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 *AMICI CURIAE* CANAVAN FOUNDATION, CLAIRE ALTMAN HEINE FOUNDATION, MARCH OF DIMES FOUNDATION, MASSACHUSETTS BREAST CANCER COALITION, NATIONAL ORGANIZATION FOR RARE DISORDERS, NATIONAL TAY-SACHS and ALLIED DISEASES ASSOCIATION IN SUPPORT OF PLAINTIFFS FOR AFFIRMANCE

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CERTIFICATE OF INTEREST

Counsel for *amici curiae* Canavan Foundation, Claire Altman Heine Foundation, March of Dimes Foundation, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, and National Tay-Sachs and Allied Diseases Association certifies the following:

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

   Canavan Foundation, Claire Altman Heine Foundation, March of Dimes Foundation, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, and National Tay-Sachs & Allied Diseases Association

2. The names of the real parties in interest represented by me are:

   Canavan Foundation, Claire Altman Heine Foundation, March of Dimes Foundation, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, and National Tay-Sachs & Allied Diseases Association

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

   None

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

   Barbara A. Caulfield
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I. STATEMENT OF INTERESTS OF *AMICI CURIAE*

All parties have consented to the filing of this amicus brief through their counsel. (See CAFC Rule 29(a)). No party's counsel authored the brief in whole or in part, and no party, party's counsel, or person—other than the amici curiae, their members, or their counsel—contributed money that was intended to fund preparing or submitting the brief.

A. Individual Organizational Interests

March of Dimes Foundation is a non-profit organization dedicated to improving the health of babies by preventing birth defects, premature births, and infant mortality. For over 70 years, March of Dimes has carried out its mission through research, community services, education, and advocacy, originally to fight polio and, for the past 50 years, more generally to save babies' lives. March of Dimes funded Jonas Salk's revolutionary research into polio vaccine. On the day the field tests were pronounced a success, Edward R. Murrow interviewed Salk live on his television show. "Who owns the patent on this vaccine?" Murrow asked. "Well, the people, I would say," Salk replied, "There is no patent. Could you patent the sun?"

Historically, March of Dimes has played an important role in the key advances of genetics, having donated substantial funds in seed money to the early research of James Watson, resulting in his milestone discovery of the double helix

structure of DNA. Today, March of Dimes funds research into genetic diseases and therapies, among many other fields. March of Dimes' mission and research are directly adversely affected by patents on gene sequences and correlations with disease, like the patents-in-suit.

Canavan Foundation is a non-profit organization founded by the parents and friends of children affected by the Canavan disease. Canavan disease is a rare but fatal, inherited degenerative brain disorder that primarily affects children of eastern and central European Jewish (Ashkenazi) descent. The disease causes loss of body control and death, generally before the children reach their teens. The Canavan Foundation's mission is to provide funding for research efforts to find an effective therapy, raise awareness of the disease, and to help avoid Canavan disease through carrier screening and prenatal testing. Although it is believed that research advances may eventually lead to treatments or even a cure, there is currently no cure for the disease. Genetic testing is an important part of prevention and early detection.

However, low-cost carrier screening and prenatal testing programs for families at risk for Canavan disease were stopped by the holder of the patent on the Canavan gene based on patent claims very similar to those in this case.

Claire Altman Heine Foundation (CAHF) is a non-profit organization and a publicly supported charity. The Foundation is dedicated to establishing

population-based pan-ethnic carrier screening for Spinal Muscular Atrophy (SMA), which is the number one genetic killer of children under two. The Foundation aims to raise awareness by educating the public and medical communities, and it works closely with medical associations, genetic counselors, leading SMA researchers, clinicians, laboratories, the NIH, Congress, industry and federal agencies such as the National Human Genome Research Institute, and others in the field of genetics research, prevention, treatment, and counseling.

In CAHF's direct experience, the enforcement and use of patent rights relating to the gene responsible for SMA, similar to the patent claims at issue in this case, adversely affects clinical access to SMA carrier screening.

Massachusetts Breast Cancer Coalition (MBCC) is dedicated to eradication of breast cancer, particularly through understanding the interaction of genes and environmental toxins. MBCC supports research into a wider variety of genetic interactions for diagnosis and treatment of breast cancer. One of the organization's primary goals is to help assure equal access to treatment and testing for breast cancer. Myriad's BRCA sequence patents and BRCA correlation patents interfere with the goals of MBCC in preventing and eliminating breast cancer, diagnosing women predisposed to breast cancer, or testing pregnant women interested in prenatal genetic testing, by restricting access to affordable genetic diagnostic testing.

