No. 2010-1406

In The 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 FOR THE INTERNATIONAL CENTER OF TECHNOLOGY ASSESSMENT, THE INDIGENOUS PEOPLES COUNCIL ON BIOCOLONIALISM, GREENPEACE, INC., FRIENDS OF THE EARTH, AND THE COUNCIL FOR RESPONSIBLE GENETICS AS AMICUS CURIAE IN SUPPORT OF PLAINTIFF-APPELLEES

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

CONSTITUTIONAL PROVISIONS

TREATISES

CASES

STATUTES

EXECUTIVE ORDERS

OTHER AUTHORITIES

STATEMENT OF INTERESTS OF *AMICI CURIAE*

Amici seek to provide this Court with insight into the broader adverse effects of human gene patents, including *inter alia* scientific, cultural, and environmental impacts. These adverse impacts could and should be avoided, because human gene patents such as the Myriad patents are not proper patentable subject matter. The Myriad patents have a direct, severe, and adverse impact on the *Amici* non-profit organizations, at risk indigenous populations, scientific progress in disease research and potentially the human community, in general.

Amicus **the International Center for Technology Assessment ("ICTA")** was formed in 1994 to assist the public and policy makers in better understanding how technology affects society. ICTA is a non-profit organization devoted to analyzing the economic, environmental, ethical, political, and social impacts that can result from the application of technology or technological systems. ICTA's *PatentWatch* Project works to expose and challenge the inappropriate use of the U.S. patent system. Over the past three decades, policies established by the U.S. Patent and Trademark Office ("USPTO") have significantly expanded the range of patentable technologies, illegally allowing for a corporate monopoly on life itself by allowing patents on human DNA, plants and animals, and their DNA and cells. ICTA's *PatentWatch* operates on the principle that life and its elements are the common heritage of all and should remain available to all to learn from, wonder at,

and utilize. ICTA's *PatentWatch* identifies pernicious patents granted by the PTO, encourages grassroots activities against such patents, and initiates and supports legal challenges against existing and future patents. The project has successfully challenged patents on various plants and animals, gaining rescission of patents on broccoli, beagles and rabbits.

Amicus **the Indigenous Peoples Council on Biocolonialism ("IPCB")** is a non-profit Indigenous people's organization established in 1999 and located on the Pyramid Lake Paiute Reservation in Nixon, NV. The IPCB seeks to protect the Indigenous knowledge, cultural heritage, and genetic materials of Indigenous peoples. The organization monitors and evaluates the complex linkages between biotechnology, intellectual property rights, and the forces of globalization in relation to Indigenous peoples' rights and concerns. Its primary focus is to develop resources, information, and tools to help Indigenous peoples address these issues from their own cultural perspectives and on their own terms in the exercise of their human right of self-determination. The IPCB works to build the capacity of Indigenous peoples to be effective advocates in defense of their rights in international fora, and to develop capacity and awareness locally.

Amicus **Greenpeace, Inc**. is a California non-profit corporation that is associated with Greenpeace offices worldwide. Greenpeace is the leading independent campaigning organization that uses peaceful direct action and creative

communication to expose global environmental problems and to promote solutions that are essential to a green and peaceful future. Greenpeace opposes all patents on genes, plants, humans, and parts of the human body and regards the biodiversity of this planet the common heritage of humankind. Greenpeace's 2004 report, "The True Cost of Gene Patents," details the severe economic and social consequences of patenting genes and living organisms.[1]

Amicus **Friends of the Earth ("FoE")** is a non-profit organization, founded in 1969, with offices in Washington, D.C. and California. Friends of the Earth has approximately 120,000 members and 76 FoE affiliates worldwide. FoE's mission is to defend the environment and champion a healthy and just world. FoE is opposed to the patenting of all DNA sequences, genes, plants, animals, humans, and any part of the human body. FoE believes that the privatization of our natural resources—including our genetic makeup—is a driving force behind many social and environmental injustices. FoE was one of the first organizations to publish concerns about the genetic modification of crops in the 1980s and exposed the fact that genetically engineered corn not approved for human consumption had entered the national food system in early 2000.

Amicus **the Council for Responsible Genetics ("CRG")** is a national non-profit organization with offices in Cambridge, Massachusetts and New York, New

[1] *Available at* http://weblog.greenpeace.org/ge/archives/1Study_True_Costs_Gene_Patents.pdf (last accessed Dec. 6, 2010).

York. CRG was founded in 1983 to represent the public interest and foster public debate about the social, ethical and environmental implications of genetic technologies. CRG is dedicated to examining the best science, interpreting the results, assessing the implications, communicating them to a general audience and creating lasting policy reform. CRG believes that no individual, institution or corporation should be able to hold patents or claim ownership rights over genes or gene sequences, whether naturally occurring or modified. CRG works with a coalition of health and patient advocacy groups to build support for a ban on gene patents. CRG's *Genetic Bill of Rights* specifically opposes such patents. CRG also publishes a magazine, *GeneWatch*, that regularly includes articles by experts in the field on issues related to gene patents.

Pursuant to Federal Rule of Appellate Procedure 29(a), Defendants-Appellants and Plaintiffs-Appellees consented to the filing of this brief.

SUMMARY OF ARGUMENT

Defendant-Appellant Myriad Genetics, Inc. seeks to reverse the district court's opinion invalidating seven patents, including fifteen composition and method claims, related to the human genes known as Breast Cancer Susceptibility Genes 1 and 2 (collectively, "BRCA1/2").. The district court's decision is based on the fundamental conclusion that the challenged patent claims cover products of

nature, specifically "the physical embodiment of laws of nature."[2] Accordingly, the grant of these patents was contrary to over a hundred years of patent law in which courts have held that products of nature are unpatentable subject matter because nature is free to all and can be reserved exclusively to none.

