United States Court of Appeals
for the Federal Circuit

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, THE AMERICAN COLLEGE OF MEDICAL GENETICS, THE AMERICAN SOCIETY FOR CLINICAL PATHOLOGY, THE COLLEGE OF AMERICAN PATHOLOGISTS, HAIG KAZAZIAN, MD, ARUPA GANGULY, PhD, WENDY CHUNG, MD, PhD, HARRY OSTRER, MD, DAVID LEDBETTER, PhD, STEPHEN WARREN, PhD, ELLEN MATLOFF, M.S., ELSA REICH, M.S., BREAST CANCER ACTION, BOSTON WOMEN'S HEALTH BOOK COLLECTIVE, LISBETH CERIANI, RUNI LIMARY, GENAE GIRARD, PATRICE FORTUNE, VICKY THOMASON, and KATHLEEN RAKER,

Plaintiffs-Appellees,

v.

UNITED STATES PATENT AND TRADEMARK OFFICE,

Defendant,

and

MYRIAD GENETICS, INC.,

Defendant-Appellant,

and

LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation,

Defendants-Appellants.

Appeal from the United States District Court for the Southern District of New York in Case No. 09-CV-4515, Senior Judge Robert W. Sweet.

BRIEF OF AMICUS CURIAE PROFESSOR EILEEN M. KANE IN SUPPORT OF PLAINTIFFS-APPELLEES AND AFFIRMANCE

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JUNE 15, 2012

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

Association for Molecular Pathology et al. v. United States Patent & Trademark Office et al.

No. 2010-1406

CERTIFICATE OF INTEREST

Counsel for the (petitioner) (appellant) (respondent) (appellee) (amicus) (name of party)
Eileen M. Kane certifies the following (use "None" if applicable; use extra sheets if necessary):

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

Eileen M. Kane

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

Eileen M. Kane

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

None

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

Eileen M. Kane, Penn State Dickinson School of Law

June 14, 2012
Date

Eileen M. Kane
Signature of counsel

Eileen M. Kane
Printed name of counsel

Please Note: All questions must be answered
cc: See Attached

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STATEMENT OF INTEREST OF *AMICUS CURIAE*

Eileen M. Kane is Professor of Law at Penn State Dickinson School of Law. Professor Kane has a Ph.D. in molecular biology, and her legal scholarship has focused on the intersection of patent law and the life sciences, with particular attention to the patent eligibility of DNA. She is a registered attorney before the United States Patent and Trademark Office. Professor Kane has no financial interest in the above referenced case. This brief is submitted because of the continuing importance of striking a balance between the patent system and the public domain. Professor Kane submits this brief as *amicus curiae* pursuant to Federal Rule of Appellate Procedure 29(a). Pursuant to Federal Circuit Rule 29(c)(5), no party's counsel authored the brief in whole or in part, no party or party's counsel contributed money that was intended to fund preparing or submitting the brief, and no person other than the *amicus* contributed money that was intended to fund preparing or submitting the brief. All parties have consented in writing to the filing of this brief.

SUMMARY OF ARGUMENT

In *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S.Ct. 1289 (2012), the Supreme Court issued a strong reaffirmation of the central role of the patentable subject matter doctrine in demarcating the boundary between a patentable inventive application or an unpatentable routine processing of basic scientific subject matter. To define this boundary, the Court uses categorical exclusions from patentable subject matter (laws of nature, natural phenomena, and abstract ideas) as a "proxy" to identify when a patent claim unjustifiably appropriates basic scientific subject matter without making an inventive contribution. *Id.* at 1303. Although *Mayo* focused on the analysis of method claims, its analytic model has generally applicability to the patentable subject matter issue in this case because it also requires that a product patent claim which bears on a product of nature or law of nature be carefully scrutinized. As the Federal Circuit requested, this *amicus* brief applies the *Mayo* analysis to the "isolated DNA" patent claims at issue (Claims 1, 2, 5, 6 and 7 of U.S. Patent No. 5,747,282, Claims 1, 6, and 7 of U.S. Patent No. 5,837,492 and Claim 1 of U.S. Patent No. 5,693,473, all of which pertain to the BRCA1 and BRCA2 genes) and concludes that these claims are attempts to patent a product of nature and to preempt a law of nature; thus, they are invalid under 35 U.S.C. § 101.

