
**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 AMICI CURIAE CHRISTOPHER M. HOLMAN AND ROBERT
COOK-DEEGAN IN SUPPORT OF NEITHER PARTY**

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OCTOBER 28, 2010

FORM 9. Certificate of Interest

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

The Association of Molecular Pathologist et al. v. USPTO and Myriad Genetics, Inc.

No. 2010-1406

CERTIFICATE OF INTEREST

Counsel for the (petitioner) (appellant) (respondent) (appellee) (amicus) (name of party)

Christopher M. Holman and Robert Cook-Deegan 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:

Christopher M. Holman and Robert Cook-Deegan

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:

Christopher M. Holman and Robert Cook-Deegan

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. [X] 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:

Christopher M. Holman, UMKC School of Law

Oct 28, 2010
Date

Signature of counsel
Christopher M. Holman
Printed name of counsel

Please Note: All questions must be answered
cc: _____

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STATEMENT OF INTEREST OF *AMICI CURIAE*

Amici curiae are academics who have studied and written about gene patent law and policy. Chris Holman has a PhD in molecular biology and is currently a law professor. In 2007 he conducted a comprehensive study of human gene patent litigation that resulted in three published articles on the subject. He has published numerous articles relating to the intersection of patent law and biotechnology, and is the author of a widely read blog dedicated to biotechnology patent law (Holman's Biotech IP Blog). Robert Cook-Deegan directs the Center for Public Genomics, which conducted eight case studies of the impact of patenting and licensing on genetic testing for ten clinical conditions commissioned by the US Secretary's Advisory Committee for Genetics, Health and Society, published in April 2010, and several other articles arising in this research. That research was supported by a center grant from the National Human Genome Research Institute and US Department of Energy.¹

Affiliations of amici are provided in Appendix A solely for the purpose of identification. No part of this brief was authored by counsel for any party, person, or organization besides *amici*. Our sole interest in this case is maintenance and development of a sensible patent system that accomplishes the constitutional goal of “promot[ing] the Progress of Science and useful Arts,” particularly in the area of

¹ A list of publications from that center grant is available at <http://www.genome.duke.edu/centers/cpg/publications/>.

genetic diagnostic testing, and more generally in biotechnology and life sciences.
Counsel of Record Daniel Ravicher and Gregory Castanias have consented to the
filing of this brief.

SUMMARY OF ARGUMENT

In their zeal to address perceived public policy concerns associated with Myriad's gene patents, and more particularly Myriad's controversial business and patent enforcement practices, plaintiffs have invoked the recently re-invigorated patent eligibility doctrine in a manner that threatens to wreak substantial collateral damage on future innovation in genetic diagnostic testing, personalized medicine, and biotechnology in general. DNA patents have created incentives critical in attracting the substantial investment necessary to fuel the discovery and development of life-saving products produced by the biotechnology industry. Although plaintiffs have identified numerous potential concerns with gene patents in the context of some types of genetic diagnostic testing, to date there is insufficient evidence that harms attributable to patents on genes justify broad, subject matter-based invalidation of all patents made of or based on DNA. More appropriate and targeted legal and policy solutions to problems associated with some gene patents and patent enforcement practices are preferable to the blunt doctrinal instrument of patent eligibility. The decision below should be reversed in order to prevent substantial unintended negative consequences for innovation in this increasingly important technology sector, and to enable adjudication of patentability using other tools that are more appropriate to the task.

ARGUMENT

I. Introduction

Plaintiffs object to Myriad's patents, and especially to some of Myriad's patent enforcement and business practices, arguably with some justification. *Amici* do not express an opinion with respect to the ultimate validity of the challenged patent claims, nor to the propriety of Myriad's business practices. Unfortunately, however, in their zeal to eradicate what they perceive to be a significant public health concern, plaintiffs have chosen a strategy which implicates not only Myriad and its patents, but if successful would invalidate, or at the very least cast substantial doubt upon, a host of patents claiming gene-based inventions, often referred to as "gene patents" and indeed many other technologies based on making and analyzing DNA. If affirmed on appeal, the decision below could have substantial negative implications for future developments in genetics and biotechnology.

This court has substantial discretion under applicable Supreme Court precedent to interpret and implement the patent eligibility doctrine in a manner that fosters innovation, and does not prematurely preclude the availability of adequate patent protection for nascent, information-based technologies. As correctly noted by the Patent Office in its recently published Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of *Bilski V. Kappos*, in most

cases issues of claim validity are better addressed using more targeted and well-established doctrines of patent law. Federal Register Vol. 75, No. 143, 43922, July 27, 2010 (“examiners should avoid focusing on issues of patent-eligibility under § 101 to the detriment of considering an application for compliance with the requirements of §§ 102, 103, and 112, and should avoid treating an application solely on the basis of patent-eligibility under § 101 except in the most extreme cases.”) We do not believe this is such an extreme case. We urge this court to refrain from interpreting the patent eligibility doctrine in a manner that broadly implicates the validity of a host of important patents, based on concerns that could be more surgically and appropriately addressed with other patent law doctrines, or legal and policy solutions addressing problematic enforcement practices rather than DNA patents in general.