BRCA1/2 genes are found naturally in humans. They carry information, in the form of DNA, that is a product of nature and is therefore not subject matter eligible for patenting. The United States has recently switched its long-standing position to agree in general with the lower court that merely isolating a gene does not make it patentable subject matter. However, the key component of DNA is genetic information, which is why—contrary to the further position recently advocated by the United States' *amicus* brief—the product of nature exception applies equally to modified DNA (or cDNA) as well as to genes in the human body and "isolated" DNA. They each represent the same information. Each type of arrangement falls outside the realm of patentable subject matter because each uses DNA in the production of *identical* proteins, all according to the laws of nature. To allow one type of arrangement to be patented while excluding another would be, in the words of the district court, just another "lawyer's trick."

[2] Although the decision below included a finding that certain claims were invalid as abstract ideas, this brief focuses on the concept and implications of genes as a product of nature.

Such legal manipulation results in harmful monopolies of nature masquerading as human invention. Plaintiff-Appellees and other *amici* have comprehensively detailed how the patenting of genes impedes crucial research and interferes with medical care to the detriment of patients, doctors, non-profit organizations and researchers. Yet, as serious as these harms are, there are unfortunately further significant scientific, cultural, and environmental impacts from these patents.

Genes are fundamentally encoded storehouses of information, and patents deny the public access to this natural genetic data, in contravention of the public good. Allowing these patents violates fundamental precepts of common heritage, the public domain, and the public trust doctrine. Worse, privatizing genes creates rights of unknown scope and significance because humanity currently lacks a holistic understanding of genes and their roles vis-à-vis non-hereditary proteins, other DNA sequences that are not genes, RNA, the cellular environment, and the extra-human environment. The patenting of one biological element in that dynamic stalls research into these processes, a result that is antithetical to the purpose of U.S. patent law. Finally, gene patents privatize genetic ancestry, making Indigenous peoples and patients into "treasure troves" to be exploited for economic gain, in violation of cultural and religious values and basic rights to informed consent.

Amici hereby request the Court affirm the district court's judgment.

ARGUMENT

I. THE INVALIDATED BRCA1 AND BRCA2 PATENTS ARE NOT COMPRISED OF PATENTABLE SUBJECT MATTER AND USPTO'S GRANT OF THESE PATENTS IS A VIOLATION OF THE PRODUCT OF NATURE DOCTRINE

Long-standing legal precedent—required by Article I, Section 8, Clause 8 of the U.S. Constitution (the patent clause of the U.S. Constitution), as well as 35 U.S.C. §101 (the patent statute subject matter requirements)—holds that products of nature are not patentable. This prohibition against patenting "physical phenomena" or "manifestations of nature" is known as the product of nature doctrine. In short, one cannot patent a product that occurs in nature in essentially the same form. The U.S. Supreme Court precedents have clearly and consistently held that products of nature are not patentable. *See, e.g.*, *Diamond v. Chakrabarty*, 447 U.S. 303 (1980); *Funk Bros. Seed Co. v. Kalo Inoculant Co*., 333 U.S. 127 (1948); *Am. Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. (23 Wall.) 566 (1874). As the Supreme Court has stated, "'[t]he relevant distinction' for purposes of §101 is . . . 'between products of nature, whether living or not, and human-made inventions.'" *J.E.M. Ag. Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 134 (2001) (quoting *Chakrabarty*, 447 U.S. at 309).

A. Products of Nature Are Not Patentable Subject Matter.

In a series of cases over the past century, the Supreme Court has held that one cannot patent products of nature, or materials isolated from products of nature, if those materials behave in the same way they would in nature. The product of nature doctrine appears as early as 1889,[3] when, in *Ex parte Latimer*, the Commissioner of Patents rejected a claim seeking to "patent purified pine needle fiber as a 'new article of manufacture' for use in textiles." *Ex parte Latimer,* 1889 Dec. Comm'r Pat. 123 (1889); *id.* at 125-26 (finding that allowing such a patent would make it "possible for an element or principle to be secured by patent," with the ultimate consequence that "successively, patents might be obtained upon the trees of the forest and the plants of the earth.").[4] *See also Gen. Elec. Co. v. DeForest Radio Co.*, 28 F.2d 641, 643 (3d Cir. 1928), *cert. denied* 278 U.S. 656 (1929) (directly applying reasoning in *Latimer* in denying patent because what patentee "discovered were natural qualities of pure tungsten...he did not create pure

[3] *See also Am. Wood Paper Co.*, 90 U.S. (23 Wall) at 593-94 (cellulose derived from wood pulp by a new process not patentable because it was indistinguishable from cellulose previously obtained from other sources via existing processes); *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293, 311 (1884) (artificial alizarine (a dye) derived from a new process unpatentable because the claimed product was indistinguishable from that obtained naturally).

[4] *See also Am. Wood-Paper Co.*, 90 U.S. (23 Wall.) at 593-94 ("A process to [extract something] from a subject from which it has never been taken may be the creature of invention, but the thing itself when obtained cannot be called a new manufacture.").

tungsten, nor did he create its characteristics…The fact that no one before [him] found it there does not negative its origin or existence.").[5]

In the 1948 case *Funk Bros. Seed Co.*, the Supreme Court reaffirmed the product of nature doctrine. 333 U.S. at 130-31. The Court held that mixtures of certain root nodule bacteria used for inoculating the seeds of plants were not patentable because the combination of bacteria species did not produce a new invention, but served more of a packaging function. *Id.* "Each species has the same effect it always had…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." *Id.* at 131. The Court further explained that "phenomena of nature. . . .are part of the storehouse of knowledge of all men," and cannot be patented. *Id.* at 130 (citing *Le Roy v. Tatham*, 55 U.S. (14 How.) 156, 175 (1853)).

