UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

ASSOCIATION FOR MOLECULAR PATHOLOGY; AMERICAN COLLEGE OF MEDICAL GENETICS; AMERICAN SOCIETY FOR CLINICAL PATHOLOGY; 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; KATHLEEN RAKER,

Plaintiffs,

v.

UNITED STATES PATENT AND TRADEMARK OFFICE; MYRIAD GENETICS; 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.

09 Civ. 4515 (RWS)

ECF Case

BRIEF FOR AMICI CURIAE

Rosetta Genomics, Ltd.
Rosetta Genomics, Inc.
George Mason University

IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

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STATEMENT OF INTEREST OF AMICI CURIAE

Rosetta Genomics, Ltd. ("Rosetta Genomics") is a leading molecular diagnostics company advancing minimally-invasive molecular tests based on the use of nucleic acids found in the human body, and platform technologies. Rosetta Genomics, Inc., is a wholly owned, U.S. subsidiary of Rosetta Genomics. Rosetta Genomics has launched three diagnostic tests for cancer and is currently developing additional tests for the diagnosis of additional human cancers. In addition, Rosetta Genomics is the owner of numerous patents claiming isolated nucleic acid sequences. See, for example, U.S. Patent Nos. 7,618,814, 7,592,441, 7,250,496, 7,217,807 and 7,642,348. Thus, issues raised in this case are of great importance to Rosetta Genomics and Rosetta Genomics, Inc.

George Mason University is a public university located in Virginia. The university includes numerous laboratories and facilities conducting cutting-edge research in the biosciences, including cancer research and proteomics. Its new biomedical research laboratory is one of 13 nationwide being built with the help of a $25 million grant from the National Institute of Allergy and Infectious Diseases. Certain research conducted by the universities' scientists is incorporated into patent applications covering cancer diagnostics. See, for example, U.S. Patent Publication No. 2009/0275546. Thus, issues raised in this case are of great importance to George Mason University.

INTRODUCTION

Why patenting exists and matters, especially regarding gene patents

The U.S. Constitution provides a clear basis for patent legal protection in the United States. Specifically, Article 1, Section 8, Clause 8, empowers Congress "[t]o promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries" (emphasis added). Congress and U.S. courts have always understood this clause to provide, for a limited time, an "exclusive right" to prevent others from unauthorized activity, i.e., the right to exclude others from practicing a patented invention for the life of a patent term.

Thus, a patent right may, for a limited time, restrict access to unauthorized use of an invention. As such, a patent right may impede certain unauthorized research, even including some basic research at universities and other non-profit organizations, prevent practitioners, such as doctors, from doing certain things, and allow certain commercial products to be more expensive initially. U.S. patent law deliberately allows for this type of activity. The right to exclude others for a limited time. and the consequences of that patent right applies to all technology, whether it be isolated DNA, diagnostic methods, or any other type. This patent right, and the benefit it provides to patentees, promotes innovation because it encourages research and development by offering the "carrot" of patent protection. In exchange for this "carrot," patentees must disclose their invention to the public, and once the limited duration of the patent expires, dedicate the invention to the public for all to use. Disclosure of the invention to the public is a stimulus for further innovation. This quid pro quo is the foundation of our patent policy.

Indeed, patent rights allow innovators to recoup significant costs for up-front investments. In biotechnology and biomedical fields in particular, such costs universally include time-consuming and expensive research and development, as well as extensive and costly regulatory approval. As stated by Judge Mayer in *Bilski*, "the pharmaceutical industry relies on patent protection in order to recoup the large sums it invests to develop life-saving and life-enhancing drugs[.]"[1] In fact, such recoupment via patent protection is especially important in biomedical fields where many products never make it to market or otherwise get into patients' hands, even after innovators have spent years and millions of dollars on up-front investment costs. As noted by Rep. Howard Coble (R-N.C.) during Congressional hearings held on gene patents in November 2007: "American biotech companies are more reliant on the Patent Act than any other industry."[2]

Moreover, cost recoupment associated with a single successful product often also must pay for other research and development that fails to bear fruit. As explained in a law review article quoted by Judge Mayer in *Bilski*:

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[1] *In re Bilski*, 545 F.3d 943, 1005-06 (Fed. Cir. 2008) (en banc) (J. Mayer dissenting from the majority opinion holding certain business method patents patentable, where J. Mayer distinguishes such patents from those directed to pharmaceutical products).

[2] *Stifling or Stimulating - The Role of Gene Patents in Research and Genetic Testing: Hearing Before the Subcomm. On Courts, the Internet and Intellectual Property of the H. Comm. On the Judiciary*, 110 Cong. 5 (2007) (statement of Rep. Howard Coble (R-N.C.), Ranking Member of House Judiciary Committee, Subcommittee on Courts, the Internet and Intellectual Property) (Exhibit 1), where Rep. Coble states:

> American biotech companies are more reliant on the Patent Act than any other industry. While a few biotech companies are large, most are smaller and lack the internal financing resources to subsidize their drug research and development. This is especially true of small start-up companies whose valuation is an exclusive function of their patent portfolios.

> [T]he "fully loaded" cost of developing a single new pharmaceutical molecule, taking it though laboratory and clinical trials, and securing FDA approval for its marketing is today about $800 million (including the cost of project failures). Furthermore, fewer than one in five drug candidates that make it out of the laboratory survive this tortuous process and reach the marketplace in the form of FDA-approved pharmaceuticals.... Only patent protection can make the innovator's substantial investment in development and clinical testing economically rational.

Bilski, 545 F.3d at 1006 (J. Mayer dissenting opinion) (quoting Jay Dratler, Jr., *Alice in Wonderland Meets the U.S. Patent System*, 38 Akron L.Rev. 299, 313 (2005) (footnotes omitted) (Exhibit 2)).