National Organization for Rare Disorders (NORD) is a non-profit federation of voluntary health organizations dedicated to helping people with rare or "orphan" diseases. An "orphan" disease is one that affects fewer than 200,000 people in the United States. There are more than 6,000 rare disorders that, taken together, affect approximately 25 million Americans. NORD assists health organizations, and is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and service. NORD provides information about diseases, referrals to patient organizations and support groups, research grants and fellowships, and advocacy for the rare-disease community. For almost twenty years, NORD has served as the primary non-governmental clearinghouse for information on rare disorders.

Many rare disorders are genetic in nature and, in NORD's experience, patents on gene sequences and correlations have a significant adverse impact on NORD's mission.

National Tay-Sachs & Allied Diseases Association (NTSAD) is a nonprofit organization founded in 1957 by the parents of children afflicted with Tay-Sachs, Canavan and related genetic diseases, as well as other lysosomal storage diseases and leukodystrophies. In general, these are progressive, degenerative disorders that cause loss of body control and death.

NTSAD's mission is to support research aimed at treating and curing these diseases, and to provide support for the individuals and families afflicted with these diseases. NTSAD strives to ensure that carrier screening for Tay-Sachs, Canavan, and other related diseases is readily available. Patent rights, like those of Myriad, limit clinical access to carrier screening for this family of diseases and the ability to conduct research for new treatments and cures.

B. Allowing Patents on Human Gene Sequences Stifles Innovation and Adversely Affects Patient Groups

This case exemplifies how too much patent protection can impede our collective efforts to minimize the pain and suffering caused by fatal diseases.[1] Patents like those at issue raise testing costs and simultaneously stifle the development of more accurate and reliable diagnostic tools. The results are concretely and tragically experienced by patients and their families whose suffering might have been minimized or prevented altogether by more effective and less expensive means of testing for the genetic disposition to certain life threatening diseases. It is therefore no exaggeration to say that the consequences of affording patent protection to human genes can be lethal.

[1] As with the BRCA genes, the genes responsible for other diseases such as Tay-Sachs disease, Canavan disease and Spinal Muscular Atrophy, are subject to similar patent claims to the gene sequences themselves and bare correlations.

Myriad[2] argues that upholding the district court's opinion would impede innovation and compromise patient diagnosis and treatment. Myriad Br. 3-4. But there is no factual or evidentiary support for Myriad's assertions. To the contrary, unless the district court's decision is upheld, the result will be less research, deficiency in diagnosing diseases, and worse outcomes for patients.

The impact that patenting genes has on research is like that of a patent on an element from the periodic table. (A2446).[3] That is, it deprives researchers of the ability to make unrestricted use of the most basic information known to humankind. If medical knowledge and testing is to advance, these basic building blocks must be free to all. (A2448). This is particularly true because, as any researcher in the field will readily admit, there are untold discoveries to be made about genes. (*Id.*)

Under current USPTO policy, one can patent a human gene even though one does not know or chose to reveal all that might be known about that patented gene. Yet, such a patent limits other research that may lead to a better understanding of that gene. In this case, Myriad's patents give it the *exclusive right* to perform genetic testing and research on the BRCA1 and BRCA2 genes in the United States. (A2727). But Myriad cannot claim that it currently knows all there is to be known

[2] "Myriad" as used herein refers to all appellants.

[3] Citations in the form "A_____" refer to Joint Appendix pages.

about the BRCA1 and BRCA2 genes and particularly the mutations thereto. Indeed, Myriad reports to many patients that they have an alteration in a BRCA gene but that the alteration has "unknown significance." (A2938). The patient does not know—and Myriad cannot tell the patient because it does not know—whether this alteration is correlated with an increased risk of cancer. Yet, Myriad is the *only* entity that the patient can look to for such answers because of its right to exclude others from researching and utilizing certain genetic sequences under the patents.[4]

Moreover, Myriad is in sole control of how or whether any new research will be incorporated into the tests that it offers—the only tests offered in the United States. (A2709). In light of its monopoly, Myriad lacks the competitive incentive to reinvent its test promptly and as necessary to reflect up-to-date research (or, for that matter, to offer its test at a reasonable price). (A2710).