In 1980 the Court applied this doctrine to biological organisms in *Chakrabarty*, holding that where an inventor introduced new genetic material within a bacterium cell, he had produced something that was not a product of nature and was thus not patentable subject matter under 35 U.S.C. § 101. 447 U.S. at 309. Significantly, the Court cited *Funk Bros.* for the proposition that one cannot patent "manifestations of . . . nature, free to all men and reserved

[5] *See also In re Marden* (Marden I), 47 F.2d 957, 957 (C.C.P.A. 1931); and *In re Marden* (Marden II), 47 F.2d 958, 958 (C.C.P.A. 1937).

exclusively to none." *Id. (*quoting *Funk Bros.*, 333 U.S. at 130 (internal quotations omitted)); *see also Gottschalk v. Benson*, 409 U.S. 63, 67 (1972); *O'Reilly v. Morse,*56 U.S. (15 How.) 62, 112-121 (1854)*; Le Roy*, 55 U.S. (14 How.) at 175. The Court's conclusion was straightforward: "His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under § 101." *Funk Bros.*, 333 U.S. at 310.[6]

The Court continues to return to *Chakabarty* for this premise that "'the relevant distinction' for purposes of § 101 is not 'between living and inanimate things, but between products of nature, whether living or not, and human-made inventions." *J.E.M. Ag Supply*, 534 U.S. at 134 (quoting *Charkabarty*, 447 U.S. at 311-12); *see also Bilski v. Kappos*, 130 S.Ct. 3218, 3225 ("these exceptions have defined the reach of the statute as a matter of statutory *stare decisis* going back 150 years...The concepts covered by these exceptions are 'part of the storehouse of knowledge of all men...free to all men and reserved exclusively to none.'") (internal citations omitted); *see also Intervet, Inc. v. Merial Ltd.*, 617 F.3d 1282, 1294-95 (Fed. Cir. 2010).

[6]It is immaterial to our argument whether *Chakrabarty* was rightly or wrongly decided in our view, as the crucial holding for this case is simply that that the product of nature doctrine emerged from *Chakrabarty* unchanged. That said, the *Chakrabarty* decision's main holding, a 5-4 decision that the addition of transgenic material is sufficient to create patentability, is far from universally accepted. *See,e.g.*, *Harvard Coll. v. Can. (Com. of Patents)*, [2002] 4 S.C.R. 45, 2002 SCC 76 (Can.) (distinguishing *Chakrabarty* and holding that a transgenic mouse was not patentable subject matter).

In summary, over a hundred years of precedent has consistently held that products of nature are not patentable subject matter and that allowing patents on products of nature violates § 101. A product whose physical characteristics are indistinguishable from those of its naturally-occurring counterpart does not constitute patentable subject matter.

B. The District Court Was Correct in Holding That the Challenged Composition Claims, Including Those Limited to cDNA, Was Not "Markedly Different" From a Product of Nature.

The court below applied the above doctrine to modern-day concepts of genetics, painstakingly elaborating on the distinction between typical chemical compounds and the "biological realities of DNA." *Ass'n for Molecular Pathology v. United States* PTO, 09-CV-4515, 2010 U.S. Dist. LEXIS 35418 at *134 (S.D.N.Y. Apr. 2, 2010). Applying the product of nature doctrine in the context of the biological realities underpinning the BRCA gene patents led to the only logical conclusion: Myriad's patents are contrary to law. There is no "invention" here.

Recent attempts by the United States to create a false distinction between "isolated" DNA and cDNA must fail.[7] As in *Funk Bros.*, the patented gene

[7] The government, in its *amicus* brief, argues that other forms of DNA are patentable, including chimeric genes, recombinant DNA, and vectors. *See* Br. for the United States as *Amicus Curiae* in Supp. of Neither Party 14-17. These DNA sequences are engineered to carry information that has utility distinct from that which exists in nature, unlike isolated DNA and cDNA. Nonetheless, we do not address the patentability of these forms of genetic material here, as they are outside the scope of the patent claims at issue.

sequences serve the ends nature originally provided and act independently of any effort of Myriad. 333 U.S. at 130-31. The information dictated by the gene is identical, whether inside or outside the body. This information is also identical whether in the form of naturally occurring, "isolated" DNA or cDNA, which merely lacks introns or other modifications that do not affect informational content. As in *Latimer* and *General Electric*, a mere description using the terms "isolated," or cDNA should not create patentable subject matter if there is not a difference in substance. *Gen. Elec.*, 28 F.2d at 642-43; *see Ex parte Latimer*, 1889 Dec. Comm'r Pat. at 123, 125, 127. The genetic compounds claimed in Myriad's patents represent the same genetic information as their natural counterpart, they do the same work as a naturally occurring gene-protein synthesis, and they employ the same processes to do it. The useful properties of a gene are not ones that a scientist invented (or created through isolation or by generating cDNA), but rather are the natural, inherent properties of genes themselves. And, as detailed in Section II *infra*, these patents improperly privatize the "storehouse of knowledge of all men," contrary to the Court's teachings. *Funk Bros.*, 333 U.S. at 132.