ARGUMENT

I. *Mayo* Confirms that Patent Eligibility Remains a Distinct Legal Inquiry In Patent Law and the Categorical Exclusions are Necessary

In *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S.Ct. 1289 (2012), the Supreme Court confronted the doctrine of patentable subject matter as applied to the life sciences. *Mayo* involved patent claims to methods for determining optimal pharmaceutical dosing by using the correlations between metabolite levels and drug toxicity, which the Court characterized as a "law of nature." *Id.* at 1296. The Court unanimously concluded that these patent claims lacked any inventive contribution beyond merely reciting the correlations; it stated that the steps recited in the method claim "add nothing of significance to the natural laws themselves," and that the claims were thus invalid under 35 U.S.C. § 101. *Id*. at 1302.

Mayo makes several general points regarding the necessity and rationale for the use of the patentable subject matter doctrine established by 35 U.S.C. § 101. First, the Court explicitly declined an invitation to avoid patentable subject matter questions by substituting the other doctrinal requirements for patentability (*e.g.*, utility under 35 U.S.C. § 101, novelty under 35 U.S.C. § 102, nonobviousness under 35 U.S.C. § 103, and the disclosure doctrines of 35 U.S.C. § 112), noting that "to shift the patent

eligibility inquiry entirely to these later sections risks creating significantly greater legal uncertainty." *Id.* at 1305.

Second, the Court turned to the actual complexity of the patentable subject matter doctrine, noting that the reach of 35 U.S.C. § 101 is not without limit: "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." *Id*. at 1293, quoting *Diamond v. Diehr*, 450 U.S. 175, 185, 101 S. Ct. 1048, 67 L. Ed. 2d 155 (1981). The Court then defined the policing of patentable subject matter by these categorical exclusions as a necessary predicate to maintaining a common stock of scientific knowledge in the public domain. "[T]he 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." *Id.* at 1303. In 2010, the Supreme Court provided additional context for these exclusions: "The concepts covered by these exceptions are 'part of the storehouse of knowledge of all men …free to all men and reserved exclusively to none.'" *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010), quoting *Funk Brothers Seed Co. v. Kalo Inoculant Co.,* 333 U.S. 127, 130 (1948). These recent statements from *Mayo* and *Bilski* echo the Supreme Court's observation

from 40 years ago: "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). The sum of these pronouncements from the Supreme Court signals that it regards the patentable subject matter doctrine as providing a guardianship of the "basic tools," the "building blocks" and the "storehouse of knowledge" of science – all of which are to be protected from private appropriation through a careful legal analysis of patent claims for compliance with 35 U.S.C. § 101.

Although the challenged patent claims to "isolated DNA" can be classified as compositions of matter with respect to the formal categories of inclusion detailed in 35 U.S.C. § 101, the analysis does not end there. Patent claims must not controvert the clear admonitions of the Supreme Court that patents not issue for laws of nature, natural phenomena, products of nature or abstract ideas; therefore, the patent claims at issue in this case must be closely examined to ascertain whether their reach exceeds the limits established by the Court's jurisprudence.

II. The Patent Claims to Isolated DNA Violate the Prohibitions on Patenting Products of Nature and Laws of Nature

A. The Patent Claims are Directed to Genes, Which Are Products of Nature

The patent claims at issue in this case recite "isolated DNA' that is removed from its biological surroundings, but the patentability of such claims is governed by the analysis provided by the product of nature doctrine.

