, do the patent claims add *enough* to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws? We believe that the answer to this question is no.

A

If a law of nature is not patentable, then neither is a process reciting a law of nature, unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself. A patent, for example, could not simply recite a law of nature and then add the instruction "apply the law." Einstein, we assume,

could not have patented his famous law by claiming a process consisting of simply telling linear accelerator operators to refer to the law to determine how much energy an amount of mass has produced (or vice versa). Nor could Archimedes have secured a patent for his famous principle of flotation by claiming a process consisting of simply telling boat builders to refer to that principle in order to determine whether an object will float.

What else is there in the claims before us? The process that each claim recites tells doctors interested in the subject about the correlations that the researchers discovered. In doing so, it recites an "administering" step, a "determining" step, and a "wherein" step. These additional steps are not themselves natural laws but neither are they sufficient to transform the nature of the claim.

First, the "administering" step simply refers to the relevant audience, namely doctors who treat patients with certain diseases with thiopurine drugs. That audience is a pre-existing audience; doctors used thiopurine drugs to treat patients suffering from autoimmune disorders long before anyone asserted these claims. In any event, the "prohibition against patenting abstract ideas 'cannot be circumvented by attempting to limit the use of the formula to a particular technological environment.'" *Bilski, supra,* at 3230.

Second, the "wherein" clauses simply tell a doctor about the relevant natural laws, at most adding a suggestion that he should take those laws into account when treating his patient. That is to say, these clauses tell the relevant audience about the laws while trusting them to use those laws appropriately where they are relevant to their decisionmaking (rather like Einstein telling linear accelerator operators about his basic law and then trusting them to use it where relevant).

Third, the "determining" step tells the doctor to determine the level of the relevant metabolites in the blood, through whatever process the doctor or the laboratory wishes to use. As the patents state, methods for determining metabolite levels were well known in the art. Indeed, scientists routinely measured metabolites as part of their investigations into the relationships between metabolite levels and efficacy and toxicity of thiopurine compounds. Thus, this step tells doctors to engage in well-understood, routine, conventional activity previously engaged in by scientists who work in the field. Purely "conventional or obvious" "[pre]-solution activity" is normally not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law. See *Bilski,* 130 S.Ct., at 3230 ("[T]he prohibition against patenting abstract ideas 'cannot be circumvented by' ... adding 'insignificant post-solution activity.'")

Fourth, to consider the three steps as an ordered combination adds nothing to the laws of nature that is not already present when the steps are considered separately. See *Diehr, supra,* at 188 ("[A] new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made"). Anyone who wants to make use of these laws must first administer a thiopurine drug and measure the resulting metabolite concentrations, and so the combination amounts to nothing signifi-

cantly more than an instruction to doctors to apply the applicable laws when treating their patients.

The upshot is that the three steps simply tell doctors to gather data from which they may draw an inference in light of the correlations. To put the matter more succinctly, the claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately. For these reasons we believe that the steps are not sufficient to transform unpatentable natural correlations into patentable applications of those regularities.

B

1

A more detailed consideration of the controlling precedents reinforces our conclusion. The cases most directly on point are *Diehr* and *Flook*, two cases in which the Court reached opposite conclusions about the patent eligibility of processes that embodied the equivalent of natural laws. The *Diehr* process (held patent eligible) set forth a method for molding raw, uncured rubber into various cured, molded products. The process used a known mathematical equation, the Arrhenius equation, to determine when (depending upon the temperature inside the mold, the time the rubber had been in the mold, and the thickness of the rubber) to open the press. It consisted in effect of the steps of: (1) continuously monitoring the temperature on the inside of the mold, (2) feeding the resulting numbers into a computer, which would use the Arrhenius equation to continuously recalculate the mold-opening time, and (3) configuring the computer so that at the appropriate moment it would signal "a device" to open the press. *Diehr*, 450 U.S., at 177–179.

The Court pointed out that the basic mathematical equation, like a law of nature, was not patentable. But it found the overall process patent eligible because of the way the additional steps of the process integrated the equation into the process as a whole. Those steps included "installing rubber in a press, closing the mold, constantly determining the temperature of the mold, constantly recalculating the appropriate cure time through the use of the formula and a digital computer, and automatically opening the press at the proper time." *Id.*, at 187. It nowhere suggested that all these steps, or at least the combination of those steps, were in context obvious, already in use, or purely conventional. And so the patentees did not "seek to pre-empt the use of [the] equation," but sought "only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process." *Ibid.* These other steps apparently added to the formula something that in terms of patent law's objectives had significance—they transformed the process into an inventive application of the formula.

The process in *Flook* (held not patentable) provided a method for adjusting "alarm limits" in the catalytic conversion of hydrocarbons. Certain operating conditions (such as temperature, pressure, and flow rates), which are continuously monitored during the conversion process, sig-

nal inefficiency or danger when they exceed certain "alarm limits." The claimed process amounted to an improved system for updating those alarm limits through the steps of: (1) measuring the current level of the variable, *e.g.*, the temperature; (2) using an apparently novel mathematical algorithm to calculate the current alarm limits; and (3) adjusting the system to reflect the new alarm-limit values. 437 U.S., at 585–587.

The Court, as in *Diehr*, pointed out that the basic mathematical equation, like a law of nature, was not patentable. But it characterized the claimed process as doing nothing other than "provid[ing] a[n unpatentable] formula for computing an updated alarm limit." *Flook, supra*, at 586. Unlike the process in *Diehr*, it did not "explain how the variables used in the formula were to be selected, nor did the [claim] contain any disclosure relating to chemical processes at work or the means of setting off an alarm or adjusting the alarm limit." *Diehr, supra*, at 192, n. 14. And so the other steps in the process did not limit the claim to a particular application. Moreover, "[t]he chemical processes involved in catalytic conversion of hydrocarbons[,] ... the practice of monitoring the chemical process variables, the use of alarm limits to trigger alarms, the notion that alarm limit values must be recomputed and readjusted, and the use of computers for 'automatic monitoring-alarming' " were all "well known," to the point where, putting the formula to the side, there was no "inventive concept" in the claimed application of the formula. *Id.*, at 594. "[P]ost-solution activity" that is purely "conventional or obvious," the Court wrote, "can[not] transform an unpatentable principle into a patentable process." *Id.*, at 589, 590.

The claim before us presents a case for patentability that is weaker than the (patent-eligible) claim in *Diehr* and no stronger than the (unpatentable) claim in *Flook.* Beyond picking out the relevant audience, namely those who administer doses of thiopurine drugs, the claim simply tells doctors to: (1) measure (somehow) the current level of the relevant metabolite, (2) use particular (unpatentable) laws of nature (which the claim sets forth) to calculate the current toxicity/inefficacy limits, and (3) reconsider the drug dosage in light of the law. These instructions add nothing specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field. And since they are steps that must be taken in order to apply the laws in question, the effect is simply to tell doctors to apply the law somehow when treating their patients. The process in *Diehr* was not so characterized; that in *Flook* was characterized in roughly this way.

***

In *Bilski* the Court considered claims covering a process for hedging risks of price changes by, for example, contracting to purchase commodities from sellers at a fixed price, reflecting the desire of sellers to hedge against a drop in prices, while selling commodities to consumers at a fixed price, reflecting the desire of consumers to hedge against a price increase. One claim described the process; another reduced the process to a mathematical formula. 130 S.Ct., at 3223–3224. The Court held that the described "concept of hedging" was "an unpatentable abstract idea." *Id.*, at 3239. The fact that some of the claims limited hedging to use in commodities and

energy markets and specified that "well-known random analysis techniques [could be used] to help establish some of the inputs into the equation" did not undermine this conclusion, for "*Flook* established that limiting an abstract idea to one field of use or adding token postsolution components did not make the concept patentable." *Id.*, at 3231.

3

The Court has repeatedly emphasized this last mentioned concern, a concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature. Thus, in *Morse* the Court set aside as unpatentable Samuel Morse's general claim for " 'the use of the motive power of the electric or galvanic current ... however developed, for making or printing intelligible characters, letters, or signs, at any distances,'" 15 How., at 86. The Court explained:

> For aught that we now know some future inventor, in the onward march of science, may discover a mode of writing or printing at a distance by means of the electric or galvanic current, without using any part of the process or combination set forth in the plaintiff's specification. His invention may be less complicated—less liable to get out of order—less expensive in construction, and in its operation. But yet if it is covered by this patent the inventor could not use it, nor the public have the benefit of it without the permission of this patentee. *Id.*, at 113.