II. GENE PATENTS ARE PROPERLY EXCLUDED FROM PATENTABLE SUBJECT MATTER BECAUSE GENE PATENTS SUCH AS MYRIAD'S BRCA1 AND BRCA2 PATENTS HAVE SIGNIFICANT NEGATIVE SCIENTIFIC, SOCIAL, CULTURAL AND ENVIRONMENTAL CONSEQUENCES

In June 2006, Justice Breyer discussed why it is important not to have patents on products of nature or laws of nature:

> The justification for the principle does not lie in any claim that "laws of nature" are obvious, or that their discovery is easy, or that they are not useful. To the contrary, research into such matters may be costly and time-consuming; monetary incentives may matter;...Rather, the reason for the exclusion is that sometimes *too much* patent protection can impede rather than "promote the Progress of Science and useful Arts," the constitutional objective of patent and copyright protection.

Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 126-27 (2006) (Breyer, J., dissenting) *denying cert. to* 370 F.3d 1354 (Fed. Cir. 2004). Plaintiff-Appellants and other *amici* have provided substantial evidence that Myriad's patents, and gene patents like them, are causing great harm by impeding the progress of necessary scientific research, patient care, and the development of cures. *See, e.g.*, Pls.' Compl. at ¶¶ 2, 7-26, 48, 81-101 (Dkt. No. 1); Pls.' Mem. of Law in Supp. of Summ. J. 5-6 (Dkt. No. 62); Br. of *Amicus Curiae* March of Dimes, *et al.* 2-5, 14-16, 21-23 (Dkt. No. 99); Br. of *Amicus Curiae* Am. Med. Assn, *et al.* 9-14 (Dkt. No. 107), 09-CV-4515 (S.D.N.Y. Apr. 2, 2010). These negative consequences are foreseeable and natural consequences of granting patents on genes in violation of the product of nature doctrine.

However, there are other important consequences, as well. The privatization of this genetic heritage violates fundamental precepts of common heritage, the public domain and the public trust doctrine. Additionally, when the USPTO grants a patent on a gene and removes it from the public domain, it does so with only very incomplete knowledge of what that gene actually does in the body. Hence these

broad patents have the additional negative result of creating exclusive rights of presently unknown scope and significance, further impeding the progress of science. Finally, granting gene patents creates a system where people are nothing more than "treasure troves" to be mined for private economic gain, violating the fundamental rights of indigenous peoples and patients.

A. The Privatization of Genetic Heritage Violates Fundamental Precepts of Common Heritage, the Public Domain and the Public Trust Doctrine.

The genetic building blocks of life and its elements are the common heritage of humanity, available to all to learn from and utilize. Patenting of human genetics, such as the BRCA1/2 genetic sequences, is antithetical to the tenets of public domain, common heritage, and public trust. As naturally occurring resources that are central to human identity and human survival, human genes are part of the common heritage of humanity and should be held as part of the public trust. Human genetics are owned by all people and a single firm should not be granted the right to exclude others from using human genetics.

The public domain is explicitly recognized in patent law by judicial exclusion of the laws of nature, natural phenomena, and abstract ideas from patent protection. The Supreme Court has held that existing knowledge and materials that exist in the public domain are the default presumption and are not to be patented: "Congress may not authorize the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials

already available." *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 6 (1966); *see also Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 151 (1989) ("free exploitation of ideas will be the rule, to which the protection of a federal patent is the exception"); *Precision Instrument Mfg. Co. v. Auto. Maint. Mach. Co.*, 324 U.S. 806, 816 (1945) ("A patent is an exception to the general rule against monopolies."). By preventing research and monopolizing genetic data, patents on gene sequences take information out of the public domain and impede the progress of science, contrary to the express intent of the Constitution. *See* U.S. Const. art. I, § 8, cl. 8 (granting Congress the power to issue patents in order to "promote the Progress of Science and the useful Arts").

Patents should not be granted for genes, which are the common heritage and inheritance of mankind. Under the common heritage theory, public resources are available for use by all, without restriction, for the benefit of humanity. *See, e.g.*, Pilar A. Ossorio, *The Human Genome as Common Heritage: Common Sense or Legal Nonsense*?, 35 J.L. MED. & ETHICS 425, 426 (2007)(hereafter "Ossorio, *The Human Genome"*).[8] Information in genes is "part of the storehouse of knowledge of all men." *Funk Bros.*, 333 U.S. at 130. The common heritage doctrine has been

[8] *See, e.g.*, Melissa L. Sturges, *Who Should Hold Property Rights to the Human Genome? An Application of the Common Heritage of Humankind*, 13 Am. U. Int'l L. Rev. 219, 245 (1997); Barbara Looney, *Should Genes Be Patented? The Gene Patenting Controversy: Ethical and Policy Foundations of an International Agreement*, 26 LAW & POL'Y INT'L BUS. 231 (1994); Hubert Curien, *The Human Genome Project and Patents*, 254 SCIENCE 1710, 1710-12 (1991).

applied to a variety of resources, including the sea floor, activities in outer space, the use of seeds, preservation of historical artifacts, and the conservation of environmental resources. *See, e.g.*, Kernal Baslar, *The Concept of the Common Heritage of Mankind in International Law*, The Hague/Boston/London: Martinus Nijhoff, 31-37, 108-109 (1998); *see also* E. Aguis, *Germ-Line Cells – Our Responsibilities for Future Generations*, Valletta, Malta: Foundation for International Studies, 133-143 (Salvino Busuttil ed.,1990) ("If there is an obvious component of the common heritage of mankind, indeed, more obvious than the resources of the sea-bed itself, it is the human genetic system.").[9]