It is not any more restrictive, unfair or costly to innovation to grant this limited exclusive right to patentees in the realm of newly discovered genetic inventions, as compared to any other technology relating to patient care or otherwise. Furthermore, as discussed in more detail below, absent a viable way to recoup significant investment costs, innovation and advances in health care and biotechnology, especially by those responsible for "applying" or "translating" basic laboratory research into actual patient benefit and products, will be profoundly and negatively effected.

As explained by the Supreme Court: "The subject-matter provisions of the patent law have been cast in broad terms to fulfill the constitutional and statutory goal of promoting 'the Progress of Science and the useful Arts' with all that means for the social and economic benefits envisioned by Jefferson." *J.E.M. AG Supply, Inc. v. Pioneer Hi-Bred Int'l.*, 534, U.S. 124, 131 (2001) (quoting *Diamond v. Chakrabarty*, 447 U.S. 303, 315, 100 S.Ct. 2204 (1980)). The contrary position advocated by plaintiffs today is short-sighted regarding the ultimate effect on biotechnology and medical innovation, particularly beyond basic science at the laboratory bench. Moreover, plaintiffs present a slippery slope that could easily be extrapolated to undermine the very existence of patent protection for any invention, whether it be genetically based, medically

related or otherwise. In short, plaintiffs position is contrary to the U.S. Constitution, statutes, regulations and federal case law, which all work as intended to promote science and innovation.

ARGUMENT

I. What this *Amici Curiae* brief will address – patentability of "isolated DNA" claims

This brief will not address certain important issues already considered in other briefs and memoranda filed in this case, and elsewhere. Specifically, this brief will not address the standing issue, nor patentability of Myriad's diagnostic method claims.

Plaintiffs' briefs and memoranda clearly indicate that they wish to knock out all patents relating to genetic material, regardless of whether such patents recite composition claims, such as those directed to nucleotide or protein sequences, or any method claims reciting genetic or recombinant material in some way. While the patents at issue in this case relate to *BRCA* genes, the overall outcome proposed by plaintiffs, and their stated rational for doing so, have sweeping implications for any patent claim reciting a gene or nucleotide sequence.

The Supreme Court is now considering relevant issues regarding patentability of certain diagnostic method claims in pending cases such as *Bilski* and *Prometheus*. *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) (en banc), cert. granted, --- U.S. ----, 129 S.Ct. 2735 (2009); *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336 (Fed. Cir. 2009) (petition for cert. filed October 22, 2009). By contrast, however, the Supreme Court and Federal Circuit are not currently addressing patentability of composition claims reciting genetic material. As such, this brief will address plaintiffs' arguments regarding patentability of Myriad's "isolated DNA" claims. This District Court should consider the patentability issue as it relates to "isolated DNA" claims, and grant defendants' motion for summary judgment in favor of patentability regarding at least these composition claims.

II. Congress Is the Proper Forum To Address Plaintiffs' Underlying Concerns

Why do the ACLU and other plaintiffs (research societies, organizations and M.D./Ph.D.s, and breast cancer patients) care about this case? As presented in their filed papers, plaintiffs' overriding concerns do not simply relate to patenting of gene technology *per se*, but broadly apply to patents covering any medically related technology. Specifically, plaintiffs concerns spurring this litigation appear to be:

- "[e]ase of access to genomic discoveries" in order for "basic research to be... expeditiously translated" into benefit to patients;[3]
- patients are allegedly prevented from obtaining information about their health risks and/or obtaining a second opinion;[4]
- the ability of uninsured and other patients to afford commercial products;[5] and
- researchers and laboratories are allegedly prevented "from independently offering testing" to patients, or from developing or implementing improvements or new tests.[6]

What plaintiffs fail to acknowledge, however, is that the above-cited concerns exist regarding any patented technology impacting medical care, whether it be in the field of genetic/diagnostics, small molecule pharmaceuticals, medical devices or otherwise.

To the extent plaintiffs have concerns about deterring research and innovation and promoting accessibility and affordability of diagnostic tests and other genetic inventions, other avenues exist to address such concerns without undermining our current patent system. For example, it is incorrect that patents on gene technology always prevent research, testing or

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[3] *See, e.g.,* Complaint, page 2 and 18-19 (¶¶ 2, 48).

[4] *See, e.g.,* Complaint, page 2 and 18-19 (¶¶ 2, 48).

[5] *See, e.g.,* Complaint, pages 2 and 10-13 (¶¶ 2, 21, 22, 24-26).

[6] *See, e.g.,* Complaint, page 2, 11 and 18-19 (¶¶ 2, 22, 23, 48).

development of improvements, as plaintiffs suggest. Even assuming an activity in question infringes a patent, one can get permission and/or pay for the right to do so. As noted by the U. S. Patent and Trademark Office ("USPTO"), "[i]t is somewhat rare for academic researchers to be sued by commercial patent owners for patent infringement. Most inventions are made available to academic researchers on very favorable licensing terms, which enable them to continue their research." U. S. Patent and Trademark Office Utility Examination Guidelines, 66 F.R. 1092, 1096, Comment (16) (2001) (addressing subject matter patentability of gene patents) ("USPTO Guidelines").

In addition, as stated by the U.S. Department of Health and Human Services ("HHS") Secretary's Advisory Committee on Genetics, Health, and Society ("SACGHS") in 2009:

> It is important to note that access to genetic tests may be hindered by high prices, fear of discrimination, difficulty in obtaining the tests, regulatory or certification requirements, lack of coverage by payers or demands by insurance payers for evidence of clinical utility, all of which could be seen to be at work to a greater or lesser extent in one or more of the case studies. Many of these factors are a function of unique aspects of the overall U.S. health care system, rather than a specific function of intellectual property rights.

Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS): Public Consultation Draft Report on Gene Patents and Licensing Practices and the Impact on Patient Access to Genetic Tests 70 (2009). http://oba.od.nih.gov/oba/SACGHS/SACGHS%20Patents%20Consultation%20Draft%203%209%202009.pdf.

Thus, plaintiffs' concerns relate to health care costs and insurance, the ability to obtain a license or otherwise get authorized access to the patented technology of interest, and/or the existence (or lack thereof) of research exemptions from infringement for non-profit organizations or individuals. Plaintiffs' concerns are improperly directed, however, as an attack on

patentability of all gene patents, a position that effectively "throws the baby out with the bathwater."

Even assuming plaintiffs' concerns are not properly balanced under current law against other considerations, the matter is one for Congress to address. Congress is the proper forum and is well positioned to address plaintiffs' raised concerns without broadly overturning patent laws. By contrast, the court system is not the venue to disrupt U.S. patent law that currently provides the financial backbone for the entire biotechnology industry in this country.

For instance, Congress could address specific cost and insurance concerns in a pending health care bill. Likewise, although not believed necessary by *Amici Curiae*, Congress could put into place broader exemptions to liability for infringement of certain types of gene patents, as applied only to non-commercial research activity of basic researchers, clinicians and non-profit research institutions. Congress could also put in place mandatory licensing requirements of gene patents, assuming it is in the public interest to do so. In fact, a Congressional hearing on October 30, 2007, addressed some of these very suggestions.[7]

Regarding such suggestions, limited exemptions to infringement liability already exist under U.S. patent law. *See, e.g.*: (1) a research exemption under the Plant Variety Protection Act;[8] (2) a narrow "experimental use defense" to infringement under *Madey v. Duke*;[9] (3) a "safe

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[7] *Stifling or Stimulating - The Role of Gene Patents in Research and Genetic Testing: Hearing Before the Subcomm. On Courts, the Internet and Intellectual Property of the H. Comm. On the Judiciary*, 110 Cong. 19-22 (2007) (statement of Lawrence Sung, Director, Intellectual Property Law Program, University of Maryland School of Law) (Exhibit 1).

[8] United States Plant Variety Protection Act, 84 Stat. 1542, as amended, 7 U.S.C. § 2321 et seq.; *J.E.M AG Supply, Inc. v. Pioneer Hi-Bred Int'l.*, 534 U.S. 124, 129 n.1 (2001) (stating that "[u]tility patents issued for plants do not contain such exemptions").

[9] *Madey v. Duke University*, 307 F.3d 1351, 1362 (Fed. Cir. 2002).

harbor" infringement exemption under the Hatch-Waxman Act (35 U.S.C. § 271(e)(1)) [10]; and (4) an infringement exemption under 35 U.S.C. § 287(c) provided to medical practitioners or related health care entities using a patented medical or surgical procedure on a human body. Notably, in § 287(c)(2)(A), Congress expressly excluded "the use of a patented machine, manufacture or composition of matter," as well as "the practice of a process in violation of a biotechnology patent" from a medical or surgical procedure infringement exemption.

Likewise, regarding licensing considerations, under the Bayh-Dole Act, Congress has already provided "march-in" rights that afford "a responsible applicant or applicants" a non-exclusive, partially exclusive, or exclusive license to inventions that were federally funded under certain circumstances. 35 U.S.C. § 203. For example, a federal agency may grant a compulsory license to inventions stemming from federally funded research if, for example, it is "necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees [to the invention]." *Id.* at § 203(a)(2).

Thus, Congress has already considered issues relevant to infringement exemptions and compulsory licensing, and in the biotechnology context in particular. To the extent that current U.S. statute and court precedent do not sufficiently promote innovation and/or health care choices as alleged by plaintiffs, Congress is the appropriate forum to address such issues. As stated by the Supreme Court, "Congress, not the courts, must define the limits of patentability",

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[10] *See Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202 (2005) (emphasis in original) (stating that the safe harbor "extends to all uses of patented inventions that are reasonably related to the development and submission of *any* information under the FDCA [Federal Food, Drug, and Cosmetic Act].").

even if it is also "true that once Congress has spoken it is 'the province and duty of the judicial department to say what the law is.'"[11]

As Congress already knows, the vast majority of those in the biotech industry advocate against any action by Congress that would broaden current infringement exemptions or compulsory licensing. For example, the Biotechnology Industry Organization ("BIO") recently stated the following when addressing a possible recommendation by the SACGHS Committee of HHS to broaden the current research use exemption under patent law as applied to genetic tests:

> This vague and ill-informed suggestion risks unintended consequences for the development and availability of important new biomedical research tools, and finds no basis of support in either the Committee's own fact-finding, or that of previous efforts by the National Academies and other expert bodies that have specifically and thoroughly reviewed the question of whether gene patents inhibit research.

Tom Dilenge, BIO Comments on the Draft report of the Secretary's Advisory Committee on Genetics, Health and Society on Gene Patenting and licensing Practices and Their Impact on Patient Access to Genetic Tests 4 (2009), http://bio.org/ip/domestic/SACGHS_Oral_Statement%2010-8-09.pdf

It is noteworthy that Congress recently considered, but chose not to take, the drastic action proposed by plaintiffs in this case. *See* H.R. 977: "Genomic Research and Accessibility Act" (a bill that never became law, introduced by Rep. Xavier Becerra [D-CA31] on February 9, 2007, in 110th Congress) (proposing to amend 35 U.S.C. "to prohibit the patenting of human genetic material") (http://www.govtrack.us/congress/bill.xpd?bill=h110-977).