II. Gene patents have for years played an important role in incentivizing innovation in applied genetics and biotechnology

The USPTO has a long-standing policy of sanctioning gene patents of the type at issue in this case, and has issued thousands of such patents over a period extending more than 30 years. Kyle Jensen & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, 310 SCIENCE 239 (2005); Georgetown DNA Patent Database, <http://dnapatents.georgetown.edu/> Gene patents constitute the core intellectual property platform for companies dedicated to translating the fruits of biomedical research into life-saving therapeutic and diagnostic agents. They

have played a critical role in providing innovators with a sufficient period of market exclusivity to recoup the sizable investment necessary to develop and secure marketing approval for biotechnology products. J.H. Graham et al., *High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey*, 24 Berkeley Technology Law Journal 1255 (2010).

In Europe, gene patents have been more controversial than in the US, but the debate ultimately has been resolved in favor of gene patents. The European Union issued a Biotechnology Directive in 1998 requiring member countries to permit gene patents. Directive 98/44/EC of the European Parliament on the Legal Protection of Biotechnological Inventions. Some European countries have limited the scope and/or enforceability of these patents to a greater extent than the United States, but all currently permit gene patents. Notably, gene patents directed towards the BRCA genes associated with inherited risk of breast and ovarian cancer recently were found valid after being challenged in opposition proceedings in the European Patent Office, although the scope of these claims appears narrower than initially granted and than some of the US claims at issue in this case. Case T 1213/ 05 *The University of Utah Research Foundation Et al.* (2007) , Case T 0080/05 *The University of Utah Research Foundation Et al.* (2008), and Case T 0666/05 *The University of Utah Research Foundation Et al.* (2008). Many of these issued European claims would appear to be patent ineligible under the decision

below. Thus, affirmance of the decision would cause US patent law to diverge from European law with respect to this important class of patents.

In biotechnology, gene patents often serve as the same function as drug patents in the traditional pharmaceutical industry. For example, a comprehensive study of gene patent litigation conducted by one of the authors of this brief in 2007 (the "Holman study") concluded that most instances of human gene patent infringement litigation have involved an innovator biotechnology company enforcing its patent against a direct competitor in order to maintain market exclusivity for a biologic drug developed by the patent owner. Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, 76 UMKC L. REV. 295 (2007). Two authoritative reports from the Congressional Office of Technology Assessment and a 2009 report issued by the Federal Trade Commission (FTC) concluded that gene patents have provided the "fuel" for the "R&D engine" bringing biologic drugs to patients. Commercial Biotechnology: An International Analysis (Washington, D. C.: U.S. Congress, Office of Technology Assessment, OTA-BA-218, January 1984); U.S. Congress, Office of Technology Assessment, *Biotechnology in a Global Economy*, OTA-BA-494 (Washington, DC: U.S. Government Printing

Office, October 1991); Emerging Healthcare Issues: Follow-On Biologic Drug Competition, Federal Trade Commission Report (June 2009).²

One of the important products of biotechnology, for example, is recombinant erythropoietin, a biologic drug first brought to the market in the 1980s by Amgen under the trade name Epogen. *Amgen, Inc. v. Chugai Pharm. Co.*, 706 F. Supp. 94, 104 (D. Mass. 1989). Recombinant erythropoietin was the product of groundbreaking research conducted by Amgen, which required a substantial investment of capital. *Amgen, Inc. v. Chugai Pharm. Co.*, Not Reported in F. Supp., 1989 WL 169006, at *7-*18. However, erythropoietin is a naturally occurring human protein that was isolated prior to Amgen's work, and the patent claiming isolated erythropoietin protein per se expired around the time Amgen entered the market with its recombinant product. As a consequence, Amgen has relied primarily on gene patent protection to protect its product. For example, when another biotechnology company attempted to bring a competing erythropoietin product to market in the US, Amgen successfully sued, using its patent claiming the erythropoietin gene. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212-14. (Fed. Cir. 1991). Significantly, Amgen's core patent claim directed toward the gene, which this court held infringed and not invalid in *Chugai*, is almost identical

² Although the FTC Report does *not* specifically identify "gene patents" as the primary "fuel," every example cited in the report of a biologic innovator successfully asserting its patent against a competitor involved a gene patent. FTC Report at 37.

to some of the composition of matter claims invalidated in the decision below (particularly the first two claims of US patent 5,747,282; the '282 patent).³