The public trust doctrine has also been invoked to understand why human genetics should be protected as public property. *See e.g.*, Looney, *supra* note 8. The public trust doctrine requires governments to hold trust property for use by the general public, and to maintain that property for certain types of public uses. *See generally* Joseph L. Sax, *The Public Trust Doctrine in Natural Resources Law: Effective Judicial Intervention*, 68 MICH. L. REV. 471 (1970). The conceptual underpinnings of the public trust doctrine are that certain interests are so

[9]Because of the unique legal status of Indigenous peoples and their rights to their genetic material, which will be discussed in section II C *infra*, the doctrine of common heritage of mankind is not applicable to them. Accordingly, specific legislation and regulations are needed to reserve the right of Indigenous peoples to determine whether or not they want to provide their genetic material for research purposes.

intrinsically important to every citizen that their free availability tends to mark the society as one of citizens rather than serfs; that certain benefits derive so directly or particularly from nature that they should be available to the entirety of a populace; and that certain uses of property have value only to the extent that they are public. *Id*. The public trust doctrine demands that human genes be available to all people. Human genes are of intrinsic importance to all people and their benefits are derived directly from human biology. *See, e.g.* Ossorio, *The Human Genome*, at 427.

Permitting the patenting of human genetics also causes the underutilization of genetic material. The proliferation of intellectual property rights on original genetic material may stifle life-saving innovations downstream from product research and development due to a phenomenon dubbed "the tragedy of the anticommons." *See, e.g.*, Michael A. Heller and Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (1998) (citing Michael A. Heller, *The Tragedy of the Anticommons: Property in the Transition from Marx to Markets*, 111 HARV. L. REV. 621 (1998)). As the right of companies to exclude others from use of genetics expands, all genetic resources become increasingly underutilized, reducing the benefit of these resources to humanity.

Accordingly, human genetic information should remain in the public domain in order to prevent the monopolization and/or underutilization of our common heritage.

B. Gene Patents Privatize Genetic Information That Scientists Lack a Full Understanding of, Creating Rights of Unknown Scope and Significance.

Gene sequences are not akin to a conventional chemical substance or a drug; they are instead fundamentally information. The patent for a particular gene sequence patents the information contained in the sequence—for example the As, Ts, Cs, and Gs of the genetic code. *See, e.g.*, Sunny Bains, *Double Helix as Engineer*, 279 Science 2043, 2043 (1998). The approximately 20,000 genes in our bodies are involved in the production of several hundred-thousand biological proteins. *See, e.g.*, Alan E. Guttmacher & Francis S. Collins, eds., *Genomic Medicine—A Primer*, 347 New Eng. J. Med. 1512, 1514 (2002). The holder of a patent purporting to describe one commercial use should not then have a monopoly on all possible functions, particularly given that the scientific scope of what those functions may be is very limited. As noted in the context of AIDS research, "[w]hoever is first to patent a DNA sequence—for any use—can lock up subsequent uses." Eliot Marshall, *AIDS Research: HIV Experts vs. Sequencers in Patent Race*, 275 Science 1263 (1997) (discussing gene sequences patented for AIDS research even though the patent specification did not mention a connection to the HIV infection).

More fundamentally, genes are substances that we still know little about. *See, e.g.*, Carl Zimmer, *Now: The Rest of the Genome*, N.Y. Times, Nov. 11, 2008, at D1 (discussing the current gene "identity crisis" and how "new large-scale studies of DNA are causing [scientists] to rethink the very nature of genes"); Brendan Maher, *Personal Genome: The Case of the Missing Hereditability*, 456 Nature 1818-21 (2008); Evelyn Fox Keller, David Harel, *Beyond the Gene,* . PLoS ONE 2(11): e1231 (2007) (noting continuing scientific debate regarding the definition of the term "gene"). Researchers once estimated that humans, because of their complexity, would probably end up having between one and two hundred thousand genes. The surprising results of the Human Genome Project revealed in 2001 that humans have only about 20,000 genes, a similar count to worms, flies and yeast. *See, e.g.*, Elizabeth Pennisi, *Working the (Gene Count) Numbers: Finally, a Firm Answer?*, 316 Science 1113 (2007). We share the vast majority of our genes with other creatures. Most genes for the same functions in animals produce proteins that are nearly identical; very few genes have been proven to be uniquely human. Still, very minor changes in an individual's DNA sequences (not just the sequences that make proteins) can cause significant differences between even individual humans.

More recently, additional research has amplified these unexpected findings, indicating that human complexity does not come primarily from genes but is

related to other elements of our biology and the outer environment including: 1) the non-coding (non-gene) elements of DNA, so-called "junk" DNA which accounts for more than 98% of all DNA, is now seen to play a far more important role in regulating gene function than previously thought; 2) a cell's RNA, often thought merely to be a "messenger" for genes, is now understood to play a more important part in heredity and the causation of hereditary disease; 3) the identity and number of the many hundreds of thousands of proteins in a cell often have a controlling influence on the action of genes and are viewed as critical biological actors in heredity and the incidences of cancer and other human disease. The ENCODE Project Consortium, *Identification and Analysis of Functional Elements in 1% of the Human Genome by the ENCODE Pilot Project*, 447 Nature 799 (2007); *see also* Rick Weiss, *Intricate Toiling Found in Nooks of DNA Once Believed to Stand Idle*, WASH POST, June 14, 2007 (reporting that "[t]he first concerted effort to understand all the inner workings of the DNA molecule is overturning a host of long-held assumptions about the nature of genes and their role in human health and evolution"); Elizabeth Pennisi, 316 Science at 1556-57 (stating that the research reveals an extremely different picture of DNA, RNA, protein, and their interactions than the one that scientists have assumed for decades); Ruth Hubbard, *The Mismeasure of the Gene*, Council for Responsible Genetics, *available at* http://www.councilforresponsiblegenetics.

org/pageDocuments/0YA8FI5N1U.pdf (discussing "the complex dialectical relationships among the material, ideological, social, political, and economic dimensions and implications of the supposedly scientific gene concept").