…. These statements reflect the fact that, even though rewarding with patents those who discover new laws of nature and the like might well encourage their discovery, those laws and principles, considered generally, are "the basic tools of scientific and technological work." *Benson, supra,* at 253. And so there is a danger that the grant of patents that tie up their use will inhibit future innovation premised upon them, a danger that becomes acute when a patented process amounts to no more than an instruction to "apply the natural law," or otherwise forecloses more future invention than the underlying discovery could reasonably justify.

The laws of nature at issue here are narrow laws that may have limited applications, but the patent claims that embody them nonetheless implicate this concern. They tell a treating doctor to measure metabolite levels and to consider the resulting measurements in light of the statistical relationships they describe. In doing so, they tie up the doctor's subsequent treatment decision whether that treatment does, or does not, change in light of the inference he has drawn using the correlations. And they threaten to inhibit the development of more refined treatment recommendations (like that embodied in Mayo's test), that combine Prometheus' correlations with later discovered features of metabolites, human physiology or individual patient characteristics. The "determining" step too is set forth in highly general language covering all processes that make use of the correlations after measuring metabolites, including later discovered processes that measure metabolite levels in new ways.

We need not, and do not, now decide whether were the steps at issue here less conventional, these features of the claims would prove sufficient to invalidate them. For here, as we have said,

the steps add nothing of significance to the natural laws themselves. Unlike, say, a typical patent on a new drug or a new way of using an existing drug, the patent claims do not confine their reach to particular applications of those laws. The presence here of the basic underlying concern that these patents tie up too much future use of laws of nature simply reinforces our conclusion that the processes described in the patents are not patent eligible, while eliminating any temptation to depart from case law precedent.

III

We have considered several further arguments in support of Prometheus' position. But they do not lead us to adopt a different conclusion. First, the Federal Circuit, in upholding the patent eligibility of the claims before us, relied on this Court's determination that "[t]ransformation and reduction of an article 'to a different state or thing' is *the clue* to the patentability of a process claim that does not include particular machines." *Benson, supra*, at 70–71. It reasoned that the claimed processes are therefore patent eligible, since they involve transforming the human body by administering a thiopurine drug and transforming the blood by analyzing it to determine metabolite levels.

The first of these transformations, however, is irrelevant. As we have pointed out, the "administering" step simply helps to pick out the group of individuals who are likely interested in applying the law of nature. And the second step could be satisfied without transforming the blood, should science develop a totally different system for determining metabolite levels that did not involve such a transformation. Regardless, in stating that the "machine-or-transformation" test is an "*important and useful clue* " to patentability, we have neither said nor implied that the test trumps the "law of nature" exclusion. *Bilski, supra,* at 3225–3227 (emphasis added). That being so, the test fails here.

Second, Prometheus argues that, because the particular laws of nature that its patent claims embody are narrow and specific, the patents should be upheld. Thus, it encourages us to draw distinctions among laws of nature based on whether or not they will interfere significantly with innovation in other fields now or in the future.

But the underlying functional concern here is a *relative* one: how much future innovation is foreclosed relative to the contribution of the inventor. A patent upon a narrow law of nature may not inhibit future research as seriously as would a patent upon Einstein's law of relativity, but the creative value of the discovery is also considerably smaller. And, as we have previously pointed out, even a narrow law of nature (such as the one before us) can inhibit future research.

In any event, our cases have not distinguished among different laws of nature according to whether or not the principles they embody are sufficiently narrow. And this is understandable. Courts and judges are not institutionally well suited to making the kinds of judgments needed to

distinguish among different laws of nature. And so the cases have endorsed a bright-line prohibition against patenting laws of nature, mathematical formulas and the like, which serves as a somewhat more easily administered proxy for the underlying "building-block" concern.

Third, the Government argues that virtually any step beyond a statement of a law of nature itself should transform an unpatentable law of nature into a potentially patentable application sufficient to satisfy § 101's demands. The Government does not necessarily believe that claims that (like the claims before us) extend just minimally beyond a law of nature should receive patents. But in its view, other statutory provisions—those that insist that a claimed process be novel, 35 U.S.C. § 102, that it not be "obvious in light of prior art," § 103, and that it be "full[y], clear[ly], concise[ly], and exact[ly]" described, § 112—can perform this screening function. In particular, it argues that these claims likely fail for lack of novelty under § 102.

This approach, however, would make the "law of nature" exception to § 101 patentability a dead letter. The approach is therefore not consistent with prior law. The relevant cases rest their holdings upon section 101, not later sections.

We recognize that, in evaluating the significance of additional steps, the § 101 patent-eligibility inquiry and, say, the § 102 novelty inquiry might sometimes overlap. But that need not always be so. And to shift the patent-eligibility inquiry entirely to these later sections risks creating significantly greater legal uncertainty, while assuming that those sections can do work that they are not equipped to do.

What role would laws of nature, including newly discovered (and "novel") laws of nature, play in the Government's suggested "novelty" inquiry? Intuitively, one would suppose that a newly discovered law of nature is novel. The Government, however, suggests in effect that the novelty of a component law of nature may be disregarded when evaluating the novelty of the whole. But §§ 102 and 103 say nothing about treating laws of nature as if they were part of the prior art when applying those sections. Cf. *Diehr,* 450 U.S., at 188 (patent claims "must be considered as a whole"). And studiously ignoring *all* laws of nature when evaluating a patent application under §§ 102 and 103 would "make all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious." *Id.*, at 189, n. 12.

Fourth, Prometheus, supported by several *amici,* argues that a principle of law denying patent coverage here will interfere significantly with the ability of medical researchers to make valuable discoveries, particularly in the area of diagnostic research. That research, which includes research leading to the discovery of laws of nature, is expensive; it "ha[s] made the United States the world leader in this field"; and it requires protection.

Other medical experts, however, argue strongly against a legal rule that would make the present claims patent eligible, invoking policy considerations that point in the opposite direction. The American Medical Association, the American College of Medical Genetics, the American

Hospital Association, the American Society of Human Genetics, the Association of American Medical Colleges, the Association for Molecular Pathology, and other medical organizations tell us that if "claims to exclusive rights over the body's natural responses to illness and medical treatment are permitted to stand, the result will be a vast thicket of exclusive rights over the use of critical scientific data that must remain widely available if physicians are to provide sound medical care." Brief for American College of Medical Genetics et al. as *Amici Curiae* 7; see also App. to Brief for Association Internationale pour la Protection de la Propriete Intellectuelle et al. as *Amici Curiae* A6, A16 (methods of medical treatment are not patentable in most of Western Europe).

We do not find this kind of difference of opinion surprising. Patent protection is, after all, a two-edged sword. On the one hand, the promise of exclusive rights provides monetary incentives that lead to creation, invention, and discovery. On the other hand, that very exclusivity can impede the flow of information that might permit, indeed spur, invention, by, for example, raising the price of using the patented ideas once created, requiring potential users to conduct costly and time-consuming searches of existing patents and pending patent applications, and requiring the negotiation of complex licensing arrangements. At the same time, patent law's general rules must govern inventive activity in many different fields of human endeavor, with the result that the practical effects of rules that reflect a general effort to balance these considerations may differ from one field to another.

* * *

For these reasons, we conclude that the patent claims at issue here effectively claim the underlying laws of nature themselves. The claims are consequently invalid. And the Federal Circuit's judgment is reversed.

Comments

5. *"Laws of Nature, Physical Phenomena, and Abstract Ideas" Not Patentable* (P. 95 - <u>Revised</u>). While *Chakrabary* noted that § 101 is intended to "'include anything under the sun that is made my man,"' the Supreme Court has repeatedly excluded "laws of nature, physical phenomena, and abstract ideas" as eligible subject matter. So why is it that E=mc2, a naturally occurring mineral, an abstract idea, or law of nature unpatentable? Why can't the businessman in *The Little Prince* own the stars? Recall the colloquy that transpires between the little prince and the businessman:

> "How is it possible for one to own the stars?"
>
> "To whom do they belong?" the businessman retorted, peevishly.
>
> "I don't know. To nobody."
>
> "Then they belong to me, because I was the first person to think of it."