III. Gene patents have not been shown to create public policy concerns so substantial or pervasive that they would warrant invocation of the doctrinal sledgehammer of patent ineligibility

Initially, much of the concern over gene patents was based on a fear that they would create a “patent anticommons” that would impede biomedical research. Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698 (1998). However, after more than a decade it is becoming increasingly apparent that the feared anticommons has for the most part failed to materialize, at least in noncommercial, academic research. For example, the Holman study of human gene patent litigation did not identify a single instance in which basic research activities or noncommercial genetic diagnostic testing led to a patent infringement lawsuit.⁴ Likewise, surveys have shown that researchers, particularly basic and academic researchers, routinely ignore patents, and that patents have had little if any limiting effect on their research. *See generally* John P. Walsh et al., *Effects of Research Tool Patents and*

³ US Patent Number 4,703,008, Claim 2 ("A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.").

⁴ Myriad did sue the University of Pennsylvania for infringement of BRCA gene patents, but the university was reportedly charging \$1900 for performing the BRCA tests.

Licensing on Biomedical Innovation, in PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285-340 (Wesley M. Cohen & Stephen A. Merrill eds., 2003).

DNA hybridization array technologies, as exemplified by the Affymetrix gene chip and Illumina bead arrays, provide a compelling example of how research has progressed apace despite fears that gene patent thickets might hinder their use. Hybridization arrays have been commercialized and widely used in basic and commercial biomedical research and diagnostics since the early 1990s, and for many years academics have pointed to hybridization arrays as a poster child for the patent thicket. John H. Barton, *Emerging Patent Issues in Genomic Diagnostics*, 24 NATURE BIOTECHNOLOGY 939 (2006). Hybridization arrays can involve the use of polynucleotide representing many thousands of genes in a single product, and it was thought that with so many issued gene patents it would be prohibitively burdensome to obtain licenses or patent clearance to make or use the arrays.

In fact, however, the Holman study found that hybridization array technology has never been the subject of a patent infringement lawsuit *involving a gene patent*. Hybridization arrays have generated copious patent litigation – Affymetrix, Illumina and other companies have been involved in many patent infringement cases - but these lawsuits have involved patents directed towards various other technologies used in hybridization arrays, not gene patents.

There are many possible explanations for the lack of human gene patent litigation over hybridization arrays, but the lack of effective remedies for the gene patent owner could be part of it. Under the *eBay* standard, it seems unlikely that a court would issue an injunction stopping the use of a product or service involving many thousands of genes based on the infringement of patents claiming one or a few of those genes, particularly if the product or service were serving an important public health function. *eBay v. Mercexchange*, 547 U.S. 388 (2006).

This would leave the award of money damages as the remedy for a prevailing patent owner. Under either a lost profits or reasonable royalty analysis, infringement of a gene patent by a hybridization array containing polynucleotides representing many thousands of genes should result in a modest award of damages to the owner of a patent on just one or a few of those genes. Most concerns about the negative impact of gene patents are based on an assumption that patents are always enforced, but experience with hybridization arrays illustrates that there are practical constraints on injudicious patent enforcement.

Today, most of the angst over gene patents centers around their potential negative effect on genetic diagnostic testing. The recently released *Revised Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient*

Access to Genetic Tests (the SACGHS Report),⁵ for example, identifies a *potential* for a substantial negative impact of gene patents on genetic diagnostic testing, but concludes that there is currently no conclusive evidence establishing that gene patents have had a net negative impact on the availability of genetic testing services. Many gene patents are non-exclusively licensed for use in genetic diagnostic testing, thus permitting competing clinical laboratories to offer the test. Some patent owners such as Myriad retain exclusive control in the US, but the SACGHS Report did not identify any instance where patents caused a test to be entirely unavailable to patients for a prolonged period of time (case studies referenced in the report did reveal problems, but not pervasive, system-wide harm).

It is important to recognize that the SACGHS Report addresses two distinct forms of restrictions on access. There are restrictions on the ability of competing commercial diagnostic testing laboratories to offer tests on a particular gene owing to the patent owner's exclusive licensing practices, and there are restrictions on the ability of patients and healthcare providers to obtain testing on a desired gene. The two should not be conflated - restrictions on the ability of competing laboratories to provide the test without licensing the patents does not necessarily imply that patients and healthcare providers are unable to obtain the testing they desire.

⁵ Available at <http://oba.od.nih.gov/oba/SACGHS/SACGHS%20Patents%20Report%20Approved%202-5-20010.pdf>.