Moreover, environmental influences can also affect DNA. New findings in the field of epigenetics show that environmental factors such as diet, stress, and prenatal nutrition can change genetic activity across at least one successive generation, even where the genetic code itself may not be altered. John Cloud, *Why Your DNA Isn't Your Destiny*, Time, (Jan. 2010), *available at* http://www.time.com/time/health/article/0,8599, 1951968-1,00.html#ixzz16fad0jch; *see also* Laura Beil, *Medicine's New Epicenter? Epigenetics*, CureToday, (Winter 2008)(hereinafter "Beil, *Medicine's New Epicenter*"); Eric J. Richards, *Inherited Epigenetic Variation—Revisiting Soft Inheritance*, 7 Nature Reviews—Genetics 395 (May 2006).

These findings have critical impacts on our understanding of BRCA1/2. First of all, no researcher claims that BRCA1/2 "cause" breast cancer. There appears to be a statistical "association" between incidences of hereditary breast cancer and these genes.[10] Since both BRCA genes are believed to be related to

[10]According to the NIH, hereditary breast cancer is believed to represent around 10-15% of all breast cancer; the remaining percentage of cancers are thought to be environmentally caused. Campeau PM, Foulkes WD, Tischkowitz MD. Hereditary breast cancer: New genetic developments, new therapeutic avenues. *Human*

tumor suppression, this may account for the percentage association with breast cancer. However, the mechanism by which such tumor suppression is accomplished remains a mystery, as do the gene "defects" that contribute to breast cancer risk. Not surprisingly given this lack of scientific understanding, virtually all studies reporting this association of BRCA1/2 with incidences of hereditary breast cancer have called for more research to verify the extent of the association and its actual biological basis. *See, e.g.*, Andrea Veronesi, et al., *Familial Breast Cancer: Characteristics and Outcomes of BRCA 1-2 Positive and Negative Cases*, 5 BMC Cancer 70 (2005); H. Eerola et al., *Survival of Breast Cancer Patients in BRCA1, BRCA2, and NON-BRCA1/2 Breast Cancer Families: A Relative Survival Analysis from Finland*, 93 Int'l J. of Cancer 368-372 (2001); Dominique Stoppa-Lyonnet, et al., *Familial Invasive Breast Cancers: Worse Outcome Related to BRCA1 Mutations*, 18(24) J. of Clinical Oncology 4053-4059 (2000); Mario Budroni, et al., *Role of BRCA2 Mutation Status on Overall Survival Among Breast Cancer Patients from Sardinia*, 9 BMC Cancer 62 (2009); Mahmond El-Tamer, el al., *Survival and Recurrence after Breast Cancer in BRCA 1/2 Mutation Carriers*, 11(2) Annals of Surgical Oncology 157-164 (2004); Colin B. Begg, et al., *Variation of Breast Cancer Risk Among BRCA1/2 Carriers*, 299(2) J. of the Am. Med. Ass'n 194-201 (2008); M.C. King, et al., *Breast and Ovarian Cancer Risks*

Genetics 2008; 124(1):31–42. from the NIH National Cancer Center webpage: http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA.

Due to Inherited Mutations in BRCA1 and BRCA2, 302 SCIENCE 643-646 (2003); A. Antoniou et al., *Average Risks of Breast and Ovarian Cancer Associated with BRCA1 or BRCA2 Mutations Detected in Case Series Unselected for Family History: A Combined Analysis of 22 Studies*, 72 Am. J. of the Human Genetics 1117-1130 (2003). A disclaimer on the NIH's National Cancer Institute webpage states the problem quite clearly: "no data are available from long-term studies of the general population comparing cancer risk in women who have harmful BRCA1 or BRCA2 mutations with women who do not have such mutations." Factsheet on BRCA1 and BRCA2: Cancer Risk and Genetic Testing, NIH National Cancer Center webpage, *available at* http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA.

Adding to the confusion is a recent 2008 study demonstrating that high risk women who did not have BRCA1/2 had a risk of new cancerous lesions considerably greater than those who were positive for the genes. Elizabeth Feldman, et al., *The Incidence of Occult Malignancy and Atypical Histopathology in Prophylactic Masectomy Specimens After Uninformative BRCA Testing*, American Society of Breast Surgeons meeting 2008. As with the association findings, these seemingly contradictory findings need further research to be better understood.

In sum, our emerging understanding of the role that genes and other biological elements play in the cell, and how the environment influences those elements, indicates that the old mechanistic view of genes "causing" complex diseases such as cancer is simply wrong. Research now shows that many cancer cells have no genetic mutations at all. *See*, *e.g.*, Beil, *Medicine's New Epicenter*. It is now understood that many human diseases are caused by complex dynamics between non-hereditary proteins, DNA, RNA, the cellular environment, and the extra-human environment. Allowing the patenting of the gene halts research into this complex dynamic process. Just as billions of dollars of government research have shown the gene is not "the dictator" of heredity and hereditary diseases, patents on genes such as the BRCA1/2 halt the progress of this new scientific paradigm to see how these DNA sequences interact with other biological elements, which may be far more important than genes in disease creation. Preventing a more comprehensive understanding of human disease causation is antithetical to the purpose of U.S. patent law, namely to "promote the Progress of Science and useful Arts." U.S. Const. art. I, § 8, cl. 8.