Not only does Myriad control what type of tests to offer, it controls who qualifies for the tests. (A2650-51). For example, Myriad initially delayed offering a test for large rearrangements that its full sequencing test would miss, which it calls BRACAnalysis Rearrangement Test ("BART"). (A2650). When it finally

[4] In fact, Myriad has accused other laboratories of infringement simply for analyzing the BRCA1 and BRCA2 genes, not because they were using a particular test that Myriad had developed. (A2851). One survey showed that more than 50% of lab directors decided not to develop a clinical test as a result of concerns over a gene patent or license. (A2672).

began offering this additional test in 2006—years after its patents issued—it imposed strict criteria on which patients would receive it. (A2651). Those who do not meet *Myriad's* criteria usually must pay out-of-pocket for BART, as it is not covered by Medicare or many insurance policies. (A2651). As a consequence, it is Myriad's judgment, and not a patient's doctor's judgment, that often determines whether BART is available for a patient. (A2651). Myriad's sole control over the only available tests related to the BRCA1 and BRCA2 genes in the United States thus impedes a doctor's ability to diagnose and treat a patient. (A2557). The consequences of this interference are especially problematic for patients who need multiple genetic tests that can each be provided only by a patent holder. At best, it is inefficient and expensive to send a patient's blood or tissue sample to multiple laboratories for genetic tests; at worst, there may simply not be enough of the patient's sample to "split up" among multiple laboratories, forcing the patient's doctor to forego testing that would otherwise be ordered.

There can be no doubt that Myriad's monopoly worsens patient outcomes. Many cannot afford Myriad's test and are left with no test option. Others who receive Myriad's test are left with uncertain outcomes (such as when they learn they have variants of unknown significance). All are prohibited from seeking a second opinion or confirmatory test results from a different provider. And all are

subject to Myriad's sole discretion in determining what test is even offered and at what cost.

In light of the foregoing, it cannot be credibly claimed that patient diagnosis and treatment will suffer if the district court's decision is affirmed. Nor is the reward of a patent necessary to encourage innovation in the field.[5] (A2675). A patent on a gene does not foster innovation. To the contrary, the value of the gene lies in the sequences created by nature (whether wild-type or mutations). (A2618). Such sequences cannot be improved upon, nor can they be designed around: "*it is the sequence created by nature that is the entire point of the gene*." (A2618). Patents on genes thus do not advance the constitutional goals of the patent system, but instead obstruct them.

II. LEGAL ARGUMENT

A. The Patent Claims in Suit

This case addresses 15 claims from 7 patents. These claims are generally categorized into (1) composition of matter claims for "isolated DNA" and (2) method claims for "comparing" and "analyzing."

Claims 1 and 2 of the '282 patent are representative of the composition claims in suit. They cover:

[5] The United States government's funding for breast cancer research was $90 million in fiscal year 1990; it had grown to $2.5 billion for fiscal year 2008. (A2700).

1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

Claim 1 of the ’999 patent and claim 20 of ’282 patent are representative of the method claims in suit.

Claim 1 of the ’999 patent covers:

> A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables l2A, 14, 18 or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1.

Claim 20 of the ’282 patent covers:

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

B. Isolated DNA is Not Patent Eligible Subject Matter Under 35 U.S.C. § 101

The district court held that Myriad's composition claims are invalid because they seek to monopolize products of nature that are ineligible for patent protection as established under a long line of U.S. Supreme Court precedents. The district court determined that the subject matter of these claims, "isolated DNA," did not possess markedly different characteristics from DNA as it occurs naturally in the human body. (A228). Central to the Court's determination is its conclusion, drawn from an analysis of key precedents, that the process of extracting DNA sequences from human cells and (in some cases) further purifying DNA sequences to eliminate noncoding portions "cannot transform it [DNA] into patentable subject matter." (A214). This applies to cDNA as well as isolated DNA; in both cases the claimed invention is nothing other than a sequence of nucleotides that function exactly as nature intended and in the same manner as they did before extraction and purification.

1. The District Court Properly Relied on the Established Exclusion for Products of Nature

Despite the broad language set forth in 35 U.S.C. § 101, the scope of what is eligible for patent protection is not limitless. The U.S. Supreme Court consistently has recognized boundaries of eligibility for patent protection by identifying general areas and subjects that are off limits to private monopolization. These subjects for

exclusion are often described in terms including "natural phenomena," "laws of nature" and "abstract ideas." *See Diamond v. Diehr*, 450 U.S. 175, 185 (1981); *Parker v. Flook*, 437 U.S. 584 (1978). But the Supreme Court has used other phrases such as "products of nature,"[6] "physical phenomena"[7] and "forces of nature"[8] interchangeably with "natural phenomena" and "laws of nature."

The rationale behind such exceptions is rooted in the idea that innovation requires unfettered access to a strata of basic concepts and natural phenomena that are prerequisite to and foundational of any advances in science and commerce. In *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948), the U.S. Supreme Court reiterated this point on its way to declaring products of nature unpatentable. "Patents cannot issue for the discovery of the phenomena of nature...[They] are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none." *Id*. at 130. Justice Breyer's recent statements in the *Metabolite* case further elaborate on the reasons for recognizing these exceptions to patentable subject matter.