> "Is that all that is necessary?"
>
> "Certainly. When you find a diamond that belongs to nobody, it is yours. When you discover an island that belongs to nobody, it is yours. When you get an idea before any one else, you take out a patent on it: it is yours. So with me: I own the stars, because nobody else before me ever thought of owning them."

Antoine de Saint-Exupéry, *The Little Prince* (Chapter 13) ----

A common response is allowing patent protection on abstract ideas and laws of nature would lead to excessive rent seeking and enormous social costs. In a precursor to his opinion in *Prometheus*, Justice Breyer wrote in 2006:

> The justification for the principle does not lie in any claim that "laws of nature" are obvious, or that their discovery is easy, or that they are not useful. To the contrary, research into such matters may be costly and time-consuming; monetary incentives may matter; and the fruits of those incentives and that research may prove of great benefit to the human race. Rather, the reason for the exclusion is that sometimes *too much* patent protection can impede rather than "promote the Progress of Science and useful Arts," the constitutional objective of patent and copyright protection.
>
> * * *
>
> Patent law seeks to avoid the dangers of overprotection just as surely as it seeks to avoid the diminished incentive to invent that underprotection can threaten. One way in which patent law seeks to sail between these opposing and risky shoals is through rules that bring certain types of invention and discovery within the scope of patentability while excluding others.

LabCorp v. Metabolite Laboratories, Inc., 126 S. Ct. 2921, 2922 (2006) (dissenting from dismissal of certiorari). Similarly, Justice Breyer wrote in *Prometheus* that "monopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it." *See also* WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 305-06 (2004) (noting transaction costs would be "enormous because the scope" of protection "often is extremely difficult to pin down, and this would make it difficult for newcomers to know when they needed to get a license"); Michael J. Meurer & Katherine J. Strandburg, *Patent Carrots and Sticks: A Model of Nonobviousness*, 12 LEWIS & CLARK L. REV. 547, 577 (2008) (stating "while offering patents for the discovery of new laws of nature might well induce private investors to fund more difficult research projects, the social cost of giving one entity control over applications of that law of nature may simply be too great to be offset by the increased investment in science that the possibility of a patent attracts").

But is the transaction/social costs argument more comfortably situated in Section

112 than in Section 101? Is the argument reminiscent of Justice Taney's concern about Morse's claim 8? Moreover, was the patentee in *Prometheus* claiming a law of nature? In referring to the relationship between concentrations of "certain metabolites in the blood" and the effectiveness or harmfulness of a dosage of thiopurine, the Court conceded that human action is needed to administer thiopurine so as to manifest this relationship, but ultimately found the relationship is an "entirely natural process" because it is nothing more than "a consequence of the ways in which thiopurine compounds are metabolized by the body." Can one reasonably argue that patent law should make an objective distinction between the aforementioned relationship between metabolites and thiopurine and, say, the law of gravity. The former — as the Court acknowledged — is variable, that is, "the way in which people metabolize thiopurine compounds varies," whereas the law of gravity is universal and invariable. Is the Court painting with too broad of a brush and likely excluding, for example, advances in the field of personalized medicine, particularly genomic-based treatments designed to address a patient's unique genetic makeup? Lastly, the Court — concerned with adroit deployment of "the draftsman's art," a concern also expressed in *Flook* —remarked how the additional steps recited in the claimed invention "consist of well-understood, routine, conventional activity already engaged in by the scientific community." Is this an eligibility or novelty argument? If a law of nature is part of a claim, *Prometheus* seems to suggest that the patentnee must set forth the law's application in a novel and nonobvious manner.

Prometheus's *Affect on* Myriad? The Supreme Court granted review of *Myriad*, vacated the Federal Circuit's opinion, and remanded for reconsideration in the light of *Prometheus*. The Federal Circuit heard oral arguments on July 27, 2012. To what extent does *Prometheus* apply to Myriad's method claims and its claims to isolated DNA? With respect to the former, Myriad claimed "a method of screening potential cancer therapeutics." The Federal Circuit may analyze the eligibility of this claim through the natural phenomena/law of nature lens, and consider any correlations between mutations and susceptibility to cancer as simply reflections of nature.

With respect to the isolated DNA claim, recall the Federal Circuit already held in *Myriad* that it is not a product of nature; rather, it is a result of sufficient human intervention. That is, isolated DNA is "markedly different" than native DNA. In this regard, *Prometheus* should be inapposite. Yet, *Prometheus* was also very concerned with blocking downstream innovation, a policy position that may be seen as applicable to Myriad's isolated DNA claims. Perhaps the more relevant question relates to novelty and nonobvious. For example, is an isolated DNA molecule obvious in the light of the native DNA from which it derives? This question may be for another day.

Read *Global-Tech* after *Lucent*

Global-Tech Appliances, Inc. v. SEB S.A

131 S.Ct. 2060 (2011)

Justice ALITO delivered the opinion of the Court.

We consider whether a party who "actively induces infringement of a patent" under 35 U.S.C. § 271(b) must know that the induced acts constitute patent infringement.

I

This case concerns a patent for an innovative deep fryer designed by respondent SEB S.A., a French maker of home appliances. In the late 1980's, SEB invented a "cool-touch" deep fryer, that is, a deep fryer for home use with external surfaces that remain cool during the frying process. The cool-touch deep fryer consisted of a metal frying pot surrounded by a plastic outer housing. Attached to the housing was a ring that suspended the metal pot and insulated the hous-

ing from heat by separating it from the pot, creating air space between the two components. SEB obtained a U.S. patent for its design in 1991, and sometime later, SEB started manufacturing the cool-touch fryer and selling it in this country under its well-known "T–Fal" brand. Superior to other products in the American market at the time, SEB's fryer was a commercial success.

In 1997, Sunbeam Products, Inc., a U.S. competitor of SEB, asked petitioner Pentalpha Enterprises, Ltd., to supply it with deep fryers meeting certain specifications. Pentalpha is a Hong Kong maker of home appliances and a wholly owned subsidiary of petitioner Global–Tech Appliances, Inc.

In order to develop a deep fryer for Sunbeam, Pentalpha purchased an SEB fryer in Hong Kong and copied all but its cosmetic features. Because the SEB fryer bought in Hong Kong was made for sale in a foreign market, it bore no U.S. patent markings. After copying SEB's design, Pentalpha retained an attorney to conduct a right-to-use study, but Pentalpha refrained from telling the attorney that its design was copied directly from SEB's.

The attorney failed to locate SEB's patent, and in August 1997 he issued an opinion letter stating that Pentalpha's deep fryer did not infringe any of the patents that he had found. That same month, Pentalpha started selling its deep fryers to Sunbeam, which resold them in the United States under its trademarks. By obtaining its product from a manufacturer with lower production costs, Sunbeam was able to undercut SEB in the U.S. market.

After SEB's customers started defecting to Sunbeam, SEB sued Sunbeam in March 1998, alleging that Sunbeam's sales infringed SEB's patent. Sunbeam notified Pentalpha of the lawsuit the following month. Undeterred, Pentalpha went on to sell deep fryers to Fingerhut Corp. and Montgomery Ward & Co., both of which resold them in the United States under their respective trademarks.

SEB settled the lawsuit with Sunbeam, and then sued Pentalpha, asserting two theories of recovery: First, SEB claimed that Pentalpha had directly infringed SEB's patent in violation of 35 U.S.C. § 271(a), by selling or offering to sell its deep fryers; and second, SEB claimed that Pentalpha had contravened § 271(b) by actively inducing Sunbeam, Fingerhut, and Montgomery Ward to sell or to offer to sell Pentalpha's deep fryers in violation of SEB's patent rights.

Following a 5–day trial, the jury found for SEB on both theories and also found that Pentalpha's infringement had been willful. Pentalpha filed post-trial motions seeking a new trial or judgment as a matter of law on several grounds. As relevant here, Pentalpha argued that there was insufficient evidence to support the jury's finding of induced infringement under § 271(b) because Pentalpha did not actually know of SEB's patent until it received the notice of the Sunbeam lawsuit in April 1998.