C. Patents on Indigenous Peoples' Genes Facilitate the Exploitation of Indigenous Peoples and Violate International Law.

Genes are fundamentally storehouses of information that has been passed down to each person from his or her ancestors, and that will be passed down to his

or her children. For Indigenous groups, their genetic materials hold traditional and spiritual significance.

The permissibility of patenting genes has caused some to view Indigenous peoples as "treasure troves." Researchers have applied for patents based on cell lines derived from Indigenous people without their consent, such as the Guyami of Panama, the Hagahai of Papua New Guinea, and the Melanese of the Solomon Islands. *See, e.g.*, Debra Harry and Le`a Malia Kanehe, *Asserting Tribal Sovereignty over Cultural Property: Towards Protection of Genetic Material and Indigenous Knowledge*, 5 Seattle J. for Soc. Just. 27 (2006). Indigenous communities are attractive to genetic researchers for several reasons, including (1) they are perceived to be more genetically homogenous than other populations, making it easier for researchers to find links between specific diseases and genetic sequences; and (2) they often have high rates of specific diseases such as Type II diabetes, heart disease, cancers, and arthritis. *Id.*

The Havasupai case demonstrates why researchers are interested in Indigenous peoples' genes. Members of the Havasupai Tribe from an isolated region of the Grand Canyon in Arizona were sought as research subjects to study the possibility of a genetic basis for the prevalence of Type II diabetes within the Tribe. Although the Tribe and some members consented to diabetes related research at Arizona State University, their blood samples were used for other

purposes, including inbreeding, schizophrenia and ancient migration theories, and transferred to other universities, all without their consent. *See, e.g.*, Lori B. Andrews, *Havasupai Tribe Sues Genetic Researchers*, 4 LAW & BIOETHICS REPORT 10 (2004). In resulting litigation, the Tribe and individual members maintained that the defendant university and researchers "violated the Havasupai Tribe's and tribal members' cultural, religious, and legal rights and have caused the Havasupai Tribe and its members severe emotional distress." *Havasupai Tribe v. Ariz. Bd. of Regents*, 204 P.3d 1063, 1069 (Ariz. Ct. App. 2008), *appeal denied*, 2009 Ariz. LEXIS 82 (Apr. 20, 2009).

The Hagahai and Guayami cases illustrate that genetic research on Indigenous peoples often results in patents. In the case of the Hagahai, NIH and Department of Health and Human Services sought and was granted a patent on a human T-cell line obtained from a Hagahai man, a member of an isolated tribe of Papua New Guinea, without his consent. *See id.* at 1067; *see also* U.S. Patent No. 5,397,696 (issued March 14, 1995). NIH eventually forfeited its patent rights, but only after an international uproar. *See, e.g.*, Gary Taubes, *Scientists Attacked for "Patenting" Pacific Tribe*, 270 SCIENCE 1112 (1995); Sally Lehrman, *U.S. Drops Patent Claim to Hagahai Cell Line*, 384 NATURE 500 (1996).

Another example is the "Guayami patent." In that case, a patent application was filed on behalf of the U.S. Department of Commerce for "Human T-

Lymphotropic Virus Type II from Guayami Indians in Panama," even though neither the tribe nor the woman whose genetic sequence was at issue knew anything about the development of the cell line or the patent application. *See, e.g.*, Marina L. Whelan, *What, If Any, Are the Ethical Obligations of the U.S. Patent Office: A Closer Look at the Biological Sampling of Indigenous Groups*, 2006 Duke L. & Tech. Rev. 14, 13-15 (2006). The President of the Guayami General Congress wrote the U.S. Secretary of Commerce, demanding that the application be withdrawn because it was made without consultation or consent and because the patent was "not an invention but a discovery of an antibody which is part of the blood of a Guayami woman." *Id.* The letter also queried what, if any, benefits the Guayami people would gain from the proposed patent application. As a result of this protest from the Guayami people, as well as from numerous public interest groups, the patent was withdrawn. *Id.*

Although the U.S. government elected to drop their patents on the Hagahai and Guayami genes due to public and diplomatic pressure, there was no legal obligation to do so. Thus, Indigenous peoples remain vulnerable to similar attempts to patent their genes, particularly with the passage of the Bayh-Dole Act in 1980, which encourages universities to patent inventions developed with federal funding. Patent and Trademark Law Amendments Act, Pub.L. No. 96-517 (1980). This legislation has facilitated the entry of universities into the marketplace by

giving them the right to patent and commercialize their inventions, including human genes.

The United Nations Declaration on the Rights of Indigenous Peoples, adopted in 2007 by the UN General Assembly, recognizes that "Indigenous peoples have the right to maintain, control, protect and develop their cultural heritage, . . . including human and genetic resources." United Nations Declaration on the Rights of Indigenous Peoples, G.A. RES. 61/295 at art. 31, U.N. Doc. A/RES/61/295 (Sept. 13, 2007). This right stems from the central right of self-determination, which includes a right to autonomy or self-government in matters relating to their internal or local affairs. *Id.* at art. 4. In the United States, this right is actualized through the recognition of the exercise of sovereignty by federally-recognized tribes. While the proper utilization and disposition of genetic material associated with a tribe is an internal matter there is no requirement in federal law to protect this right.