> 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

[6] *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 130 (2001); *Diamond v. Chakrabarty*, 447 U.S. 303, 311 (1980).

[7] *Bilski v. Kappos*, 130 S. Ct. 3218, 3221 (2010); *Chakrabarty*, 447 U.S. at 309.

[8] *Dolbear v. Am. Bell Tel. Co.*, 126 U.S. 1, 532 (1888).

> and time-consuming; monetary incentives may matter; and the fruits of those incentives and that research may prove of great benefit to the human race. Rather, the reason for the exclusion is that sometimes too much patent protection can impede rather than "promote the Progress of Science and useful Arts," the constitutional objective of patent and copyright protection.

Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 136 (2006) (Breyer, J., dissenting). As Justice Breyer's comment suggests, the grant of a private monopoly through the issuance of a patent is not intrinsically beneficial; there are cases of "too much patent protection," and patents on universal principles, abstract ideas, and the basic elements of nature are paradigmatic of such cases.

2. Under *Funk Bros.* and *Chakrabarty*, Isolated Human Gene Sequences are not Patentable Subject Matter

In *Funk Bros.*, the patent applicant claimed a new product for inoculating plants comprising six well-recognized species of bacteria. This product could be used on many different types of plants because of the applicant's alleged discovery that certain strains of root-nodule bacteria do not exert a mutually inhibitive effect on each other. By virtue of this discovery, a farmer could use one composite inoculate product to treat many different crops.

The Supreme Court, while acknowledging that the product was a "new" and useful composition, concluded that "[i]t is no more than the discovery of some handiwork of nature and hence is not patentable." *Funk Bros.*, 333 U.S. at 131.

Crucial to the Court's analysis is its understanding that "[t]he 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." *Id.* As these statements reflect, the critical inquiry in *Funk Bros.* is whether naturally occurring properties lie at the core of the claimed invention. When the claimed advantages of an invention are little more than natural properties of the ingredients behaving in the manner for which nature intended them, the subject matter is not patent eligible.

Myriad and several amici argue that the facts of the present case are more analogous to those addressed by the Supreme Court in *Diamond v. Chakrabarty*, and that *Chakrabarty* more than any other case supports the conclusion that Myriad's composition claims are drawn to patentable subject matter. But the Court in *Chakrabarty* does not deviate from the criteria employed in *Funk Bros.* and makes even clearer why the composition claims in the present case are invalid for lack of patentable subject matter.

In *Chakrabarty*, the Supreme Court held that where an inventor introduced new genetic material within a bacterium cell, he had created something that was not a product of nature and was thus patentable subject matter under 35 U.S.C. § 101. In reaching its holding, the Court expressly recognized that patentable subject matter must exclude "laws of nature, physical phenomena and abstract

ideas." The Court explained that the subject matter at issue fell outside of these categories because the "patentee has produced a new bacterium with *markedly different characteristics* from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly, it is patentable subject matter under § 101." *Chakrabarty*, 447 U.S. at 310.

To explain how the newly engineered bacterium was "markedly different" from natural products, the Supreme Court points primarily to the functional properties of the product. It differentiates the new subject matter from products of nature by observing that its utility is based on a property "which is possessed by no naturally occurring bacteria." *Id*. at 305. The new bacterium in *Chakrabarty* fell on the side of human manufacture because its utility and suitability for claimed purposes derived from a property that did not occur in any bacteria naturally.

The same cannot be said of the subject matter of Myriad's BRCA1 and BRCA2 patents. Isolated human gene sequences, whether extracted from cells or extracted and further purified into cDNA, are structurally and functionally identical to human gene sequences as they naturally occur. The characteristics and function of a gene reside in the gene sequence—that is, the A's, C's, G's, and T's that code for the expression of a specific protein. These characteristics and functions (the active portion of the gene sequence) have not been changed in "isolated" DNA.

The person claiming ownership of an isolated gene is seeking a monopoly on its natural functions—the ability of a gene sequence to anneal to its complementary strand (which allows diagnosis) and the ability to produce proteins. The standard and criteria adopted in *Funk Bros.* and *Chakrabarty* for distinguishing unpatentable products of nature from patentable products of human manufacture clearly establish the unpatentability of "isolated DNA" whether it be merely extracted or further purified to cDNA. The district court thus correctly held that isolated DNA cannot be patented under section 101.