Congress has every reason to refuse to take such action. Gene patents, such as those directed to isolated DNA, have allowed genetic research and the biotechnology industry to grow

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[11] *J.E.M AG Supply*, 534 U.S. at 130 (quoting *Chakrabarty*, 447 U.S. at 315) (quoting *Marbury v. Madison*, 1 Cranch 137, 177 [2 L.Ed. 60] (1803)).

and thrive. For example, as noted in Myriad's Summary Judgment Memo, over 18,000 scientists have conducted research on the *BRCA1* and *BRCA2* genes, and have published more than 7,000 papers on those genes since the relevant patents issued. Myriad Defendants' Memorandum of Law (1) In Support of Their Motion for Summary Judgment and (2) In Opposition to Plaintiffs' Motion for Summary Judgment ("Myriad's Summary Judgment Memo"), pages 1 and 6. In fact, such scientists include eight plaintiffs and plaintiffs' declarants in this case, who have themselves published over 48 scientific papers on the *BRCA1* and *BRCA2* genes. *Id.* at page 46.

III. Abolishing Gene Patents Will Deter, Not Promote, Innovation

Plaintiffs inaccurately assume that relevant scientific progress is hindered by the existence of patents on genetic inventions. Contrary to plaintiffs' short-sighted view, abolishing patents on genetic inventions will have more of a dampening effect on research and development in relevant medical fields than any patent right could ever do.

For starters, abolishing patent rights for genetic technology will certainly, at minimum, deter "translational" research and innovation. A closer examination of plaintiffs' position indicates their narrow understanding that abolishing gene patenting will not deter basic research performed at the bench at universities and non-profit research institutions, such as the NIH. The plaintiff scientists, for example, wish to ensure that their specific research in the laboratory or clinic is not deterred. It may be the case that abolishing gene patents will allow them unfettered access to certain genetic discoveries publicly disclosed by others, reduce a possible hindrance to publishing research papers (critical to the livelihood of researchers), and otherwise allow the scientists to rely and piggyback on the hard work of others.

What plaintiffs fail to consider, however, are the astronomical costs and inherent large risks associated with "translating" basic science to something actually used by patients. *See, e.g.*, Skolnick Decl. ¶¶10, 15, 17 and 18; Critchfield ¶ 41. The reality is that most "translational"

aspects of genetic innovations (i.e., going from laboratory to market to bedside) are not funded or even performed by scientists or clinicians at non-profit entities, which usually do not have the finances or know-how needed to obtain FDA-approval and/or scale up for mass production and clinical use.

As stated by Rep. Howard Coble during relevant Congressional hearings in 2007:

> The National Institutes of Health is the world's largest agency for conducting basic medical and biological research with a budget in excess of $28 billion, but the pharmaceutical and biotech industries devote more than $50 billion annually to research. The process of identifying a DNA sequence through clinical testing and manufacturing of an FDA-approved drug may cost the patent holder in excess of a billion dollars, yet only a third of all drugs ever generate revenues sufficient to cover those costs, and the great majority ... do not realize a profit.[12]

In other words, even the NIH—a non-profit entity that collectively has the biggest budget for biomedical R&D (including all extramural funding going to researchers and institutions outside NIH)—does not come close to having the same resources or ability that the private sector has to provide actual medical therapies and tests to patients.

Thus, much important R&D, and certainly nearly all "translational" or "applied" aspects, are established and performed by for-profit companies, which are themselves often funded by investors who are able to take large financial risks.[13] Such risks, regardless of who takes them,

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[12] *Stifling or Stimulating - The Role of Gene Patents in Research and Genetic Testing: Hearing Before the Subcomm. On Courts, the Internet and Intellectual Property of the H. Comm. On the Judiciary*, 110 Cong. 4 (2007) (statement of Rep. Howard Coble (R-N.C.), Ranking Member of House Judiciary Committee, Subcommitte on Courts, the Internet and Intellectual Property) (Exhibit 1).

[13] *See* Tom Dilenge, BIO Comments on the Draft report of the Secretary's Advisory Committee on Genetics, Health and Society on Gene Patenting and licensing Practices and Their Impact on Patient Access to Genetic Tests 4 (2009), http://bio.org/ip/domestic/SACGHS_Oral_Statement%2010-8-09.pdf stating:

> While [the Committee's] contention that patenting does not serve as a powerful incentive in this particular area [regarding "association" patent claims] may have

must also involve some prospect of reward to recoup, at minimum, the high costs associated with "translating" the specific innovation in question into a viable benefit for patients. Otherwise, the entire system that currently exists in the U.S. to provide diagnostics and therapies to patients becomes unworkable, as it necessarily leads to a significant financial loss for any initial innovator.

This significant loss will occur, not in small part, due to the fact that other non-innovating for-profit entities will have every incentive to piggyback and freeload off the significant effort and investment of an original innovator. As explained by the USPTO, "[o]ther researchers may discover higher, better or more practical uses, but they are advantaged by the starting point that the original disclosure provides." USPTO Guidelines, 66 F.R. at 1094, Comment (7).

In fact, if gene patents no longer exist, particularly in a difficult economy, many biotech/pharma companies will have no choice but to either freeload off others, or rely on previously established products. Biotech/pharma companies, who are otherwise solely responsible for getting products to patients, simply will not have the finances (nor the potential of finances) to do otherwise. In the absence of viable patenting or other meaningful exclusive rights, innovators will be immediately subject to instant competition by others who will take advantage of the innovator's investment costs while providing nothing in return. This phenomenon will deter anyone from being the initial innovator.

More specifically to the current case, abolishing gene patents could also effectively kill the relatively new diagnostic and personalized medicine industries altogether, especially in the

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some basis with respect to basic research performed by purely academic researchers, such an analysis ignores the fact that great research in this area is also done by for-profit entities, and that the applied research and development process is the more difficult and costly part and is largely carried out by the private sector.

current economy. Diagnostic and other biotech companies and investors will be unwilling and/or unable to make the needed financial upfront investments. *See, e.g.*, Critchfield Decl. ¶ 25; Linck Decl. ¶¶ 74-75.