For example, Myriad's assertion of exclusive rights to perform BRCA testing has caused some competing laboratories to exit the US market, but there is no clear evidence that this has resulted in less patients being tested in the US. To the contrary, as exclusive provider in the US Myriad has invested substantially in facilitating insurance reimbursement and in promoting awareness of BRCA testing, which arguably has resulted in more individuals being tested for BRCA mutations in the US than would have been the case otherwise. Indeed, one concern raised in the case studies was overutilization of BRCA tests SACGHS case study.

Similarly, SACGHS looked for evidence that patent-based exclusivity resulted in higher costs for genetic testing services, but was unable to document any consistent effect. The SACGHS Report states that "[O]ne surprising finding from the case studies was that the per-unit price of the full-sequence BRCA test, which often is cited as being priced very high, was actually quite comparable to the price of other full-sequence test done by polymerase chain reaction (PCR), at both nonprofit and for-profit testing laboratories."

To date, there has been little patent litigation involving gene patents and genetic diagnostic testing. The Holman study identified several instances in which lawsuits have been filed asserting human gene patents against a provider of genetic diagnostic testing services, but in every case the parties settled quickly. Until the decision below, it appears that no court had ever addressed substantive issues of

patent validity or claim scope with respect to a gene patent asserted in the context of diagnostic testing. Thus, providers of genetic diagnostic testing services have never attempted to challenge human gene patents on more conventional grounds, such as noninfringement or invalidity under section 102, 103 or 112, and so it is premature to assume that these less sweeping patent challenges would be ineffective to deal with the policy concerns alleged by plaintiffs with respect to the patent claims at issue.

IV. Concerns raised with respect to Myriad's patents, and gene patents in general, could be better addressed using other doctrines of patentability and appropriate claim interpretation

Plaintiffs assert that at the time Myriad identified and characterized the BRCA genes, the existence of the genes was well known and multiple laboratories were actively engaged in efforts to isolate and sequence the genes. They argue that it was inevitable that one of these laboratories would have succeeded, and thus BRCA genetic testing would have been made available regardless of Myriad's contribution. The decision below states that "the consensus among the scientific community" is that Myriad was not the first to sequence the BRCA2 gene.

In essence, statements such as these question the inventiveness of Myriad's claimed compositions and methods. But the appropriate legal doctrines for addressing these concerns are novelty and nonobviousness, not patent eligibility. If the allegations are accurate, and at the time of Myriad's invention there was

widespread knowledge that the BRCA genes existed, motivation to isolate them, and methods for isolating and sequencing the gene with a reasonable likelihood of success were available, recent case law suggests that the patent claims could have been invalidated for obviousness under Section 103 of the patent statute. *KSR International Co. v. Teleflex Inc.*, 550 US 398 (2007); *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009). And if in fact the “consensus” is correct that others had succeeded in isolating the BRCA2 gene prior to Myriad, the novelty requirement under Section 102 is likewise implicated.

The policy advantage of using the nonobviousness and novelty requirements to address these concerns, rather than patent ineligibility, lies in the ability of these doctrines to distinguish between new and nonobvious inventions warranting patent protection, and non-inventions that are either anticipated by the prior art, or which would have been obvious to those skilled in the art at the time of the invention.

Plaintiffs also argue that challenged claims are overly broad, completely blocking the ability of others to perform any sort of genetic testing, or to perform research, and even preventing doctors from communicating with their patients. In so doing, they (like many critics of gene patents) fail to heed the most fundamental maxim of patent law, to wit, "the name of the game is the claim."⁶ Some of those claims may be invalid. Or when properly interpreted, at least some of the

⁶ Quoting Judge Giles S. Rich.

challenged claims likely would likely not have the broad preclusive effect that plaintiffs attribute to them.

For example, the product claims reciting the full-length BRCA coding sequence would not appear to be infringed by conventional BRCA mutation testing as it is currently practiced, which involves the amplification and sequencing of relatively short fragments of the full-length gene sequence. Robert Cook-Deegan et al., *Impact of gene patents and licensing practices on access to genetic testing for inherited susceptibility to cancer: comparing breast and ovarian cancers with colon cancers*, 12 *Genetics in Medicine* S15 (2010). Since the full-length BRCA coding sequence is not made or used in the process of diagnostic sequencing, it is hard to see how infringement could be shown for these claims.

Some of the other challenged claims appear broader on their face, and more likely to be infringed by conventional genetic diagnostic testing, but that does not necessarily mean these claims are valid, or could not be circumvented by future technological advances in DNA analysis and diagnostic technology. To date there have been no judicial decisions addressing the interpretation and scope of human gene patent claims in the context of genetic testing, so it is difficult to predict how expansive the scope of these claims would be once they emerge from the crucible of patent litigation.