3. The District Court Properly Applied the Teachings of *Funk Bros.* and *Chakrabarty*

Myriad concedes, as it must, that the exclusion of physical phenomena, natural laws, and abstract ideas from patentable subject matter is well-established by Supreme Court precedent. Myriad Br. 17 and 33. It instead faults the district court for using the term "products of nature" and for relying on the "markedly different characteristics" language from *Chakrabarty*. Myriad Br. 41. These arguments are specious. First, the terms "physical phenomena" and "laws of nature," which Myriad presumably accepts, are as broad or broader than the term "products of nature" and do not imply a different result when applied to the facts of this case. Abstract terms such as these do not provide a self-sufficient interpretive means of distinguishing between patentable and unpatentable subject matter. Regardless of which term is used, the challenge for courts addressing patent

eligibility has been how to classify subject matter using general categories such as product of nature vs. human manufacture. In facing this task, the district court properly relied on language from *Chakrabarty* to explain the considerations that should be analyzed on this issue.

Myriad contends that the district court misuses the language "markedly different characteristics" to create a new legal standard. This too is a red herring. The district court has properly adopted precise language employed by the *Chakrabarty* court as explanation for that Court's holding. These words are stated in *Chakrabarty* not as a passing observation, but as the Court's explanation of what differentiates newly engineered bacterium from unpatentable products of nature.

Myriad apparently introduces the dispute over nomenclature in order to obscure the fact that it can find no substantive basis for challenging the district court's analysis of the precedents. Certainly, Myriad has not proffered a more credible interpretive scheme.[9]

[9] Myriad seems to prefer the *Chakrabarty* court's reference to language in *Hartranft v. Wiegmann*, 121 U.S. 609 (1887) describing a nonnaturally occurring human manufacture as "having a distinctive name, character [and] use." Myriad Br. 47. Myriad does not explain how "having a distinctive name" might serve as a means of distinguishing between patentable and unpatentable subject matter. Moreover, the language of "distinctive character and use" does not advance the interpretive goal beyond, or even as far as, the *Chakrabarty* court's own analysis in terms of "markedly different characteristics."

4. The Mere Extraction and Purification of Human DNA Does Not Render it Patentable Subject Matter

Myriad's arguments wrongly suggest that the amount of human energy expended to extract and purify "isolated DNA" is prima facie evidence of human manufacture. As Justice Breyer's comments in *Metabolite Labs.* make clear, the amount of human energy exerted on a discovery is not material to its patent eligibility. *Metabolite Labs., Inc.*, 548 U.S. at 136 (Breyer, J., dissenting). Moreover, a long line of cases have held that an isolated and purified product of nature is not patentable if the product functions in a way that is not significantly different than what occurs in nature. As the Supreme Court wrote over a century ago:

> There are many things well known and valuable in medicine or in the arts which may be extracted from...substances. But the extract is the same, no matter from what it has been taken. A process to obtain it 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.

American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 593-94 (1874).

In *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884), the Supreme Court considered a synthetic version of a dye that already existed in nature (alizarine), but the synthetic version had a brighter hue. The Court held that "calling it artificial alizarine did not make it a new composition of matter, and

patentable as such, by reason of its having been prepared artificially for the first time from anthracine, if it was set forth as alizarine, a well known substance." *Id.* at 311.

Most lower courts' have held that isolated and purified products of nature are not patentable. *See e.g. In re Marden* (Marden I), 47 F.2d 957 (C.C.P.A. 1931) (purified uranium); *In re Marden* (Marden II), 47 F.2d 958 (C.C.P.A. 1931) (purified vanadium); *In re Merz*, 97 F.2d 599 (C.C.P.A. 1938) (purified ultramarine dye); *Dennis v. Pitner*, 106 F.2d 142 (7th Cir. 1939) (purified cube plant root); *Gen. Elec. Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d Cir. 1928), *cert. denied*, 278 U.S. 656 (1928) (purified tungsten); *Ex parte Latimer*, 1889 Dec. Comm'r Pat. 123 (purified pine needle fiber).[10]

These cases further support the conclusion that any labor expended by Myriad in isolating the DNA sequence or isolating the coding region does not transform the natural product into a manufacture. The resulting molecules and genetic sequences obtained are "fit only for the same beneficial uses as

[10] The one notable exception is *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95 (C.C.S.D.N.Y 1911), *aff'd in part, rev'd in part*, 196 F. 496 (2d Cir. 1912), where Judge Learned Hand held that purified adrenaline met the statutory requirement for novelty. *Parke-Davis & Co.*, 189 F. at 101-102. Despite Judge Learned Hand's reputation as an important jurist, *Parke-Davis* has been heavily criticized and suffers from numerous infirmities. Moreover, even if the decision had reflected the law at that time, the Supreme Court's subsequent decisions in *Funk Bros.* and *Chakrabarty* make clear that *Parke-Davis* is not good law.

theretofore." *American Fruit Growers, Inc. v. Brogdex, Co.*, 283 U.S. 1, 12 (1931).