In short, without involvement of for-profit groups/investors, most basic research will stay exactly where it will start—in academia or with other non-profit basic research institutions. Skolnick Decl. ¶ 18. Very little new and truly innovative research will get past the basic research stage. Thus, the availability of entirely new diagnostics and treatments for patents will slow to a trickle and eventually dry up.

The current debate on biosimilars (also called follow-on biologics) in Congress likewise provides many details as to why exclusive rights are necessary for innovators in the area of biologics. *See, e.g.,* BIO SMARTBRIEF SPECIAL REPORT, December 15, 2009, "*An interview with Ceregene co-founder/Chairman and BIO Board Chair Dr. Stephen Sherwin*" (stating that "we must be careful to preserve the intellectual property protections that support continued innovation. The incentive to invest in developing a novel biologic therapy, diagnostic or vaccine is removed if the novel therapy cannot recoup the substantial research and development capital invested.") (Exhibit 3). While a debate may still exist regarding an appropriate time frame for market exclusivity, no pending legislation relating to this issue suggests that patenting of biologics should be abolished altogether.

IV. Patent Claims Directed to "Isolated DNA" Do Not Impede Research or Innovation

Plaintiffs inaccurately assume, based on what appears to be a misconception of science and/or patent law, that researchers are unable to work within, work around or "invent around" currently existing gene patents.[14]

[14] *See, e.g.,* Complaint, pages 25-26.

As recently explained regarding gene patents in the scientific journal *Nature*:

> A survey last year revealed that for more than 40,000 gene patents, only six instances of litigation came up in relation to diagnostic testing (C. M. Holman, *Science* **322**, 198-199, 2008). All six were settled or dismissed within a year and a half, suggesting that the scale of litigation is not as high as some suspected. Reports of researchers being blocked from access to patented DNA sequences or being sued for infringement are extremely rare, and workarounds are not difficult from a legal perspective.

Property rights: The granting of patents on human genes has so far not been the disaster it was predicted to be. 458 Nature 386 (2009) (Exhibit 4). Thus, gene patents, such as Myriad's patents at issue, do not block researchers from access to patented DNA sequences. Moreover, "workarounds" are viable.[15]

Regarding Myriad's gene patents in particular, as recently stated by the SACGHS at HHS:

> Myriad's monopoly and enforcement activities may have inhibited research—more clearly, clinical research on the use of genetic testing rather than basic research. Nonetheless, a considerable amount of research has proceeded, and any chilling effect has been at the margins. Myriad states that it has no intention of inhibiting research. Indeed, in most (but not all) instances, it is in Myriad's interest to promote research and application, because Myriad garners profits from any U.S. testing.

Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS): Public Consultation Draft Report on Gene Patents and Licensing Practices and the Impact on Patient Access to Genetic Tests 75 (2009) http://oba.od.nih.gov/oba/SACGHS/SACGHS%20Patents%20Consultation%20Draft%203%209%202009.pdf. In other words, even Myriad's own patents have not impeded research and

[15] *See also Impact of Gene Patents and Licensing Practices on Access to Genetic Testing Compendium of Case Studies Commissioned for SACGHS by the Duke University Center for Genome Ethics, Law & Policy*. A31 and A36 (2009), http://oba.od.nih.gov/oba/SACGHS/Appendix%201%20SACGHS%20Patents%20Consultation%20Draft%20Compendium%20of%20Case%20Studies.pdf

development in relevant scientific areas, or even patient or clinical access to tests. *See also* Myriad's Summary Judgment Memo, pages 6 and 46 (citing Parvin Decl. ¶¶ 3-6; Baer Decl. ¶¶ 3-6; Li Decl. ¶¶ 3-6; Critchfield Decl. ¶¶ 3, 13).

In fact, Myriad's patents in this case have significantly stimulated relevant research. As noted above, over 18,000 scientists (including plaintiffs and plaintiffs' declarants in this case) have conducted research on the *BRCA1* and *BRCA2* genes, and have published more than 7,000 papers on those genes since the relevant patents issued. Myriad's Summary Judgment Memo, pages 1, 6 and 46 (citing numerous declarations in support).

Lastly, all the patents here will expire in 2014 or 2015. The scientific community will have full benefit of inventors' innovation and patentee's investment at that time. Notably, the USPTO issued all patents in this case by 1998, except one patent reciting certain method claims, which issued in 2000. Plaintiffs chose, however, not to file their Complaint in this case until May 2009, i.e., more than a decade after relevant patents issued. Thus, plaintiffs waited to file its case until after Myriad commercially launched its BRAC*Analysis*® test, invested significant time and money to raise awareness and understanding of genetic testing to patients and health care providers, and achieved tremendous medical success with the test over the last ten years. *See* Crichfield Decl., ¶¶ 26-30. Skolnick Decl. ¶¶ 19-23.

It is only now, after countless patients and scientists have benefited from patentees' innovation, investment and public disclosure, that plaintiffs ask to abolish these patents altogether. The timing of the Complaint indicates an effort by plaintiffs to take unfair advantage of what Myriad and its scientists have spent years establishing as a useful and available test for breast cancer patients.

V. Patentability under 35 U.S.C. § 101 – "Isolated DNA" Claims

The Supreme Court has interpreted §101 broadly.[16] As stated by the Supreme Court in *Chakrabarty*: "Anything under the sun that is made by man" is patentable. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980); *see also* S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952); H.R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952). That said, limits on patentable subject matter do exist. Specifically, the following are not patentable under current U.S. law: laws of nature, natural phenomena, abstract ideas, mathematical formulas or algorithms, mental process, as well as products and processes of nature, including genes, proteins, cells or organisms as occurring in nature. *See, e.g.*, *Diamond v. Diehr*, 450 U.S. 175, 185 (1981); *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972).