The District Court rejected Pentalpha's argument, as did the Court of Appeals for the Federal Circuit, which affirmed the judgment. Summarizing a recent en banc decision, the Federal Cir-

cuit stated that induced infringement under § 271(b) requires a "plaintiff [to] show that the alleged infringer knew or should have known that his actions would induce actual infringements" and that this showing includes proof that the alleged infringer knew of the patent. Although the record contained no direct evidence that Pentalpha knew of SEB's patent before April 1998, the court found adequate evidence to support a finding that "Pentalpha deliberately disregarded a known risk that SEB had a protective patent." Such disregard, the court said, "is not different from actual knowledge, but is a form of actual knowledge."

II

Pentalpha argues that active inducement liability under § 271(b) requires more than deliberate indifference to a known risk that the induced acts may violate an existing patent. Instead, Pentalpha maintains, actual knowledge of the patent is needed.

A

In assessing Pentalpha's argument, we begin with the text of § 271(b)—which is short, simple, and, with respect to the question presented in this case, inconclusive. Section 271(b) states: "Whoever actively induces infringement of a patent shall be liable as an infringer."

Although the text of § 271(b) makes no mention of intent, we infer that at least some intent is required. The term "induce" means "[t]o lead on; to influence; to prevail on; to move by persuasion or influence." Webster's New International Dictionary 1269 (2d ed.1945). The addition of the adverb "actively" suggests that the inducement must involve the taking of affirmative steps to bring about the desired result, see *id.*, at 27.

When a person actively induces another to take some action, the inducer obviously knows the action that he or she wishes to bring about. If a used car salesman induces a customer to buy a car, the salesman knows that the desired result is the purchase of the car. But what if it is said that the salesman induced the customer to buy a *damaged* car? Does this mean merely that the salesman induced the customer to purchase a car that happened to be damaged, a fact of which the salesman may have been unaware? Or does this mean that the salesman knew that the car was damaged? The statement that the salesman induced the customer to buy a damaged car is ambiguous.

So is § 271(b). In referring to a party that "induces infringement," this provision may require merely that the inducer lead another to engage in conduct that happens to amount to infringement, *i.e.*, the making, using, offering to sell, selling, or importing of a patented invention. See § 271(a). On the other hand, the reference to a party that "induces infringement" may also be read to mean that the inducer must persuade another to engage in conduct that the inducer knows is infringement. Both readings are possible.

B

Finding no definitive answer in the statutory text, we turn to the case law that predates the enactment of § 271 as part the Patent Act of 1952. As we recognized in *Aro Mfg. Co. v. Convertible Top Replacement Co.*, 377 U.S. 476 (1964) *(Aro II),* "[t]he section was designed to 'codify in statutory form principles of contributory infringement' which had been 'part of our law for about 80 years.' " *Id.*, at 485–486, n. 6, 84 S.Ct. 1526 (quoting H.R.Rep. No. 1923, 82d Cong., 2d Sess., 9 (1952)).

Unfortunately, the relevant pre–1952 cases are less clear than one might hope with respect to the question presented here. Before 1952, both the conduct now covered by § 271(b) (induced infringement) and the conduct now addressed by § 271(c) (sale of a component of a patented invention) were viewed as falling within the overarching concept of "contributory infringement." Cases in the latter category—*i.e.*, cases in which a party sold an item that was not itself covered by the claims of a patent but that enabled another party to make or use a patented machine, process, or combination—were more common.

The pre–1952 case law provides conflicting signals regarding the intent needed in such cases. In an oft-cited decision, then-Judge Taft suggested that it was sufficient if the seller of the component part intended that the part be used in an invention that happened to infringe a patent. He wrote that it was "well settled that where one makes and sells one element of a combination covered by a patent with the intention and for the purpose of bringing about its use in such a combination he is guilty of contributory infringement." *Thomson–Houston Elec. Co. v. Ohio Brass Co.*, 80 F. 712, 721 (C.A.6 1897).

On the other hand, this Court, in *Henry v. A.B. Dick Co.*, 224 U.S. 1 (1912), overruled on other grounds, *Motion Picture Patents Co. v. Universal Film Mfg. Co.*, 243 U.S. 502 (1917), stated that "if the defendants [who were accused of contributory infringement] *knew of the patent* and that [the direct infringer] had unlawfully made the patented article ... with the intent and purpose that [the direct infringer] should use the infringing article ... they would assist in her infringing use." 224 U.S., at 33, 32 S.Ct. 364 (emphasis added and deleted). Our decision in *Metro–Goldwyn–Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913 (2005), which looked to the law of contributory patent infringement for guidance in determining the standard to be applied in a case claiming contributory copyright infringement, contains dicta that may be read as interpreting the pre–1952 cases this way. In *Grokster*, we said that "[t]he inducement rule ... premises liability on purposeful, culpable expression and conduct." *Id.*, at 937, 125 S.Ct. 2764.

While both the language of § 271(b) and the pre–1952 case law that this provision was meant to codify are susceptible to conflicting interpretations, our decision in *Aro II* resolves the question in this case. In *Aro II*, a majority held that a violator of § 271(c) must know "that the combination for which his component was especially designed was both patented and infringing," 377 U.S., at 488, and as we explain below, that conclusion compels this same knowledge for liability under § 271(b).

C

As noted above, induced infringement was not considered a separate theory of indirect liability in the pre–1952 case law. Rather, it was treated as evidence of "contributory infringement," that is, the aiding and abetting of direct infringement by another party. When Congress enacted § 271, it separated what had previously been regarded as contributory infringement into two categories, one covered by § 271(b) and the other covered by § 271(c).

Aro II concerned § 271(c), which states in relevant part:

> Whoever offers to sell or sells ... a component of a patented [invention] ..., constituting a material part of the invention, *knowing the same to be especially made or especially adapted for use in an infringement* of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer." (Emphasis added.)

This language contains exactly the same ambiguity as § 271(b). The phrase "knowing [a component] to be especially made or especially adapted for use in an infringement" may be read to mean that a violator must know that the component is "especially adapted for use" in a product that happens to infringe a patent. Or the phrase may be read to require, in addition, knowledge of the patent's existence.

This question closely divided the *Aro II* Court. In a badly fractured decision, a majority concluded that knowledge of the patent was needed. 377 U.S., at 488, and n. 8. Four Justices disagreed with this interpretation and would have held that a violator of § 271(c) need know only that the component is specially adapted for use in a product that happens to infringe a patent. These Justices thought that this reading was supported by the language of § 271(c) and the pre–1952 case law, and they disagreed with the inference drawn by the majority from the amendment of § 271(c)'s language.

While there is much to be said in favor of both views expressed in *Aro II*, the "holding in *Aro II* has become a fixture in the law of contributory infringement under [section] 271(c),"—so much so that SEB has not asked us to overrule it. Nor has Congress seen fit to alter § 271(c)'s intent requirement in the nearly half a century since *Aro II* was decided. In light of the " 'special force' " of the doctrine of *stare decisis* with regard to questions of statutory interpretation, we proceed on the premise that § 271(c) requires knowledge of the existence of the patent that is infringed.

Based on this premise, it follows that the same knowledge is needed for induced infringement under § 271(b). As noted, the two provisions have a common origin in the pre–1952 understanding of contributory infringement, and the language of the two provisions creates the same difficult interpretive choice. It would thus be strange to hold that knowledge of the relevant patent is needed under § 271(c) but not under § 271(b).

Accordingly, we now hold that induced infringement under § 271(b) requires knowledge that

the induced acts constitute patent infringement.

III

Returning to Pentalpha's principal challenge, we agree that deliberate indifference to a known risk that a patent exists is not the appropriate standard under § 271(b). We nevertheless affirm the judgment of the Court of Appeals because the evidence in this case was plainly sufficient to support a finding of Pentalpha's knowledge under the doctrine of willful blindness.

A

The doctrine of willful blindness is well established in criminal law. Many criminal statutes require proof that a defendant acted knowingly or willfully, and courts applying the doctrine of willful blindness hold that defendants cannot escape the reach of these statutes by deliberately shielding themselves from clear evidence of critical facts that are strongly suggested by the circumstances. The traditional rationale for this doctrine is that defendants who behave in this manner are just as culpable as those who have actual knowledge. It is also said that persons who know enough to blind themselves to direct proof of critical facts in effect have actual knowledge of those facts.