5. The DOJ's Effort to Distinguish cDNA from Isolated DNA is Insupportable and Legally Immaterial

The U.S. Department of Justice ("DOJ") has submitted an Amicus brief agreeing with the district court that isolated DNA is not patent eligible, but asserting that cDNA is a human manufacture. The DOJ does not and cannot provide a credible reading of legal precedent that would support the inclusion of cDNA among human-made products that differ markedly from native DNA. The fact that cDNA requires additional procedures to isolate only the coding portions of DNA does not support a conclusion that cDNA is patent eligible.[11] Regardless, the DOJ's "middle position" on this subject turns out to be irrelevant to this Court's decision because there are no claims at issue that are limited to cDNA. It is not clear why the DOJ believes that it is entitled to read in such a limitation in claims 2 and 6 of the '282 patent, but Myriad does not do so, nor has it challenged the district court's broader construction of these particular claims. Consequently, even if the DOJ's distinction between isolated DNA having both coding and

[11] The DOJ's arguments rest on the misconception that the amount of time and human energy expended to reveal natural tendencies is evidence of human manufacture. As Justice Breyer's comments in *Metabolite Labs.* point out, neither the amount of effort nor the cost of discovering a force of nature renders it patentable. *See also American Wood-Paper Co.*, 90 U.S. (23 Wall.) at 593-94*; American Fruit Growers, Inc.*, 283 U.S. at 12-13; *Funk Bros.*, 333 U.S. at 131.

noncoding sequences and cDNA having only the coding sequence were supportable (and it is not), this Court need not reach that issue to affirm the district court's Opinion in all respects.

C. Myriad's Patent Claims for Methods of "Comparing" Human Gene Sequences or Cell Growth Rates are Invalid

The district court held that the method claims were invalid because they are directed to the abstract mental processes of comparing or analyzing gene sequences or even to the scientific method itself.

Myriad challenges the disposition of its method claims by arguing various ways that the claims in-suit implicitly include certain processing and/or transformation steps that render the claimed subject matter more than mere observation and/or comparison of natural phenomena. Myriad's arguments rest on an impermissible attempt to read limitations into the method claims and must be rejected.

1. The District Court Properly Construed the Claims Not to Include Additional Limitations

The challenged method claims for "analyzing" or "comparing" DNA sequences require only a single step of "analyzing" or "comparing" sequences. For example, the only identified step of claim 1 of the '999 patent is (1) analyzing a sequence of (a) a BRCA1 gene or (b) BRCA1 RNA from a human sample, or (2)

analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample.

Myriad does not dispute that the challenged claims do not explicitly claim the steps of isolating DNA or sequencing DNA.[12] Instead, Myriad argues that the court should have construed the claims to include *additional limitations* of isolating and sequencing DNA based upon the phrase "sequence … from a human sample" found in some of the claims.[13] Myriad Br. 17. Myriad's premise is that these claims "require extraction and processing of human tissue or blood samples." Myriad Br. 55.

But Myriad only identifies alleged transformations that are not found in the claim language. Specifically, Myriad impermissibly attempts to import at least the following steps into the claims based on the phrase "from a human sample": (1) breaking open cells of a tissue sample; (2) extracting DNA or RNA from those

[12] None of the method claims include any version of the word "isolate," and the term "sequence" is always used as a noun to describe the information being analyzed or compared.

[13] The district court correctly concluded that "from a human subject" "serve[s] only to specify the identity of the DNA or RNA sequence to be 'analyzed' or 'compared," i.e., from a human sample as opposed to an animal sample or cell culture." (A235). The identification of a sequence's source is a reasonable, plain, and ordinary interpretation of the construed phrase "from a human subject" and is not at odds with the specification. Moreover, the district court only needed to apply one reasonable interpretation of the phrase "from a human subject" in order to determine that the claim read on patent ineligible subject matter and was therefore invalid. *See Titanium Metals Corp. of Am. v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985).

cells; and (3) using a diagnostic probe or primer to hybridize to the target DNA or RNA to initiate a sequencing reaction. *See* Myriad Br. 56-57. Despite well-settled law that patent claims cannot be limited to a specific embodiment unless the specification so teaches,[14] Myriad asserts that these additional steps are required to practice the claimed steps of "analyzing" or "comparing."