At the same time, case law has established that "while a claim drawn to a fundamental principle"—i.e., a law of nature, natural phenomenon, or abstract idea—"is unpatentable, 'an application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.'" *Bilski*, 545 F.3d at 953 (quoting *Diehr*, 450 U.S. at 187). As well stated by the USPTO in its Utility 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." USPTO Guidelines 66 F.R. at 1093, Comment (1).

Notably, contrary to plaintiffs' assertions, a substantial body of case law supports patentability of chemical compounds, such as DNA, that are isolated from nature. *See, e.g.*, Linck Decl., ¶¶ 29-42, 50-77; Rebecca S. Eisenberg, *Genetics and the Law: Patenting the*

[16] 35 U.S.C. § 101 states: "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."

Human Genome, 39 Emory. L.J. 721, at 727 and n. 27 (1990) (listing "a substantial body of case law" on point) (Exhibit 5). As stated by the USPTO, "[p]atenting compositions or compounds isolated from nature follows well-established principles, and is not a new practice." USPTO Guidelines 66 F.R. at 1093, Comment (1) (citing numerous cases).

The Declaration of Dr. Nancy Linck submitted by defendant Myriad in this case, as well as other *Amicus Curiae* briefs filed in support of defendants, discusses relevant case law at length, and addresses plaintiffs' misinterpretation of the law as relating to subject matter patentability of gene patents. *Amici Curiae* here would like to simply add a short discussion pertaining to *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948). As done with other case law, plaintiffs erroneously rely on this Supreme Court decision to support an assertion that isolated DNA are products of nature. In fact, a close reading of *Funk Bros.* affirmatively supports current case law and determinations by the USPTO dictating that isolated DNA may be patentable subject matter.

In his majority opinion in *Funk Bros.*, Justice Douglas considered claims directed to an inoculant for plants "comprising a plurality of selected mutually non-inhibitive strains of different species of bacteria of the genus *Rhizobium*, said strains being unaffected by each other in respect to their ability to fix nitrogen ...." *Id.* at 128 n.1 Notably, the claims at issue did not recite any specific strains of bacteria, but only that the bacteria be "unaffected by each other." As stated by Justice Douglas:

> No species acquires a different use. The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect it always had. The bacteria perform in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee.

Funk Bros., 333 U.S. at 131 (emphasis added). Thus, the majority held that such claims were not

patentable.

The above-quoted factors relied upon by the Supreme Court in *Funk Bros.* distinguish claims at issue there from claims directed to "isolated DNA" at issue in the current case. "Isolated DNA" differs from a gene existing in the body, not least of which because an "isolated DNA" provides an "enlargement of the range of [the] utility" of the gene, as discussed by Justice Douglas. For instance, isolated DNA can be used in recombinant techniques to make purified protein in a large amount, in a form and manner that never exists inside the body. Petricoin Decl., ¶ 22. At minimum, isolated DNA allows one to isolate an expressed protein in a purified form that that might otherwise be difficult, expensive or even impossible to obtain. *Id.* Isolated DNA and recombinant techniques may also avoid undue burden on a humans or animals, as might otherwise be needed to extract a sufficient amount of a protein of interest. *Id.*

Moreover, isolated DNA does not merely "serve the ends nature originally provided." *Funk Bros.*, 333 U.S. at 131. Isolated DNA can be used to do all sorts of things that do not otherwise naturally occur. For example, unlike naturally-occurring DNA, isolated DNA may be used as a primer for synthesis of DNA in a polymerase chain reaction (PCR). Petricoin Decl., ¶ 21. In addition, one can use isolated DNA to create a transgenic animal, such as a mouse over-expressing a human gene of interest. Petricoin Decl., ¶ 23. In any event, isolated DNA, by definition, simply cannot "act quite independently of any effort of the patentee," as discussed by Justice Blackman. *Funk Bros.*, 333 U.S. at 131. *See also* Petricoin Decl., ¶ 20.

In his concurrence in *Funk Bros.*, Justice Frankfurter also notes the following:

> It only confuses the issue, however, to introduce such terms as 'the work of nature' and the 'laws of nature.' For these are vague and malleable terms infected with too much ambiguity and equivocation. Everything that happens may be deemed 'the work of nature,' and any patentable composite exemplifies in its properties 'the laws of nature.' Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every

patent.

Id. at 134-35 (emphasis added). In other words, one must take care when determining that subject matter is unpatentable because it is allegedly a product of nature. Nearly everything is arguably a product of nature, which can lead to a slippery slope of undermining all patents. It is exactly this slippery slope that plaintiffs pursue today.

In this case, the recited "isolated DNA" is a man-made, non-naturally occurring composition of matter, and therefore patentable subject matter. "Isolated DNA" only comes about as a result of human intervention. Petricoin Decl., ¶ 20.

Judge Learned Hand of the Southern District of New York wrote a pivotal early decision, which acts as direct binding precedent on this District Court. *Parke-Davis & Co. v. H.K. Mulford & Co.*, 189 F. 95, 103 (S.D.N.Y. 1911), *aff'd*, 196 F. 496 (2d Cir. 1912) (finding purified adrenalin composition patentable in view of fact that patent holder was the first to make adrenalin available for therapeutic use by removing it from the other gland-tissue in which it was found). Plaintiffs summarily dismiss this case law by asserting that "[w]hereas the human body does not possess a natural process for purifying adrenaline, the human body does possess a natural process for isolating and purifying genes." Plaintiffs' Memorandum of Law in Support of Motion for Summary Judgment ("Plaintiffs' Summary Judgment Memo"), page 25. This statement is scientifically incorrect.