However, in the context of biologic drugs, human gene patents have been litigated extensively on a number of occasions, and there have been multiple instances in which an alleged infringer successfully designed around a human gene patent that on first inspection might have appeared quite broad. Christopher M. Holman, *Learning from Litigation: What Can Lawsuits Teach Us About the Role of Human Gene Patents in Research and Innovation?* 18 Kansas Journal of Law & Public Policy 215, 223-29 (2009) (examples discussed include *Genzyme v. Transkaryotic Therapies*, 346 F.3d 1094 (Fed. Cir. 2003) (claims broadly reciting methods for recombinant production of human α -galactosidase A not infringed by method employing gene activation technology); *Regents of University of California v. Eli Lilly*, 119 F.3d 1559, 1571-74 (Fed. Cir. 1997) (patent on insulin gene circumvented by expressing protein as a fusion); *Novo Nordisk v. Genentech*, 77 F.3d 1364, 1371 (Fed. Cir. 1996) (apparently broad gene patent circumvented by the use of protein fusion technology); *Berlex v. Biogen Laboratories*, 318 F.3d 1132 (Fed. Cir. 2003) (claims to cells that have been genetically engineered to express the human interferon gene not literally infringed by cells produced using alternate transformation method); *Schering v. Amgen*, 222 F.3d 1347 (Fed. Cir. 2000) (patent claiming naturally occurring interferon gene not infringed by consensus interferon product).

All of Myriad's composition of matter claims recite isolated polynucleotides (i.e., DNA and/or RNA molecules). It is not a foregone conclusion that these claims would necessarily cover any and all technologies that could be used to perform BRCA diagnostic testing. For example, this court recently held that diagnostic testing procedure that employs peptide nucleic acids (PNAs), which are synthetic, non-naturally occurring DNA analogs, did not literally infringe a method claim reciting the use of "nucleic acids," because PNA is not a nucleic acid. *Regents of the Univ. of Cal. v. Dakocytomation*, 517 F.3d 1364 (Fed. Cir. 2008). PNAs can substitute for DNA molecules in at least some diagnostic applications, and in some respects perform better than their naturally occurring DNA counterparts.⁷ This example is provided not to suggest that Myriad's composition of matter claims could necessarily be circumvented by use of synthetic DNA molecules, but it illustrates that claims to isolated polynucleotides are not necessarily impervious to being designed around in the context of diagnostic testing.

Similarly, it is not clear that all formats of genetic diagnostic testing necessarily require the making or using of "isolated" DNA molecules in the way

⁷Petra P. Paulasova & Franck Pellestor, *The Peptide Nucleic Acids (PNAs): A New Generation of Probes for Genetic and Cytogenetic Analyses*, 47 ANNALS DE GÉNÉTIQUE 349 (2004), available at http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15581832.

courts might interpret the term. There is no definitive case law on the question of exactly how "isolated" should be interpreted in diagnostics. Does "isolated" apply to "copied as found in nature" or not? Some assume that a claim reciting an isolated DNA molecule should be interpreted as broadly encompassing the DNA in any context outside its native context in the human body. However, there is reason to think that if the issue were litigated, a narrower interpretation might be imposed. For example, a 2002 district court decision seems to imply (without addressing the issue head-on) that a claim to an isolated DNA molecule does not cover recombinant cells genetically engineered by the introduction of a plasmid containing the claimed DNA molecule. *Synaptic Pharmaceuticals Corp. v. MDS Panlabs*, 265 F.Supp.2d 452 (D.N.J. 2002). Claims on "isolated" DNA might require some transformation from DNA as found in nature, or a functional change, but such case law interpretations would leave some DNA inventions patentable. If DNA is ruled to be patent-ineligible *per se*, such case law cannot develop.

Some whole genome sequencing technologies currently in development rapidly scan a single molecule of DNA in order to determine its sequence. Kevin Davies, *THE \$1000 GENOME* (New York:Free Press 2010). It is not clear whether or not these technologies involve the making or using of "isolated" DNA molecules as that term is properly interpreted in the context of issued human gene patents. If "isolated" is so expansive that full-genome sequencing infringes thousands of

individual gene claims, then a serious patent thicket could arise. Yet case law could narrow the scope of “isolated” under existing patent doctrines without invoking patent-eligibility.

It is important to bear in mind that the broader the term "isolated" is interpreted, the more vulnerable the claim is to validity challenges under Sections 102, 103 and 112. The broader the scope of a patent claim, the more susceptible it is to invalidation for violating one of the requirements of patentability. *See* Giles S. Rich, *The Proposed Patent Legislation: Some Comments*, 35 Geo. Wash. L. Rev. 641, 644 (1967) (explaining that “the stronger a patent the weaker it is and the weaker a patent the stronger it is.”).