Myriad looks to *Prometheus Labs., Inc. v. Mayo Collaborative Services*, 581 F.3d 1336 (Fed. Cir. 2009), *cert. granted, judgment vacated, and remanded*, 130 S. Ct. 3543 (2010), to support its argument. In *Prometheus*, this Court held that the claimed processes satisfied section 101 because they taught the transformation of the human body following administration of a drug and/or determination of the levels of the drug's metabolites. This Court concluded that "the presence of those two steps in the claimed process is not 'merely' for the purpose of gathering data," but rather ***central*** to the invented process. *Id.* at 1347.

Prometheus is readily distinguishable. The claims at issue in *Prometheus* were drafted to expressly include one or more of the two transformative steps. *Prometheus*, 581 F.3d at 1340. In contrast, Myriad's claims were not drafted to

[14] *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed. Cir. 2005) (*en banc*). The interpretation of the claim language should be consistent with the specification of the patent. *See id.* at 1315-17. For example, the inventor may give a special definition to a term other than its ordinary meaning, or may intentionally disclaim, or disavow, a claim's scope. *Id.* at 1316. Myriad's asserted additional limitations are not based upon these exceptions to a term's ordinary meaning, but are an improper attempt to redefine the challenged claims.

include the proposed transformative steps that Myriad faults the district court for not importing as limitations. For example, the ***claimed*** "determining" step in *Prometheus* is akin to Myriad's ***unclaimed*** would-be limitations for the steps of "isolating" and "sequencing."

Moreover, Myriad's asserted transformation steps are only performed to make the sequence information that naturally occurs in the body observable so that the analysis or comparison can be performed. In fact, it is imperative that the sequence information is not altered by the additional steps or the claimed analysis is useless.[15] In other words, they are merely data-gathering steps. In contrast, in *Prometheus*, a transformation of the body achieved via an administered drug was central to the patent's end—the claims in the *Prometheus* patent all required the determination of metabolites in relation to red blood cells, where the metabolites were based upon bodily changes to an administered drug.[16]

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[15] Despite Myriad's contradictions, the ordinary meaning of "sequence" to one skilled in the art would include a series of letters representing a linear order of nucleotides, as the specification confirms. *See e.g.*, '999 patent 5:65-67 (describing the series of letters in Figure 10 as "showing a genomic sequence of BRCA1"); '857 patent 5:10-11 (describing the series of letters in Figure 3 as "the DNA sequence of the BRCA2 gene."). Regardless, the sequence information is the necessary aspect of the claims regardless if the term "sequence" is referred to as a molecule or a series of letters representing a nucleotide order. In both cases, it is the information shown by the sequence that is being observed.

[16] *See* Patent No. 6,355,623 (showing that even claim 46 which did not include an "administering step" explicitly called for "determining the level … in a subject *administered a drug*") (emphasis added).

The patent applicant for Myriad's patents could have included the steps of determining a sequence from a sample in its claims if the applicant had intended to limit the claims to include such steps—as the applicant in the *Prometheus* patent did.[17] Myriad cannot now seek to read in claim limitations without violating the prohibition against importing claim limitations from the specification. *See Phillips*, 415 F.3d at 1323-24.

2. Even Under Myriad's Proposed Claim Construction, the Method Claims at Issue Are Directed to Patent Ineligible Subject Matter

Under Myriad's claim construction, the method claims for "analyzing" and "comparing" DNA sequences would include routine "isolating" and "sequencing" steps to determine the "sequence" for analysis or comparison. *See* Myriad Br. 56-57. But even assuming these are "required"—though unclaimed—elements in the claims, they are "data gathering steps" that "are not central to the purpose of the claimed process." (A238). Accordingly, even if it was proper, Myriad's attempt to import limitations of "isolating" and "sequencing" DNA cannot save its invalid method claims. *See In re Bilski*, 545 F.3d 943, 953 (Fed. Cir. 2008).

For example, claim 1 of the '999 patent is "[a] method for detecting a germline alteration in a BRCA1 gene." (A463). This is accomplished by "analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample

[17] However, Myriad's additional limitations would not be sufficient to render the abstract ideas patent eligible. *See, infra*, Section C2.

…." (A463). The only step central to the claim's purpose of detecting a germline alteration is to analyze a sequence of a BRCA1 gene to presumably observe whether or not a specified alteration is within the sequence. In other words, the "process"—retrieving the sequence of a BRCA1 gene from a human—is nothing more than data gathering for the purpose of the claim (i.e., the actual analysis of the sequence).[18]

Myriad's method claims for "analyzing" and "comparing" DNA sequences are patent-ineligible for an additional reason: the claims as a whole read on scientific principles—namely, the identification of a predisposition to breast cancer based on "analyzing" or "comparing" BRCAl/2 gene sequences. *See Diehr*, 450 U.S. at 191 (instructing that "when a claim recites a mathematical formula (or scientific principle or phenomenon of nature), an inquiry must be made into whether the claim is seeking patent protection for that formula in the abstract.") *See Bilski*, 130 S. Ct. at 3231 (citing *Flook*, 437 U.S. 584) (recognizing that a limitation to one field of use or a limitation to token post-solution activity will not save a claim that, taken as a whole, is directed to patent ineligible subject matter and invalid).