The UN Declaration also recognizes the obligation upon States to obtain the free, prior and informed consent ("FPIC") of Indigenous peoples when legislative or administrative actions may affect them, as well as prior to the extraction of their resources. *Id.* at arts. 19, 32. This principle of international law is closely related to the rights of individual human research subjects and patients to informed consent under federal law except that FPIC is a right uniquely applicable to

Indigenous peoples as collective groups rather than as individuals. Given the demonstrated history of utilization of genetic material of Indigenous peoples without their informed consent, USPTO's extension of patent protection to human genes obtained from Indigenous peoples without their free, prior and informed consent is an infringement of their internationally recognized rights.

All federal agencies have a duty to consult with tribes when "formulating or implementing agency policies that have tribal implications." Exec. Order No. 13, 175 (2000). The issuance of a patent on genes taken from tribal members necessarily has significant legal, social, cultural and economic implications for tribes. Yet federal regulations do not require USPTO to inquire into the origin of the genetic material, tribal or otherwise, or require their consent, and therefore the agency does not have any mechanism to ensure that appropriate tribes are consulted before issuance of a patent. Accordingly, properly excluding gene sequences as impermissible subject matter pursuant to the product of nature doctrine would serve to protect the rights, under international and federal law, of Indigenous peoples, that are currently being violated.

D. The Granting of Gene Patents Such as Myriad's BRCA1/2 Patents Creates a System That Violates the Rights of Patients' to Informed Consent.

Human gene patents such as Myriad's patents violate basic notions of informed consent as well. Doctors, health care institutions, researchers, and

hospitals have gone to court to gain ownership of patients' cell lines, tissue, and genes in order to commercialize them, even over the patients' objections. *See, e.g.*, *Moore v. Regents of the Univ. of Cal.*, 793 P.2d 479 (Cal. 1990); *Wash. Univ. v. Catalona*, 490 F.3d 667 (8th Cir. 2007). Justice Cardozo was one of the first to acknowledge the existence of a basic right to informed consent, concluding that "[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body." *Schloendorff v. Soc'y of New York Hosp.*,105 N.E. 92, 93 (N.Y. 1914). Indeed, the concept is "fundamental in American jurisprudence." *Canterbury v. Spence*, 464 F.2d 772, 780 (D.C. Cir. 1972). Informed consent requires disclosure of all the information that is material to a patient's intelligent and informed decision. *See, e.g.*, *Johnson v. Kokemoor*, 545 N.W.2d 495, 501 (Wis. 1996). Yet, the current patenting of gene sequences allows for indiscriminate patenting without consent or knowledge.

In *Moore*, the seminal case regarding an individual's right to informed consent in medical sampling and research, the patient suffered from hairy-cell leukemia and was admitted to the UCLA Medical Center for treatment. 793 P.2d at 481. Before advising Moore that he needed to have his spleen removed, his physician decided that he would use Moore's spleen for research purposes. *Id.* The physician did not advise Moore of his research intentions when he suggested Moore undergo surgery and later derived a cell line from Moore's T-lymphocytes,

valued at $3 billion, over which the University of California applied for a patent. *Id*. Moore sued, alleging, among other things, that he was not able to make an informed decision about whether to undergo his surgery because he was unaware of his physician's ulterior motives. *Id.* at 482. The California Supreme Court agreed, holding that "a physician must disclose personal interests unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgment." *Id.* at 483.

The *Moore* decision, however, has been limited to physicians and other individuals with whom a patient shares a fiduciary relationship. *See Greenberg v. Miami Children's Hosp. Research Inst., Inc*., 264 F. Supp. 2d 1064, 1070-71 (S.D. Fla. 2003). In *Greenberg*, a researcher patented the genetic sequence for Canavan disease after studying the blood and tissue samples of several donors. *Id.* at 1067. The individuals who provided the samples alleged that the researcher violated principles of informed consent when he did not disclose his economic intentions to patent the genetic sequence and commercialize it. *Id.* at 1068. The court disagreed, distinguishing *Moore* on the ground that it applied to physicians and patients, but not to researchers and donors. *Id.* at 1070-71. *Greenberg* illustrates how donors who intend to contribute to the public domain can be misled by researchers and left without a remedy.

Genetic research is being undertaken on people without their consent, as researchers prospect for genes. The United Nations Educational, Scientific and Cultural Organization (UNESCO) warned in 2002:

> Industry is naturally interested in human genetic data as well. The legal battle between several European institutions, including France's Institut Curie, and the US firm Myriad Genetics shows this . . . . because the firm refuses to grant manufacturing licences, all DNA samples will have to be sent to the Myriad Genetics headquarters in Salt Lake City for processing, *providing the company with a unique databank about people at high risk*.
>
> The stock of human genetic data is sure to continue increasing. So we have to think about possible misuses . . . At the collecting stage, there is the problem of consent, which is not new to the medical profession. "Free, informed and express" consent is not always self-evident. Suppose researchers in rich countries decide to obtain raw genetic data from people living in countries with less developed economies and legal protection systems, with no legislation about genetic data or even basic information about it, what kind of consent can they give?[11]

CONCLUSION

For the above stated reasons, the Court should affirm the judgment below.

[11] UNESCO, *Ethical Guidelines Urgently Needed For Collecting, Processing, Using and Storing Human Genetic Data*, Press Release No. 2002-93 (2002), *available at* http://portal.unesco.org/en/ev.php-URL_ID=7791&URL_DO=DO_PRINTPAGE&URL_SECTION=201.html.

Respectfully submitted,

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