Some of the claims at issue in the case below might illustrate this principle. Claim 5 of US patent number 5,747,282, for example, recites any “isolated DNA having at least 15 nucleotides of the [full length BRCA-encoding DNA sequence].” In principle, fragment claims such as this provide much broader coverage than claims reciting full-length genes, and would appear to encompass conventional BRCA mutation testing that involves the amplification and analysis of DNA fragments as used in diagnostic testing. If the claim is interpreted that broadly, however, it raises significant validity issues.

In particular, a recent study found that 80% of the cDNA and mRNA sequences that were contributed to GenBank (and hence presumably published)

before the effective filing date of the '282 patent contain at least one DNA fragment falling within the scope of Claim 5, and thus would apparently be encompassed by the claim. Thomas B. Kepler, Colin Crossman and Robert Cook-Deegan, *Metastasizing patent claims on BRCA1*, Genomics (2010), doi:10.1016/j.ygeno.2010.03.003. Follow-up studies have shown many “hits” of 15-mer sequences in GenBank sequences that had already been deposited more than a year before patent application, thus implicating 35 USC 102(b). It thus appears that either this claim (and the similar claim 6) is invalid because it is not novel, or courts would have to interpret the claim in a narrower sense than suggested by a plain reading of the claim language.

More generally, enablement and written description are the appropriate doctrinal tools for challenging overly broad patent claims, not patent eligibility. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991) (overly broad gene patent claim invalidated for lack of enablement); *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed.Cir.1997)(overly broad gene patent claim invalidated for lack of adequate written description).

Recent lawsuits filed by Ariad Pharmaceuticals against Eli Lilly and Amgen exemplify the effective use of limiting claim interpretation and claim invalidation under section 112 as alternatives to patent ineligibility. Eli Lilly attempted to invalidate Ariad's claims by arguing they are patent ineligible, but ultimately

succeeded in obtaining the same result using the written description requirement. *Ariad Pharmaceuticals v. Eli Lilly*, 598 F.3d 1336 (Fed. Cir 2010). Amgen, on the other hand, avoided liability by successfully arguing that the claims when properly construed do not cover their allegedly infringing products. *Amgen v. Ariad Pharmaceuticals*, 333 Fed.Appx. 549 (Fed. Cir 2009). In both cases, conventional patent doctrine was sufficient to fend off Ariad's allegations of infringement, without slamming the gate on patent eligibility.

Arguably, some of the claims at issue in the case below exceed a scope that is commensurate with the nature of the inventors' contribution to the art. One of the broadest claims among the contested patents is claim 1 of US Patent 5,753,441, which on its face appears to encompass the identification of any difference between a sample sequence and a standard (normal or "wild type") reference sequence for BRCA1. While it is true that the inventors identified the genes' location and some disease-associated variations, many of the more than 2000 known BRCA variants, some of which confer cancer risk and some of which do not, were only identified after Myriad applied for these patents. The claim would appear to encompass the detection of any variation, even variations that were not known to be associated with disease at the time of the invention. Even in 2010--that is, 16 years after gene discovery and 12 years after patent grant--some *BRCA* tests are reported as "variants of unknown significance," i.e., the clinical

implications of the genetic variation are unknown. The scope of the claim appears on its face to include not only the variants known to confer risk, and disclosed in the patent, but also gives exclusive rights to detect any variants of the gene including those discovered since and yet to be discovered, regardless of clinical or scientific utility.

To its credit, Myriad has tracked the clinical significance newly discovered variants it finds.⁸ But it is clear that the clinical significance of such variants has required hard work over a decade and a half by Myriad and many other clinical researchers; and this important task remains incomplete. Myriad may well have invented a genetic test for inherited risk of breast and ovarian cancer, but Myriad's patents arguably claim more than they invented. A careful claim-by-claim review of those patents could restrict their patent exclusivity to the scope of their actual invention. This kind of review would narrow the scope of the patents without endangering patents on genes that enable production of valuable therapeutic proteins, vaccines, and other useful molecules. Yet case law cannot determine proper claim scope if no claims on DNA are allowed at all.

Properly drafted and interpreted, gene patent claims should not have the broad inhibitory effect on access and innovation asserted by the critics. The remedy to unduly broad scope is invalidation based on insufficient enablement or

⁸ Cook-Deegan, DeRienzo, et al. 2010.

inadequate written description, not a blanket prohibition on the patenting of anything made of or based on DNA. Once again, these other doctrines of patentability can limit gene-based patent claims to an appropriate scope, rather than using the patent eligibility doctrine that would unnecessarily invalidate all DNA-based patents indiscriminately and regardless of their merit.

V. Concerns with Myriad's patent enforcement and business practices could be better addressed by other means

Most of the current anxiety surrounding gene patents in general, and Myriad's patents in particular, centers around their potential negative impact on genetic diagnostic testing and research. The extent of the problem is currently unclear and the subject of much debate. However, if society determines that the business and enforcement practices of some gene patent owners is problematic in some contexts, it would be more appropriate to consider alternatives that more directly address the enforcement concerns, rather than interpreting patent eligibility in a manner that broadly precludes effective patent protection for DNA-based inventions in general.