The Supreme Court has instructed that the mere removal of a natural product from its environment – a preexisting product of nature – does not qualify as an inventive act which authorizes the grant of a patent on the product. In a case that considered whether a genetically engineered bacterium was a patentable invention, the Court noted that the patentable subject matter inquiry must distinguish "between products of nature, whether living or not, and human-made inventions." *Diamond v. Chakrabarty*, 447 U.S. 303, 313 (1980). To aid in identifying when inventive alteration of natural subject matter has occurred, *Chakrabarty* recognized that inventive status may be conferred when a claimed product has "markedly different characteristics" than the natural product. *Id*. at 310. The Court recognized that patent eligibility could be satisfied by a "product of human ingenuity" "having a distinctive name, character [and] use." *Id*. at

309-10. This search for difference echoes *Mayo's* insistence that "significant" and "sufficient" inventive work on the laws of nature in the patent claims was required for patent eligibility. *Mayo*, 132 S. Ct. at 1298.

The relevant analysis for the "isolated DNA" patent claims which pertain to the BRCA1 and BRCA2 genes is whether these claims can be meaningfully distinguished from the naturally occurring genes. Although described in the language of "isolated DNA," the challenged patent claims faithfully correlate to the naturally occurring wild-type genes or naturally occurring mutated genes that correspond to the human BRCA1 gene (Claims 1, 2, and 7 of U.S. Patent No. 5,747,282 and Claim 1 of U.S. Patent No. 5,693,473), the human BRCA2 gene (Claims 1, 6, and 7 of U.S. Patent No. 5,837,492) or comprise fragments of the BRCA1 gene that may operate to cover the use of that full-length gene (Claims 5 and 6 of U.S. Patent No. 5,747,282).

A formal comparison of the "isolated DNA" in the challenged patent claims on wild-type and mutant genes to the naturally occurring genes has two separate inquiries. These are the questions of structure and function. Is the isolated DNA structurally identical to the native gene? Does the isolated DNA function in the same manner as the native gene? The purified gene is claimed as an isolated complementary DNA (cDNA) – the abbreviated,

message-bearing form of the gene – produced by routine, conventional laboratory protocols. Jonathan Pevsner, *Bioinformatics and Functional Genomics* 302*,* 2nd edition (Wiley-Blackwell 2009). This isolated DNA has minimal structural alterations from its natural counterpart, none of which qualify as "the markedly different characteristics" sought by *Chakrabarty*. The chemical processing of the gene to produce an "isolated DNA" molecule is performed with a goal of producing a molecule that can faithfully reproduce its biological function as a genetic template outside its natural environment because the native informational content of the gene is preserved. The description from one of the challenged patents makes that equivalence clear ("the present invention provides an isolated polynucleotide comprising all, or a portion of the BRCA1 locus or of a mutated BRCA1 locus."). U.S. Patent No. 5,747,282, column 6, lines 25-27. In fact, any deviation from the natural DNA sequence would compromise the use of the isolated DNA as the functional equivalent of the gene in the cell. The fidelity of the DNA sequences in the patent claims to the native biological genes, coupled with an analysis of the routine technical protocols that produce the isolated gene, undermines any assertion that an inventive alteration has occurred, and leads to the conclusion that the patent claims are directed to genes, which are unpatentable products of nature.

Accordingly, the patent claims to "isolated DNA" (Claims 1, 2, 5, 6 and 7 of U.S. Patent No. 5,747,282, Claims 1, 6, and 7 of U.S. Patent No. 5,837,492 and Claim 1 of U.S. Patent No. 5,693,473) are invalid for lack of patentable subject matter under 35 U.S.C. § 101 as products of nature.

B. The Patent Claims to Genes Preempt the Genetic Code, Which is a Law of Nature

The patent claims at issue in this case recite "isolated DNA" that is removed from its biological surroundings, but the patentability of such claims is also governed by the analysis provided by the law of nature doctrine.