Given the long history of willful blindness and its wide acceptance in the Federal Judiciary, we can see no reason why the doctrine should not apply in civil lawsuits for induced patent infringement under 35 U.S.C. § 271(b).

Pentalpha urges us not to take this step, arguing that § 271(b) demands more than willful blindness with respect to *the induced acts* that constitute infringement. This question, however, is not at issue here. There is no need to invoke the doctrine of willful blindness to establish that Pentalpha knew that the retailers who purchased its fryer were selling that product in the American market; Pentalpha was indisputably aware that its customers were selling its product in this country.

B

While the Courts of Appeals articulate the doctrine of willful blindness in slightly different ways, all appear to agree on two basic requirements: (1) the defendant must subjectively believe that there is a high probability that a fact exists and (2) the defendant must take deliberate actions to avoid learning of that fact. We think these requirements give willful blindness an appropriately limited scope that surpasses recklessness and negligence. Under this formulation, a willfully blind defendant is one who takes deliberate actions to avoid confirming a high probability of wrongdoing and who can almost be said to have actually known the critical facts. By contrast, a reckless defendant is one who merely knows of a substantial and unjustified risk of such wrongdoing, and a negligent defendant is one who should have known of a similar risk but, in fact, did not, see § 2.02(2)(d).

The test applied by the Federal Circuit in this case departs from the proper willful blindness standard in two important respects. First, it permits a finding of knowledge when there is merely a "known risk" that the induced acts are infringing. Second, in demanding only "deliberate indifference" to that risk, the Federal Circuit's test does not require active efforts by an inducer to avoid knowing about the infringing nature of the activities.

In spite of these flaws, we believe that the evidence when viewed in the light most favorable to the verdict for SEB is sufficient under the correct standard. The jury could have easily found that before April 1998 Pentalpha willfully blinded itself to the infringing nature of the sales it encouraged Sunbeam to make.

SEB's cool-touch fryer was an innovation in the U.S. market when Pentalpha copied it. As one would expect with any superior product, sales of SEB's fryer had been growing for some time. Pentalpha knew all of this, for its CEO and president, John Sham, testified that, in developing a product for Sunbeam, Pentalpha performed "market research" and "gather[ed] information as much as possible." Pentalpha's belief that SEB's fryer embodied advanced technology that would be valuable in the U.S. market is evidenced by its decision to copy all but the cosmetic features of SEB's fryer.

Also revealing is Pentalpha's decision to copy an overseas model of SEB's fryer. Pentalpha knew that the product it was designing was for the U.S. market, and Sham—himself a named inventor on numerous U.S. patents—was well aware that products made for overseas markets usually do not bear U.S. patent markings. Even more telling is Sham's decision not to inform the attorney from whom Pentalpha sought a right-to-use opinion that the product to be evaluated was simply a knockoff of SEB's deep fryer. On the facts of this case, we cannot fathom what motive Sham could have had for withholding this information other than to manufacture a claim of plausible deniability in the event that his company was later accused of patent infringement. Nor does Sham's testimony on this subject provide any reason to doubt that inference. Asked whether the attorney would have fared better had he known of SEB's design, Sham was nonresponsive. All he could say was that a patent search is not an "easy job" and that is why he hired attorneys to perform them.

Taken together, this evidence was more than sufficient for a jury to find that Pentalpha subjectively believed there was a high probability that SEB's fryer was patented, that Pentalpha took deliberate steps to avoid knowing that fact, and that it therefore willfully blinded itself to the infringing nature of Sunbeam's sales.

Comments

1. *Inducement's Knowledge Requirement.* The nature of the knowledge requirement for active inducement is not without confusion. For instance, in *Insituform Technologies, Inc. v. CAT Contracting, Inc.*, 385 F.3d 1360, 1377 (Fed. Cir. 2004), the court conceded "there is a lack of clarity

concerning whether the required intent must be merely to induce the specific acts or additionally to cause an infringement."

The *DSU* case (cited in *Lucent*) concluded inducement requires evidence of culpable conduct, directed to encouraging another's infringement, not merely that the inducer had knowledge of the direct infringer's activities. In quoting *Manville*, the "plaintiff has the burden of showing that the alleged infringer's actions induced infringing acts *and* that he knew or should have known his actions would induce actual infringements." In other words, "inducement requires 'that the alleged infringer knowingly induced infringement and possessed *specific intent* to encourage another's infringement.'" *DSU*, 471 F.3d 1304 (emphasis added).

In *DSU*, the accused infringer had actual knowledge of the patent, thus whether such knowledge is required was not before the court. *DSU*, 471 F.3d at 1311 (Michel, J., concurring) (the "'knowledge of the patent' issue is not before us"). So what then does it mean to have "specific intent to encourage another's infringement" or to have "actual or constructive knowledge of the patent?"

2. *Knowledge of the Patent.* Prior to *Global-Tech*, it was clear that a patentee must prove "that the alleged infringer knew or should have known that his actions would induce actual infringement." *DSU Medical Corp. v. JMS Co.*, 471 F.3d 1293, 1304 (Fed. Cir. 2006) (en banc). What was unclear was whether the accused infringer's knowledge also requires knowledge of the patent, an issue that was not present in *DSU*. Relying on *Aro Manufacturing Co. v. Convertible Top Replacement Co.*, 377 U.S. 476 (1964) and its § 271(c) jurisprudence, the Supreme Court in *Global-Tech* held that knowledge of infringement and of the patent are both required for induced infringement. And knowledge can be shown through willful blindness, that is when an accused infringer "who takes deliberate actions to avoid confirming a high probability of wrongdoing and who can almost be said to have actually known the critical facts." This knowledge threshold is higher than negligence, recklessness, and what the Federal Circuit called "deliberate indifference," all of which are insufficient for induced infringement because they do "not require active efforts by an inducer to avoid knowing about the infringing nature of the activities."

Pages 721-34
Replace *Kingsdown Med* and *Agfa* with *Therasense*

Therasense, Inc. v. Becton, Dickinson and Co.

649 F.3d 1276 (Fed. Cir. 2011) (en banc)

RADER, CHIEF JUDGE.

The United States District Court for the Northern District of California found U.S. Patent No. 5,820,551 ("the '551 patent") unenforceable due to inequitable conduct. ("*Trial Opinion* "). Therasense, Inc. (now Abbott Diabetes Care, Inc.) and Abbott Laboratories (collectively, "Abbott") appeal that judgment. This court vacates and remands for further proceedings consistent with this opinion.

I

The '551 patent involves disposable blood glucose test strips for diabetes management. These strips employ electrochemical sensors to measure the level of glucose in a sample of blood. When blood contacts a test strip, glucose in the blood reacts with an enzyme on the strip, resulting in the transfer of electrons from the glucose to the enzyme. A mediator transfers these electrons to an electrode on the strip. Then, the electrons flow from the strip to a glucose meter, which calculates the glucose concentration based on the electrical current.

> The '551 patent claims a test strip with an electrochemical sensor for testing whole blood without a membrane over the electrode:
>
> 1. A single use disposable electrode strip for attachment to the signal readout circuitry of a sensor to detect a current representative of the concentration of a compound in a drop of a whole blood sample comprising:

> a) an elongated support having a substantially flat, planar surface, adapted for releasable attachment to said readout circuitry;
>
> b) a first conductor extending along said surface and comprising a conductive element for connection to said readout circuitry;
>
> c) an active electrode on said strip in electrical contact with said first conductor and positioned to contact said whole blood sample;
>
> d) a second conductor extending along said surface comprising a conductive element for connection to said read out circuitry; and
>
> e) a reference counterelectrode in electrical contact with said second conductor and positioned to contact said whole blood sample,
>
> *wherein said active electrode is configured to be exposed to said whole blood sample without an intervening membrane or other whole blood filtering member ....*

′551 patent col. 13 l.29–col. 14 l.3 (emphasis added). "Whole blood," an important term in the claim, means blood that contains all of its components, including red blood cells.