The human body does not have a mechanism for isolating a gene sequence, and consequently, isolated DNA is not found in the body. Gene expression involves the production of mRNA through transcription and translation, i.e., processes that occur in the naturally-occurring environment of the cell. At no time during these processes, however, is DNA "removed from its naturally occurring environment." Petricoin Decl., ¶ 26.

Specifically, while a human body does transcribe a gene into mRNA, which is then translated into a protein, the human body never, at any time, isolates or purifies a gene as recited in an "isolated DNA" patent claim. A gene naturally exists on one of two strands of DNA (the coding strand) within a chromosome, where the coding strand remains intact during cellular processes, such as transcription or DNA replication. Likewise, genes exist on chromosomes as DNA transcription units, which contain not only the sequence that is ultimately translated into a protein (the coding sequence), but also regulatory sequences that exist both before (upstream from) and after (downstream from) the coding sequence, including promoters, transcription factors, enhancers and termination sequences. Petricoin Decl., ¶ 27 Many isolated DNA sequences (e.g., SEQ ID NOs) recited in gene patents do not include endogenous regulatory sequences or, in the case of cDNA, introns (which are not necessarily transcribed) normally present between exons in genes in the body. Petricoin Decl., ¶ 15 (also noting that genomic *BRCA1* and *BRCA2* genes contain introns).

Accordingly, isolated DNA are necessarily obtained by the hand of man, who must use highly sophisticated genetic and molecular techniques to identify and isolate genes. Petricoin Decl., ¶ 31. Dr. Sulston, a declarant for plaintiffs, also recognizes that "many *inventive* steps have been necessary to allow us to extract and read a genetic sequence . . . ." Sulston Decl., ¶17 (emphasis added).

Regarding the *BRCA1* and *BRCA2* genes in particular, isolation of these genes and corresponding nucleotide sequences claimed in the Myriad Genetics' patents required skillful and inventive enterprise. When the work began, the inventors did not know which of three billion nucleotide sequences in the human genome comprised the *BRCA1* and *BRCA2* genes. As a result of the inventive work of the Myriad inventors, we now know that the longest form of a

BRCA gene has about 80,000 nucleotides. A gene comprised of 80,000 nucleotides represents about 0.003% of the human genome, an infinitesimally small portion of the total number of nucleotides in the human genome. Petricoin Decl., ¶ 30.

Isolated DNA comprising the *BRCA1* or *BRCA2* gene has a very different structure from that which occurs naturally. The isolated sequences are no longer located on a human chromosome and therefore are not necessarily assembled in the native chromatin structure. Depending on how the isolated DNA is produced, it may not be methylated, or it may have a very different pattern of methylation than the naturally-occurring gene. Petricoin Decl., ¶ 18.

In addition, the environment of a DNA molecule dictates not only its structure, but also its uses. Petricoin Decl., ¶ 18.; Linck Decl., ¶48. For example, as discussed above, isolated DNA can be used in primer synthesis for a PCR reaction, to make large amounts of protein recombinantly, and to create transgenic animals, to name a few. *See* Petricoin Decl., ¶¶ 21, 22, 23. These, and a vast number of other uses and properties, are unique to isolated DNA and cannot be duplicated with naturally-occurring DNA. Petricoin Decl., ¶ 21. In addition, the isolated *BRCA1* and *BRCA2* genes are useful for, *inter alia*, diagnosing a predisposition to breast and ovarian cancer.

Thus, contrary to plaintiffs' allegations, it is not scientifically correct that isolated DNA are "products of nature" or "functionally and informationally identical" to the corresponding genes in the body. *See* Plaintiffs' Summary Judgment Memo, pages 4-5; *see also* Plaintiff Complaint, page 19, ¶ 51; Plaintiffs' Summary Judgment Memo, page 20 (incorrectly suggesting that isolated DNA "has the exact same function and informational content as the genes as they exist in the body" and that "[a]ll of these claims [in the Myriad patents] embody products or laws of nature").

Rather, isolated DNA is distinct from endogenous genomic DNA for at least the following reasons: (1) isolated DNA is chemically different in size and composition from a corresponding gene contained in a chromosome in a body; (2) isolated DNA is no longer surrounded by, and therefore not regulated by, its natural environment; (3) isolated DNA has different, additional functions/uses, as compared to a gene existing in a body; and (4) regarding cDNA, non-coding introns may be absent. Petricoin Decl., ¶ 24.

In sum, isolated DNA is DNA that has been removed from the environment in which it naturally occurs, and isolated genes and genetic sequences have a different chemical structure and unique properties and uses that are not found associated with naturally-occurring nucleotide sequences. Petricoin Decl., ¶ 11. As such, isolated DNA composition claims, such as the ones at issue in this case, correspond to patentable subject matter under 35 U.S.C. § 101.

VI. Tens of Thousands of Gene Patents Currently Exist

Numerous innovators have obtained patents directed to isolated nucleic acids. Specifically, the USPTO has issued tens of thousands of patents relevant to isolated nucleic acids that could be negatively impacted by any adverse decision here.

For example, a search conducted on December 7, 2009, on the USPTO website for U.S. issued patents filed within the last 17 years (i.e., since December 7, 1992), having claims that recite: (isolated or purified) and (nucleotide or DNA or RNA or "nucleic acid" or "SEQ ID NO"), brought up 22,556 patents alone. Likewise, a search conducted on the USPTO website for U.S. issued patents having claims reciting "SEQ ID NO" brought up 33,624 patents. The first patent issued in 1991. These types of search results are consistent with the survey published last year in *Science* discussing "more than 40,000 gene patents." 458 *Nature* 386 (2009) (Exhibit 4) (citing C. M. Holman, *Science* 322, 198-199 (2008)).