A detailed look at the patent claims to "isolated DNA" in these three patents reveals that all claims are either directed to or derive from explicit claims of patent rights to the "coding" sequences for the wild-type or mutated BRCA1 and/or BRCA2 genes. For example, Claim 1 of U.S. Patent No. 5,747,282 recites an "isolated DNA coding for a BRCA1 polypeptide," while Claim 1 of U.S. Patent No. 5,837,492 recites an "isolated DNA molecule coding for a BRCA2 polypeptide." All of these claims examined in the context of their patents reveal that these particular molecules and the DNA sequences they contain were chosen because of their biological and genetic relevance. The coding sequences use the genetic code to specify a specific sequence of nucleotides that dictate the amino acids which comprise

the BRCA1 and BRCA2 proteins. The correlation between DNA sequence and amino acid sequence, which has been described as the "central dogma" of molecular biology, is facilitated by the use of the genetic code. Pevsner, *Bioinformatics and Functional Genomics*, at 492. The genetic code defines the relationship between a DNA sequence and its cognate protein, without human intervention. Lily E. Kay, *Who Wrote The Book Of Life?: A History Of The Genetic Code* 276 (2000). As such, the genetic code qualifies as a law of nature. Eileen M. Kane, *Splitting the Gene: DNA Patents and the Genetic Code*, 71 Tennessee Law Review 707, 753 (2004). The genetic code is thus conceptually analogous to the correlation between drug metabolite level and biological effect which the *Mayo* court described as a "law of nature." *Mayo*, 132 S. Ct. at 1289**.** Following the analytic scheme in *Mayo*, where the Court went on to consider whether any inventive features had been added to the law of nature in the patent claim, concluding they had not, the same logic can be applied to the claims at issue in this case. There is no ambiguity about the fact that the patent claims faithfully recite naturally occurring embodiments of the genetic code, which are the genes. Genes are not invented; they are nature's exemplars of the genetic code. It is not possible to identify any value-added contribution from the defendants to the naturally occurring DNA sequence, and as a result, the claims do no more

than preempt a law of nature. The *Mayo* court expressed sharp disapproval of such an outcome. "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." *Id.* at 1301.

Accordingly, the patent claims to "isolated DNA" (Claims 1, 2, 5, 6 and 7 of U.S. Patent No. 5,747,282, Claims 1, 6, and 7 of U.S. Patent No. 5,837,492 and Claim 1 of U.S. Patent No. 5,693,473) are invalid for lack of patentable subject matter under 35 U.S.C. § 101 because they preempt laws of nature.

III. Patent Claims with No Inventive Contribution to a Product of Nature or Law of Nature Are Invalid Under *Mayo*

In *Mayo,* the Supreme Court was very clear about the need to measure the potentially preemptive or inhibitory effect of a patent against the weight of any inventive contribution provided by the subject matter of the patent. "[T]he underlying functional concern here is a *relative* one: how much future innovation is foreclosed relative to the contribution of the inventor." *Mayo*, 132 S. Ct. at 1303 (italics in original). In the view of the Supreme Court, a worst-case scenario is presented when a patent with potentially occlusive impact on the future development of a field because it will control the use of a basic scientific law is not supported by an inventive contribution that justifies such a grant of private rights. "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." *Id*. at 1303.

Such a worst-case scenario is presented by the DNA claims at issue here. Two points are critical. First, as the foregoing analysis in Parts I and II, *supra,* has detailed, the "isolated DNA" claims are directed to or derived from naturally occurring wild-type or mutant forms of the BRCA1 and BRCA2 genes or have a scope that may include naturally occurring genes. Because the "isolated DNA" is both a chemical and a template, these claims effectively capture products of nature and effectively preempt a law of nature. The presentation of a gene sequence as an "isolated DNA" molecule in the patent claims is the result of routine, well-established protocols in the field of molecular biology that do not alter or enhance the naturally occurring DNA sequence of the gene, and are conceptually analogous to the additional steps in the invalidated *Mayo* method claims which "add nothing of significance to the laws of nature." *Id*. at 1299.