In the prior art, some sensors employed diffusion-limiting membranes to control the flow of glucose to the electrode because the slower mediators of the time could not deal with a rapid influx of glucose. Other prior art sensors used protective membranes to prevent "fouling." Fouling occurs when red blood cells stick to the active electrode and interfere with electron transfer to the electrode. Protective membranes permit glucose molecules to pass, but not red blood cells.

Abbott filed the original application leading to the ′551 patent in 1984. Over thirteen years, that original application saw multiple rejections for anticipation and obviousness, including repeated rejections over U.S. Patent No. 4,545,382 ("the ′382 patent"), another patent owned by Abbott. The ′382 patent specification discussed protective membranes in the following terms: "Optionally, but preferably when being used on live blood, a protective membrane surrounds both the enzyme and the mediator layers, permeable to water and glucose molecules." Col.4 ll.63–66. "Live blood" refers to blood within a body.

In 1997, Lawrence Pope, Abbott's patent attorney, and Dr. Gordon Sanghera, Abbott's Director of Research and Development, studied the novel features of their application and decided to present a new reason for a patent. Pope presented new claims to the examiner based on a new sensor that did not require a protective membrane for whole blood. Pope asserted that this distinction would overcome the prior art ′382 patent, whose electrodes allegedly required a pro-

tective membrane. The examiner requested an affidavit to show that the prior art required a membrane for whole blood at the time of the invention.

To meet this evidentiary request, Dr. Sanghera submitted a declaration to the U.S. Patent and Trademark Office ("PTO") stating:

> [O]ne skilled in the art would have felt that an active electrode comprising an enzyme and a mediator would require a protective membrane if it were to be used with a whole blood sample.... [O]ne skilled in the art would not read lines 63 to 65 of column 4 of U.S. Patent No. 4,545,382 to teach that the use of a protective membrane with a whole blood sample is optionally or merely preferred.

Pope, in submitting Sanghera's affidavit, represented:

> The art continued to believe [following the '382 patent] that a barrier layer for [a] whole blood sample was necessary....
>
> One skilled in the art would *not* have read the disclosure of the ['382 patent] as teaching that the use of a protective membrane with whole blood samples was optional. He would not, especially in view of the working examples, have read the "optionally, but preferably" language at line 63 of column [4] as a technical teaching but rather mere patent phraseology.
>
> ....
>
> There is no teaching or suggestion of unprotected active electrodes for use with whole blood specimens in [the '382 patent]....

Several years earlier, while prosecuting the European counterpart to the '382 patent, European Patent EP 0 078 636 ("EP '636"), Abbott made representations to the European Patent Office ("EPO") regarding the same "optionally, but preferably" language in the European specification. On January 12, 1994, to distinguish a German reference labeled D1, which required a diffusion-limiting membrane, Abbott's European patent counsel argued that their invention did not require a diffusion-limiting membrane:

> *Contrary to the semipermeable membrane of D1, the protective membrane optionally utilized with the glucose sensor of the patent is [sic] suit is not controlling the permeability of the substrate....* Rather, in accordance with column 5, lines 30 to 33 of the patent in suit:

> Optionally, but preferably when being used on live blood, a protective membrane surrounds both the enzyme and the mediator layers, permeable to water and glucose molecules.
>
> See also claim 10 of the patent in suit as granted according to which the sensor electrode has an outermost protective membrane (11) permeable to water and glucose molecules.... Accordingly, *the purpose of the protective membrane of the patent in suit, preferably to be used with in vivo measurements, is a safety measurement to prevent any course [sic] particles coming off during use but not a permeability control for the substrate.*

(emphases added).

On May 23, 1995, Abbott's European patent counsel submitted another explanation about the D1 reference and EP ′636.

> "Optionally, but preferably when being used on live blood, a protective membrane surrounds both the enzyme and the mediator layers, permeable to water and glucose molecules."
>
> *It is submitted that this disclosure is unequivocally clear. The protective membrane is optional, however, it is preferred when used on live blood in order to prevent the larger constituents of the blood, in particular erythrocytes from interfering with the electrode sensor. Furthermore it is said, that said protective membrane should not prevent the glucose molecules from penetration, the membrane is "permeable" to glucose molecules.* This teaches the skilled artisan that, whereas the [D1 membrane] must ... control the permeability of the glucose ... the purpose of the protective membrane in the patent in suit is not to control the permeation of the glucose molecules. For this very reason *the sensor electrode as claimed does not have (and must not have) a semipermeable membrane in the sense of D1.*

(first and third emphases added).

II

In March 2004, Becton, Dickinson and Co. ("Becton") sued Abbott in the District of Massachusetts seeking a declaratory judgment of noninfringement of U.S. Patent Nos. 6,143,164 ("the ′164 patent") and 6,592,745 ("the ′745 patent"). Becton's product was a blood glucose test strip, the BD Test Strip. Abbott countersued Becton in the Northern District of California alleging that Becton's strip infringed the ′164, ′745, and ′551 patents.

… Of primary relevance here, the district court held the ′551 patent unenforceable for inequitable conduct because Abbott did not disclose to the PTO its briefs to the EPO filed on January 12, 1994 and May 23, 1995. Abbott appealed…. On unenforceability, the panel also affirmed, but with a dissent…. Recognizing the problems created by the expansion and overuse of the inequitable conduct doctrine, this court granted Abbott's petition for rehearing en banc and vacated the judgment of the panel. This court now vacates the district court's inequitable conduct judgment and remands.

III

Inequitable conduct is an equitable defense to patent infringement that, if proved, bars enforcement of a patent. This judge-made doctrine evolved from a trio of Supreme Court cases that applied the doctrine of unclean hands to dismiss patent cases involving egregious misconduct:

IV

The unclean hands cases of *Keystone, Hazel–Atlas,* and *Precision* formed the basis for a new doctrine of inequitable conduct that developed and evolved over time. Each of these unclean hands cases before the Supreme Court dealt with particularly egregious misconduct, including perjury, the manufacture of false evidence, and the suppression of evidence. Moreover, they all involved "deliberately planned and carefully executed scheme[s] to defraud" not only the PTO but also the courts. As the inequitable conduct doctrine evolved from these unclean hands cases, it came to embrace a broader scope of misconduct, including not only egregious affirmative acts of misconduct intended to deceive both the PTO and the courts but also the mere nondisclosure of information to the PTO. Inequitable conduct also diverged from the doctrine of unclean hands by adopting a different and more potent remedy—unenforceability of the entire patent rather than mere dismissal of the instant suit.

In line with this wider scope and stronger remedy, inequitable conduct came to require a finding of both intent to deceive and materiality. *Star Scientific Inc. v. R.J. Reynolds Tobacco Co.*, 537 F.3d 1357, 1365 (Fed.Cir.2008). To prevail on the defense of inequitable conduct, the accused infringer must prove that the applicant misrepresented or omitted material information

with the specific intent to deceive the PTO. *Id.* The accused infringer must prove both elements—intent and materiality—by clear and convincing evidence. *Id.* If the accused infringer meets its burden, then the district court must weigh the equities to determine whether the applicant's conduct before the PTO warrants rendering the entire patent unenforceable. *Id.*

As inequitable conduct emerged from unclean hands, the standards for intent to deceive and materiality have fluctuated over time…. This court embraced reduced standards for intent and materiality to foster full disclosure to the PTO. This new focus on encouraging disclosure has had numerous unforeseen and unintended consequences. Most prominently, inequitable conduct has become a significant litigation strategy. A charge of inequitable conduct conveniently expands discovery into corporate practices before patent filing and disqualifies the prosecuting attorney from the patentee's litigation team. *See* Stephen A. Merrill et al., Nat'l Research Council of the Nat'l Academies, *A Patent System for the 21st Century* 122 (2004).[*] Moreover, inequitable conduct charges cast a dark cloud over the patent's validity and paint the patentee as a bad actor. Because the doctrine focuses on the moral turpitude of the patentee with ruinous consequences for the reputation of his patent attorney, it discourages settlement and deflects attention from the merits of validity and infringement issues. Committee Position Paper, *The Doctrine of Inequitable Conduct and the Duty of Candor in Patent Prosecution: Its Current Adverse Impact on the Operation of the United States Patent System,* 16 AIPLA Q.J. 74, 75 (1988). Inequitable conduct disputes also "increas[e] the complexity, duration and cost of patent infringement litigation that is already notorious for its complexity and high cost." Brief and Appendix of the American Bar Ass'n as Amicus Curiae at 9.