Presumably, the vast majority of these U.S. patent are valid today. A search on Westlaw in "ALLFEDS" (containing all U.S. district court, U.S. court of appeals or Supreme Court opinions) for decisions including the terms: (patent) and (isolated or purified) and (nucleotide or DNA or RNA or "nucleic acid" or "SEQ ID NO"), identified 92 cases.[17] Even if every one of the 92 cases invalidated a patent (which is not the case here), it would affect 92 out of tens of thousands of issued patents (in addition to numerous pending patent applications). Moreover, none of those 92 cases challenged subject matter patentability of a gene patent under 35 U.S.C. § 101 or the Constitution. As noted in the *Nature* editorial, "[r]eports of researchers being blocked from access to patented DNA sequences or being sued for infringement are extremely rare," despite the fact that tens of thousands of relevant U.S. valid patents currently exist. 458 *Nature* 386.

VII. First and Fourteen Amendments Do Not Preclude Patentability

The "Causes of Action" section in plaintiffs' Complaint presents paragraphs 102 and 103. Only Paragraph 103 refers to the 1st and 14th Amendment, where it states in full: "All of the challenged claims represent patents on abstract ideas or basic human knowledge and/or thought and as such are unconstitutional under the First and Fourteenth Amendments to the United States Constitution" (emphasis added). As discussed in detail above, "isolated DNA" claims recite man-made compositions of matter. As such, they do not represent "abstract ideas or basic human knowledge and/or thought," as asserted in the Complaint.

In Plaintiffs' Summary Judgment Memo, plaintiffs also argue that "isolated DNA" claims are unconstitutional under the First Amendment. Plaintiffs' Summary Judgment Memo, page 35-37. Specifically, plaintiffs assert that such composition claims "limit pure information." *Id.*

[17] All above searches were conducted on December 7, 2009.

at 36. This assertion indicates a misunderstanding of what the term "isolated DNA" means to one skilled in the art, and/or as defined by the patents at issue in this case. Petricoin Decl., ¶ 12.

Isolated DNA is a chemical compound, and not "pure information." Petricoin Decl., ¶ 12; Linck Decl., ¶ 46. Of course, all chemical compounds, such as isolated DNA, inherently carry information. As stated by Dr. Linck, "[t]he mere fact that the DNA molecules of the invention inherently carry information is not a bar to patentability." Linck Decl., ¶ 46. The human body does not infringe a patent claim directed to an isolated gene. *See, e.g.*, USPTO Guidelines, 66 F.R. at 1093, Comment (2). Moreover, an "isolated DNA" claim does not prevent a researcher from using sequence information itself (i.e., the "pure information"), but rather may affect (for a limited time) whether a researcher may make or use an isolated form of the DNA, i.e., a chemical compound present, for example, in a plasmid or otherwise physically existing outside of a living organism as it naturally occurs.

Plaintiffs' Summary Judgment Memo, pages 36-37, also suggests that "isolated DNA" claims "cannot be invented around," and that the "USPTO has given entire control over a body of knowledge and over pure information to a private company." Again, for the many reasons discussed above, the term "isolated DNA" itself dictates that this suggestion is without merit.

VIII. Article 1, Section 8, Clause 8, of the Constitution Strongly Supports Patentability

As discussed the Introduction section of this brief, Article 1, Section 8, Clause 8, provides the Constitutional basis for granting a patent rights, i.e., the right to exclude others from practicing a patented invention for the life of a patent term. Nothing in this clause remotely suggests that "isolated DNA" claims are not patentable subject matter. Rather, plaintiffs rely on Second Circuit case law addressing copyright law to turn this clause on its head regarding patent protection and policy behind patent law. Plaintiffs' Summary Judgment Memo, pages 37-38.

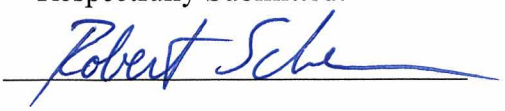
Plaintiffs also suggest that gene patents impede science. Plaintiffs' Summary Judgment Memo, page 38. As discussed in detail above, gene patents play an important role in stimulating innovation in an area of research and development that requires a great deal of money and know-how to get relevant products into patients' hands. As stated by a Committee for HHS regarding Myriad's gene patents in particular, "a considerable amount of research has proceeded, and any chilling effect has been at the margins." *Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS): Public Consultation Draft Report on Gene Patents and Licensing Practices and the Impact on Patient Access to Genetic Tests* 75 (2009). http://oba.od.nih.gov/oba/SACGHS/SACGHS%20Patents%20Consultation%20Draft%203%209%202009.pdf. . Thus, for this and the many reasons discussed above, plaintiff's constitutional arguments have no factual basis.

CONCLUSION

U.S. Congress, U.S. courts and the USPTO, not to mention the scientific community and biotechnology industry, have long relied upon an understanding that claims directed to "isolated DNA" recite patentable subject matter under 35 U.S.C. § 101 and the Constitution (assuming the claims otherwise meet patentability requirements under 35 U.S.C.). To hold otherwise for the first time in American history would have a dramatic negative effect on biotech research as we know it, the entire business of biotechnology, not to mention other technological areas, in ways unforeseen or addressed by plaintiffs in this case. Such a sweeping shift in paradigm is best left to Congress, which is the proper forum to address any considerations raised by plaintiffs. Thus, for the reasons set out above, *Amici Curiae* respectfully urge that the Court uphold the patentability of the "isolated DNA" claims at issue under 35 U.S.C. § 101 and the Constitution, and consequently deny plaintiffs motion for summary judgment, and grant defendant's motion for summary judgment, on at least this issue.

Dated: January 11, 2010

Respectfully Submitted:

By: 

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CERTIFICATE OF SERVICE

This is to certify that on January 11, 2010, a true and correct copy of the foregoing document has been served on registered counsel of record via the Court's ECF system.

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