[18] The other claims for "analyzing" and "comparing" are in accord with this example, and do not include a transformation that is central to the claim purpose of the claims even under Myriad's construction.

Simply put, to consider Myriad's proposed transformations[19] as sufficient to satisfy section 101 "would effectively vitiate the limitations to claiming mental processes … since 'to use virtually any natural phenomenon for virtually any useful purpose could well involve the use of empirical information obtained through an unpatented means that might have involved transforming matter.'" (A238) (citing *Metabolite Labs.*, 548 U.S. at 136 (Breyer, J., dissenting)); *see also Bilski*, 130 S. Ct. at 3231 (finding that instructing the use of well-known techniques to help establish inputs into the equation does not make the abstract idea patentable). "To hold otherwise would allow a competent draftsman to evade the recognized limitations on the type of subject matter eligible for patent protection." *Diehr*, 450 U.S. at 192.

3. Application of the Scientific Method to a Natural Phenomena is an Abstract Process

Myriad asserts that the step of "administering a substance to a cell in the expectation that the substance will slow its growth" in claim 20 of the '282 patent is transformative and sufficient to render the claim patent eligible. But Myriad's claim broadly covers the scientific method for testing a reaction, which is a formulaic approach to determining cause and effect relationships. In simple terms, this is a test wherein you (1) prepare a test sample having the hypothesized element

[19] In addition, the "isolating" and "sequencing" steps are not transformative as they are designed to determine and maintain the coding sequence of natural DNA, because the comparison step is useless if the coding sequence is transformed.

(*i.e.*, the compound) and a control sample without the hypothesized element; (2) allow a reactionary process to occur (*i.e.*, time for "growing"); (3) observe the results of both samples (*i.e.*, compute and compare cell growth rates); and (4) draw a conclusion related to the original hypothesis (*i.e.*, whether the compound is indicative of a cancer therapeutic). This claim does nothing more than apply the scientific method to the particular technological environment surrounding the BRCA1 gene—a natural phenomena. Merely limiting patent-ineligible material to a single field of use does not make a concept patentable. *See Bilski*, 130 S. Ct. at 3231 (finding a patent claim for the use of an abstract idea in the energy market was not patent eligible) (citing *Flook*, 437 U.S. 584); s*ee also Diehr*, 450 U.S. at 191 ("A mathematical formula as such is not accorded the protection of our patent laws, and this principle cannot be circumvented by attempting to limit the use of the formula to a particular technological environment").

4. Observing a Natural Phenomena is an Abstract Process

In addition to simply applying the scientific method to the BRCA1 environment, claim 20 of the '282 patent is directed to observing laws of nature dictating cell growth reactions and mentally correlating the cell growth reactions to a conclusion. As the district court stated "the essence of the claim, when considered in its entirety, is the act of comparing cell growth rates and concluding that 'a slower growth of said host cell in the presence of said compound is

indicative of a cancer therapeutic.'" (A241). Administering a substance to a cell is not sufficiently transformative to be patent eligible when considering the claim as a whole. The purpose of administering a substance is to gather cell growth data for comparison with control cell growth data. The information is evaluated to determine whether the substance is a potential cancer therapeutic—a mental process of observing a natural phenomenon.

III. CONCLUSION

In this case, decisions concerning the proper limits of patent protection have profound consequences for the lives of patients and their families. For the reasons stated above, Amici urge the Court to affirm the district court's opinion.

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December 8, 2010

CERTIFICATE OF FILING AND SERVICE

I hereby certify that on this 8th day of December, 2010, I caused two copies of the Brief for Amici Curiae Canavan Foundation, Claire Altman Heine Foundation, March of Dimes Foundation, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, National Tay-Sachs and Allied Diseases Association to be sent to counsel for Appellants, Gregory A. Castanias, by hand delivery and to all other parties by U.S. Mail as follows:

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I certify that the foregoing Brief of Amici Curiae Canavan Foundation, Claire Altman Heine Foundation, March of Dimes Foundation, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, National Tay-Sachs and Allied Diseases Association contains 6,984 words as measured by the word processing software used to prepare this brief.

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