Perhaps most importantly, the remedy for inequitable conduct is the "atomic bomb" of patent law. *Aventis Pharma S.A. v. Amphastar Pharm., Inc.*, 525 F.3d 1334, 1349 (Fed.Cir.2008) (Rader, J., dissenting). Unlike validity defenses, which are claim specific, inequitable conduct regarding any single claim renders the entire patent unenforceable. *Kingsdown Med. Consultants, Ltd. v. Hollister Inc.*, 863 F.2d 867, 877 (Fed.Cir.1988). Unlike other deficiencies, inequitable conduct cannot be cured by reissue, or reexamination. Moreover, the taint of a finding of inequitable conduct can spread from a single patent to render unenforceable other related patents and applications in the same technology family. Thus, a finding of inequitable conduct may endanger a substantial portion of a company's patent portfolio. A finding of inequitable conduct may also spawn antitrust and unfair competition claims. Further, prevailing on a claim of inequitable conduct often makes a case "exceptional," leading potentially to an award of attorneys' fees under 35 U.S.C. § 285. A finding of inequitable conduct may also prove the crime or fraud exception to the attorney-client privilege.

[*] [Ed. Footnote: The Merrill et al. study is available on the casebook website - http://law.case.edu/lawofpatents/ - under "Documents and Literature."

While honesty at the PTO is essential, low standards for intent and materiality have inadvertently led to many unintended consequences, among them, increased adjudication cost and complexity, reduced likelihood of settlement, burdened courts, strained PTO resources, increased PTO backlog, and impaired patent quality. This court now tightens the standards for finding both intent and materiality in order to redirect a doctrine that has been overused to the detriment of the public.

V

To prevail on a claim of inequitable conduct, the accused infringer must prove that the patentee acted with the specific intent to deceive the PTO. A finding that the misrepresentation or omission amounts to gross negligence or negligence under a "should have known" standard does not satisfy this intent requirement. "In a case involving nondisclosure of information, clear and convincing evidence must show that the applicant *made a deliberate decision* to withhold a *known* material reference." *Molins*, 48 F.3d at 1181 (emphases added). In other words, the accused infringer must prove by clear and convincing evidence that the applicant knew of the reference, knew that it was material, and made a deliberate decision to withhold it. This requirement of knowledge and deliberate action has origins in the trio of Supreme Court cases that set in motion the development of the inequitable conduct doctrine. In each of those cases, the patentee acted knowingly and deliberately with the purpose of defrauding the PTO and the courts.

Intent and materiality are separate requirements. A district court should not use a "sliding scale," where a weak showing of intent may be found sufficient based on a strong showing of materiality, and vice versa. Moreover, a district court may not infer intent solely from materiality. Instead, a court must weigh the evidence of intent to deceive independent of its analysis of materiality. Proving that the applicant knew of a reference, should have known of its materiality, and decided not to submit it to the PTO does not prove specific intent to deceive.

Because direct evidence of deceptive intent is rare, a district court may infer intent from indirect and circumstantial evidence. However, to meet the clear and convincing evidence standard, the specific intent to deceive must be "the single most reasonable inference able to be drawn from the evidence." *Star*, 537 F.3d at 1366. Indeed, the evidence "must be sufficient to *require* a finding of deceitful intent in the light of all the circumstances." *Kingsdown*, 863 F.2d at 873 (emphasis added). Hence, when there are multiple reasonable inferences that may be drawn, intent to deceive cannot be found. This court reviews the district court's factual findings regarding what reasonable inferences may be drawn from the evidence for clear error.

Because the party alleging inequitable conduct bears the burden of proof, the "patentee need not offer any good faith explanation unless the accused infringer first ... prove[s] a thresh-

old level of intent to deceive by clear and convincing evidence." *Star*, 537 F.3d at 1368. The absence of a good faith explanation for withholding a material reference does not, by itself, prove intent to deceive.

VI

This court holds that, as a general matter, the materiality required to establish inequitable conduct is but-for materiality. When an applicant fails to disclose prior art to the PTO, that prior art is but-for material if the PTO would not have allowed a claim had it been aware of the undisclosed prior art. Hence, in assessing the materiality of a withheld reference, the court must determine whether the PTO would have allowed the claim if it had been aware of the undisclosed reference. In making this patentability determination, the court should apply the preponderance of the evidence standard and give claims their broadest reasonable construction. Often the patentability of a claim will be congruent with the validity determination—if a claim is properly invalidated in district court based on the deliberately withheld reference, then that reference is necessarily material because a finding of invalidity in a district court requires clear and convincing evidence, a higher evidentiary burden than that used in prosecution at the PTO. However, even if a district court does not invalidate a claim based on a deliberately withheld reference, the reference may be material if it would have blocked patent issuance under the PTO's different evidentiary standards.

As an equitable doctrine, inequitable conduct hinges on basic fairness. "[T]he remedy imposed by a court of equity should be commensurate with the violation." *Columbus Bd. of Educ. v. Penick*, 443 U.S. 449, 465 (1979). Because inequitable conduct renders an entire patent (or even a patent family) unenforceable, as a general rule, this doctrine should only be applied in instances where the patentee's misconduct resulted in the unfair benefit of receiving an unwarranted claim. Moreover, enforcement of an otherwise valid patent does not injure the public merely because of misconduct, lurking somewhere in patent prosecution, that was immaterial to the patent's issuance.

Although but-for materiality generally must be proved to satisfy the materiality prong of inequitable conduct, this court recognizes an exception in cases of affirmative egregious misconduct. This exception to the general rule requiring but-for proof incorporates elements of the early unclean hands cases before the Supreme Court, which dealt with "deliberately planned and carefully executed scheme[s]" to defraud the PTO and the courts. When the patentee has engaged in affirmative acts of egregious misconduct, such as the filing of an unmistakably false affidavit, the misconduct is material. After all, a patentee is unlikely to go to great lengths to deceive the PTO with a falsehood unless it believes that the falsehood will affect issuance of the patent. Be-

cause neither mere nondisclosure of prior art references to the PTO nor failure to mention prior art references in an affidavit constitutes affirmative egregious misconduct, claims of inequitable conduct that are based on such omissions require proof of but-for materiality. By creating an exception to punish affirmative egregious acts without penalizing the failure to disclose information that would not have changed the issuance decision, this court strikes a necessary balance between encouraging honesty before the PTO and preventing unfounded accusations of inequitable conduct.

[T]he materiality standard set forth in this opinion includes an exception for affirmative acts of egregious misconduct, not just the filing of false affidavits. Accordingly, the general rule requiring but-for materiality provides clear guidance to patent practitioners and courts, while the egregious misconduct exception gives the test sufficient flexibility to capture extraordinary circumstances. Thus, not only is this court's approach sensitive to varied facts and equitable considerations, it is also consistent with the early unclean hands cases—all of which dealt with egregious misconduct.

This court does not adopt the definition of materiality in PTO Rule 56. As an initial matter, this court is not bound by the definition of materiality in PTO rules. While this court respects the PTO's knowledge in its area of expertise, the routine invocation of inequitable conduct in patent litigation has had adverse ramifications beyond its effect on the PTO. Tying the materiality standard for inequitable conduct to PTO rules, which understandably change from time to time, has led to uncertainty and inconsistency in the development of the inequitable conduct doctrine.

This court declines to adopt the current version of Rule 56 in defining inequitable conduct because reliance on this standard has resulted in the very problems this court sought to address by taking this case en banc. Rule 56 provides that information is material if it is not cumulative and:

> (1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or
>
> (2) It refutes, or is inconsistent with, a position the applicant takes in:
>
> (i) Opposing an argument of unpatentability relied on by the Office, or
>
> (ii) Asserting an argument of patentability.