For example, since the real concern with gene patents is the potential for restrictions on research and genetic testing, a more targeted approach could involve the creation of some sort of limitation on infringement liability for those using patented genetic technology in research or genetic testing. This was the recommendation of the SACGHS Report. Along similar lines, the Genomic

Research and Diagnostic Accessibility Act, introduced in Congress in 2002 but never enacted, would have amended the patent statute to eliminate liability for use of certain patented genetic technologies in basic research and diagnostic testing. Genomic Research and Diagnostic Accessibility Act of 2002, H.R. 3967, 107th Cong. (2002). In fact, the patent statute already contains a provision that shields healthcare providers from liability for acts of patent infringement occurring during the performance of "medical activities." 35 USC 287(c). If Congress concludes that gene patents do pose a threat to genetic testing, the statutory safe harbor could be expanded to explicitly encompass providers of genetic diagnostic testing services.

If necessary, other approaches such as compulsory licensing, invocation of march-in rights, and assertion of state sovereign immunity could be considered. Joshua D. Sarnoff & Christopher M. Holman, *Recent Developments Affecting the Enforcement, Procurement, and Licensing of Research Tool Patents*, 23 Berkeley Tech. L.J. 1299 (2008). These approaches would be extreme, and would not appear to be justified at the present time, but are available should some gene patent enforcement practices prove to be as deleterious to the public interest as plaintiffs allege in this case.

International experience with BRCA testing reinforces this point. Myriad has established a *de facto* BRCA testing monopoly in only one jurisdiction, the

United States. In the United Kingdom, the National Health Service rebuffed Myriad's business plan. Shobita Parthasarathy. 2007. *Building Genetic Medicine: Breast Cancer, Technology, and the Comparative Politics of Health Care*. Cambridge, MA: MIT Press. In Canada, Australia, and Europe Myriad has not become the sole provider of even first-line BRCA testing. E. Richard Gold and Julia Carbone. 2010. Myriad Genetics: in the eye of the policy storm. *Genetics in Medicine*. 12 Supplement (April): S39–S70. This suggests that what most distinguishes the United States from other countries is not the strength of its patent system but the weakness and inaction of other stakeholders in the US health system.

The National Institutes of Health, as a partial funder of this research, has rights in the inventions through both the Stevenson-Wydler and Bayh-Dole Acts, and under Bayh-Dole has authority to march in if “health and safety needs” are not met by the patent holder. The government pays for almost half of health services through Medicare, Medicaid, the Veterans Health Administration, Indian Health Service, military health system, Tricare, and Federal Employee Health Benefits plan. And private payers can condition coverage and reimbursement decisions on compliance with business practices to promote access to tests and interpretation of their results. Experience in the rest of the world suggests that to the extent there are problems with Myriad's business practices, the remedy can be found in

awakening US agencies and institutions from their stupor rather than foregoing the patent incentive for all inventions based on DNA.

Some have expressed concern that Myriad has leveraged its patent-based status as exclusive BRCA testing provider in the US to amass a proprietary database of sequence variants associated with cancer risk that could serve to maintain market dominance, even after the relevant patents have expired. Clinicians rely on this information to interpret test results. Until November 2004, Myriad was a major contributor to public databases of BRCA mutations. But since 25 November 2004, Myriad has not shared data on mutations they discover, or about their clinical significance except through selective publication.

The practical consequence is that clients sending samples to Myriad can benefit from its proprietary database of mutations and clinical findings, while others cannot. In effect, Myriad could leverage its US patent exclusivity—which makes it the largest BRCA testing service in the world—into a permanent proprietary database. Interpreting the clinical significance of variants characterized since Myriad stopped sharing data with public databases will depend on either Myriad's sharing them or on others replicating the work that Myriad used its US sole provider status to develop.

But it is important to bear in mind that using patent exclusivity to leverage other forms of exclusivity is not unique to diagnostics, and there are mechanisms

for dealing with it. For example, anticompetitive business practices used to maintain a monopoly are more properly addressed by the antitrust laws. There are also potential market-based solutions. For example, as noted above, most genetic diagnostic testing is paid for by third-party providers, including the US government. Payers can demand that Myriad share data if interpreting test results depends on such sharing.

VI. The lower court's invalidation of claim 20 of the '282 patent illustrates the problem with using patent eligibility to address a perceived problem with gene patents

Claim 20 of the '282 patent covers what is commonly referred to as a cell-based assay, used to identify potential drugs for the treatment of cancer. The claimed method involves substantial human intervention, including genetic engineering of a recombinant cell culture to express a BRCA variant, and use of the resulting cell culture in a laboratory screening procedure to identify pharmaceutically active chemical compounds.