Second, the patenting of DNA – as genes – removes critical scientific tools from widespread use in research and medicine by genetic scientists and

medical practitioners, with adverse consequences for patients. Patented genes significantly impact the emerging field of genetic testing, despite empirical research demonstrating that such patents are not necessary to incentivize genetic research. The Secretary's Advisory Committee on Genetics, Health and Society, *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* 15-16, 23 (2010). The BRCA1 and BRCA2 genetic testing field is a signature example of how unjustified patent claims have exerted undue weight in limiting the development of breast cancer and ovarian cancer genetic medicine. The record in this case is replete with instances where scientists had to abandon the offering of genetic testing services, doctors could not provide genetic information as part of medical care, and patients encountered limited or faulty genetic testing options for the BRCA1 and BRCA2 genes, all as a result of the restricted climate created by these patents. *Association for Molecular Pathology v. U.S. Patent &Trademark Office*, 702 F. Supp.2d 181, 205-207 (S.D.N.Y. 2010). The genes are basic scientific tools which have no effective substitutes. Rochelle C. Dreyfuss and James P. Evans, *From Bilski Back to Benson: Preemption, Inventing Around and the Case of Genetic Diagnostics*, 63 Stanford Law Revew 1349, 1371 (2011). As a result, these patent claims have produced the "danger" that *Mayo* warned

against: creating obstacles to the use of basic scientific tools, while adding "nothing of significance" to the already existing natural product. *Mayo*, 132 S. Ct. at 1302, 1303. Where exclusive control of the relevant patent portfolio for a particular disease field is used to frustrate a competitive genetic testing environment, the *de facto* clinical testing standards are set by a patent holder, rather than the scientific community. The clinical standard then becomes a function of the marketplace, rather than the laboratory. Eileen M. Kane, *Patent-Mediated Standards in Genetic Testing*, 2008 Utah Law Review 835, 849.

To emphasize its concern for maintaining the boundaries of patent eligibility, *Mayo* explicitly recognized that even if patenting were to encourage research into laws of nature and basic scientific principles, the cost of patenting basic scientific knowledge would still be too high: "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.'" *Mayo*, 132 S. Ct. at 1301, quoting *Benson*, 409 U.S. at 67.

Patent rights are reserved for truly inventive work, and patent claims to genes controvert both *Mayo* and the essential patent bargain. "A patent by

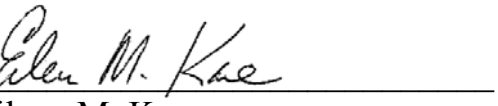
its very nature is affected with a public interest. As recognized by the Constitution, it is a special privilege designed to serve the public purpose of promoting the 'Progress of Science and useful Arts.'" *Precision Instrument Mfg. Co. v. Auto. Maint. Mach. Co*., 324 U.S. 806, 816 (1944) (quoting U.S. CONST. art I, § 8, cl.8).

CONCLUSION

The inventive precision enforced through the proper application of 35 U.S.C. § 101 – as *Mayo* has demonstrated - will allow creative applications of fundamental knowledge to emerge and legitimately solicit legal protection, while the intellectual substrates for research and innovation remain unowned. For the reasons stated, the judgment of the District Court that the patent claims on isolated DNA are invalid for lack of patentable subject matter under 35 U.S.C. § 101 should be affirmed.

Dated: June 15, 2012

Respectfully Submitted,



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ASSOCIATION FOR MOLECULAR v. PTO, 2010-1406

CERTIFICATE OF SERVICE

I, John C. Kruesi, Jr. being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

Counsel Press was retained by Eileen M. Kane, *Amicus Curiae* to print this document. I am an employee of Counsel Press.

On the **15th Day of June, 2012**, I served the within **Brief of Amicus Curiae** upon:

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June 15, 2012