37 C.F.R. § 1.56. Rule 56 further provides that a "prima facie case of unpatentability is established when the information compels a conclusion that a claim is unpatentable ... *before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability*." *Id.* (emphasis added). The first prong of Rule 56 is overly broad be-

cause information is considered material even if the information would be rendered irrelevant in light of subsequent argument or explanation by the patentee. Under this standard, inequitable conduct could be found based on an applicant's failure to disclose information that a patent examiner would readily agree was not relevant to the prosecution after considering the patentee's argument. Likewise, the second prong of Rule 56 broadly encompasses anything that could be considered marginally relevant to patentability. If an applicant were to assert that his invention would have been non-obvious, for example, anything bearing any relation to obviousness could be found material under the second prong of Rule 56. Because Rule 56 sets such a low bar for materiality, adopting this standard would inevitably result in patent prosecutors continuing the existing practice of disclosing too much prior art of marginal relevance and patent litigators continuing to charge inequitable conduct in nearly every case as a litigation strategy.

VII

In this case, the district court held the ′551 patent unenforceable for inequitable conduct because Abbott did not disclose briefs it submitted to the EPO regarding the European counterpart of the ′382 patent. Because the district court found statements made in the EPO briefs material under the PTO's Rule 56 materiality standard, not under the but-for materiality standard set forth in this opinion, this court vacates the district court's findings of materiality. On remand, the district court should determine whether the PTO would not have granted the patent but for Abbott's failure to disclose the EPO briefs. In particular, the district court must determine whether the PTO would have found Sanghera's declaration and Pope's accompanying submission unpersuasive in overcoming the obviousness rejection over the ′382 patent if Abbott had disclosed the EPO briefs.

The district court found intent to deceive based on the absence of a good faith explanation for failing to disclose the EPO briefs. However, a "patentee need not offer any good faith explanation unless the accused infringer first ... prove[s] a threshold level of intent to deceive by clear and convincing evidence." *Star*, 537 F.3d at 1368. The district court also relied upon the "should have known" negligence standard in reaching its finding of intent. *See Trial Opinion* at 1113 ("Attorney Pope knew or should have known that the withheld information would have been highly material to the examiner"). Because the district court did not find intent to deceive under the knowing and deliberate standard set forth in this opinion, this court vacates the district court's findings of intent. On remand, the district court should determine whether there is clear and convincing evidence demonstrating that Sanghera or Pope knew of the EPO briefs, knew of their materiality, and made the conscious decision not to disclose them in order to deceive the PTO.

For the foregoing reasons, this court vacates the district court's finding of inequitable conduct and remands for further proceedings consistent with this opinion.

Comments
(replace current comments with the following)

1. ***The "Atomic Bomb of Patent Law."*** The Federal Circuit stressed the devastating consequences resulting from a finding of inequitable conduct. These consequences — coupled with what the court viewed as the relatively low evidentiary requirements of intent and materiality and a laundry list of "unintended consequences" — influenced the court's opinion. Accordingly, with an eye towards greater certainty, the court "tighten[ed] the standards for finding both intent and materiality in order to redirect a doctrine that has been overused to the detriment of the public." Will this tightening also result to unintended consequences? Will fewer prior art disclosures lead to lower patent quality?

2. ***Intent.*** The court adopted a "specific intent" standard. This standard is likely to be particularly germane to *undisclosed* material information. The omission of certain types of material information can be troubling from a patent law perspective. For example, as the court noted in a prior case, "concealment of sales information can be particularly egregious because, unlike the applicant's failure to disclose a material patent reference, the examiner has no way of securing the information on his own." *Paragon Podiatry Lab., Inc. v. KLM Labs. Inc.*, 984 F.2d 1182, 1193 (Fed. Cir. 1993). In *Therasense*, the court, while presumably aware of the perils of non-disclosure, nonetheless expressly reaffirmed the principle that "clear and convincing evidence must show that the applicant made a deliberate decision to withhold a known material reference." As such, the applicant must not only have known of the reference, but deliberately withheld it.

Moreover, the court eliminated the so-called "sliding scale" approach whereby a court could require less evidence of intent in the light of a highly material reference. In jettisoning this inverse relationship, the court stressed that intent and materiality are separate elements that should be weighed independent of each other.

Lastly, proving intent in any setting is difficult. In the context of inequitable conduct, rarely is there a "smoking gun." But this type of explicit evidence has not been necessary to satisfy the intent prong, as courts have inferred intent from the facts and circumstances relating to

the applicant's conduct. Inferential findings of intent are still permitted under *Therasense*, but the court adopted the "single most reasonable inference" principle, which means that "the evidence must be sufficient to *require* a finding of deceitful intent in the light of all the circumstances." Thus, when multiple reasonable inferences are present, intent to deceive cannot be found.

3. ***Materiality.*** Rule 1.56 (commonly referred to as "rule 56") of the Code of Federal Regulations – a USPTO promulgation − defines "material" as information that "is not cumulative to information already of record or being made of record," and

> (1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or
>
> (2) It refutes, or is inconsistent with, a position the applicant takes in:
>
> > (i) Opposing an argument of unpatentability relied on by the Office, or
> >
> > (ii) Asserting an argument of patentability.

37 C.F.R. § 1.56(b) (1999). The *Therasense* court rejected this definition, and adopted the more rigorous "but-for" approach; that is, a reference will be deemed material "if the PTO would not have allowed a claim had it been aware of the undisclosed" reference. The but-for test is thought to provide more certainty than prior definitions of materiality and discourage the disclosure of marginally relevant references. The dissent bemoaned the majority's new "hard and fast rules" that replaced the doctrine's longstanding flexibility, which, according to the dissent, could accommodate divergent scenarios. (The dissent's point reflects yet another instance of the rules-standards debate that we first encountered in Chapter Five - *see* page 324, Comment 3.) The dissent would have adopted the USPTO's Rule 56 definition because the (1) "PTO is in the best position to know what information examiners need to conduct effective and efficient examinations, i.e., what information is material to the examination process;" and "the higher standard of materiality adopted by the majority will not provide appropriate incentives for patent applicants to comply with the disclosure obligations the PTO places upon them."

In addition to the "but-for" test, the majority notably attached the preponderance of the evidence standard to this determination, rather than the more demanding clear and convincing evidence standard. By definition, a reference that leads to a finding of invalidity (which is subject to a clear and convincing evidence standard) is material under the "but for" test. Yet given the lower standard of proof under the but-for analysis, a reference may still be material even if it does not give rise to an invalidity finding.

The but-for test was also viewed by the court as consistent with social welfare. Enforcement of a valid patent does not harm the public, even though the applicant may have withheld a reference that a reasonable examiner would consider relevant to the claimed invention. Is there public harm if a patent would nonetheless have issued if the examiner was aware of the reference? Is there any harm to the public in this context? The dissent asserted that the majority — particularly its definition of materiality — "comes close to abolishing" the doctrine of inequitable conduct. Is this accurate? What about patent quality, a common concern over the past several years? Given the specific intent and materiality definitions, will applicants disclose fewer references, leading to lower quality patents?

4. The Carve Out: *"Affirmative Acts of Egregious Misconduct."* The court seemed to think the public could be harmed by egregious behavior such as filing an "unmistakenly false affidavit" with the PTO. This type of behavior, according to the court, is material. Is this "misconduct" material only if a patent would not have issued but-for the misconduct? The courts writes of "encouraging honesty before the PTO," but are all dishonest acts "egregious?" Can an applicant tell a non-material lie to an examiner? Is there a difference between an "unmistakenly false affidavit" and a mere "false affidavit?"

This carve out was intended to provide "sufficient flexibility to capture extraordinary circumstances." Yet what these circumstances are remains to be determined. The majority noted that the three Supreme Court cases dealing with unclean hands concerned "perjury, the manufacture of false evidence, and the suppression of evidence" as well as "deliberately planned and carefully executed scheme[s] to defraud not only the PTO but also the courts." If the exception proves to be overly accommodating as applied by the district courts, the majority's tilt towards rule-based certainty could be diluted.

5. *Supplemental Examination*. The AIA's new post-grant supplemental examination serves as a sort of amnesty or second chance for patentees who may be concerned about plausible charges of inequitable conduct. The AIA amends § 257 allows patentees to submit relevant information post-issuance. If the new information survives supplemental review without prompting a reexamination, or survives reexamination, the submitted information cannot be used later as a basis for an inequitable conduct claim. But, as the prior sentence implies, the new prior art may give rise to a "substantial new question of patentability" and potentially lead to the invalidation of the claims in question. Supplemental examination becomes effective on September 16, 2012.