Nonetheless, the decision below invalidated this claim for patent ineligibility. If this claim is patent ineligible, it is hard to imagine a biotechnology claim that is eligible for patent protection. This illustrates the unsuitability of patent eligibility for distinguishing between patentable and unpatentable biotechnology inventions, and the danger of unintended negative consequences for biotechnology if the decision below is affirmed.

VII. Affirmance of the decision below could result in substantial unintended consequences impeding the development of future genetic diagnostic tests, personalized medicine and biotechnology

Looking forward, companies focused on the development of pharmacogenomics and personalized medicine—technologies widely viewed as critical to the future of pharmaceutical development and healthcare—point to gene patents as critical to securing the funding necessary to bring these products to market. See, for example, *Amici Curiae* briefs filed in the court below on behalf of BayBio et al., Genetic Alliance, and the Biotechnology Industry Organization. Affirmance of the decision below could dramatically reduce the private incentive for investment in innovation in these and related fields.

The decision below could also undermine incentives for the development of new biologics, an increasingly important class of life-saving drugs. As noted above, gene patents have historically played a role in providing market exclusivity for biologic innovators in the past, and they could be even more important now that Congress has created an abbreviated approval process for follow-on biologics. Affirmance of the decision below could have an unintended but nonetheless substantial negative impact on patent protection to develop these often life-saving therapeutic products.

The availability of patent protection for genetic inventions could become more important if the cost of bringing future genetic tests to market increases.

Some would argue that gene patents are not required to promote innovation in genetic diagnostic testing, based on an assumption that the relevant genes and mutations will be discovered with or without the incentive of a patent, and that once the genetic variations have been identified and correlated with disease it requires little investment to commercialize a genetic test. Given that patent holders and those holding exclusive licensing to first-generation diagnostic gene patents were rarely “first to market,” this argument might be valid with respect to the BRCA genes and other single genes highly correlated with disease. Cho M, Illangasekare S, Weaver M, Leonard, D, Merz J. 2003. Effects of patents and licenses on provision of clinical genetic testing services. *J. Mol. Diagnostics* 5(1):3–8; see also the eight case studies of ten clinical conditions prepared for the Secretary’s Advisory Committee on Genetics, Health and Society and published in a supplement to *Genetic in Medicine* (April 2010), in which none of the companies that patented or exclusively licensed gene patents for Mendelian medical conditions was first to market. It does not follow, however, that publicly funded research will suffice to discover and develop the next generation of genetic testing technologies. Indeed, the complexity of nascent diagnostics suggests they will be expensive to develop.

Much of the future of genetic testing will lie in identifying more complex patterns of genetic variation involving a large number of genes dispersed

throughout the genome, or identification of complex gene expression patterns. Personalized medicine will involve identifying correlations between genetic variation and specific therapeutic compounds. These next-generation diagnostic testing products and services might very well require a substantial private investment, increasing the importance of the patent incentive. A wholesale elimination of patent protection for genetic inventions, as embodied in the decision below, could impair future innovation in diagnostics.

Another factor to be considered is the likelihood that at some point the Food and Drug Administration (FDA) will take a more active role in regulating genetic diagnostic testing, and require a submission of data demonstrating safety and efficacy, similar to the current requirements with respect to drugs and medical devices. FDA regulation would substantially increase the investment necessary to commercialize new genetic diagnostic tests compared to past genetic tests, and patents might be necessary to induce adequate private investment. Finally, if the Centers for Medicare and Medicaid Services or private health plans and insurers begin to demand clinical studies before they cover and reimburse for genetic tests, development costs would rise dramatically to pay for long-term clinical studies to supply evidence of clinical validity and utility.

CONCLUSION

For these reasons, this Court should reverse the district court on its determination that the claims at issue are patent ineligible.

Respectfully submitted;

A handwritten signature in black ink, appearing to read 'C. M. Holman', written over a horizontal line.

Christopher M. Holman

*Counsel for Amici Curiae Christopher
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APPENDIX A –LIST OF *AMICI CURIAE*

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**United States Court of Appeals
for the Federal Circuit**

ASSOCIATION FOR MOLECULAR V PTO, 2010-1406

**DECLARATION OF AUTHORITY PURSUANT TO
28 U.S.C. § 1746 AND FEDERAL CIRCUIT RULE 47.3(d)**

I, Elissa Matias, being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

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October 28, 2010


Elissa Matias

**United States Court of Appeals
for the Federal Circuit**

ASSOCIATION FOR MOLECULAR V PTO, 2010-1406

CERTIFICATE OF SERVICE

I, Elissa Matias, being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

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