CERTIFICATE OF INTEREST

Counsel for amici curiaeCanavan 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:

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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 the 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

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 the cost of tests 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,

began offering this additional test in 2006—years after its patents issued—it imposed strict criteria on which patients w

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.

1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ

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 sa

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 strata of basic concepts and natural phenomena that are prerequisite to and foundational of 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 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

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 end 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. Where 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 compositions claimed 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

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 patent 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 bacteria 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. Clearly, Myriad has not proffered a more credible interpretive scheme.[9]

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[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.

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.[10] 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).

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

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

noncoding sequences and cDNA may only the coding sequence were

supportable (and it is not), this Court need not reach that issue to affirm the district

cells; and (3) using a diagnostic probe oligomer 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 TJ 17.60 rometheiTc 2d m0 TwMyr[adThis not

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 additional steps or the claimed analysis is useless.[15] In other words, they are merely data-gathering steps. In contrast, in Prometheus

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 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

…." (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

Simply put, to consider Myriad's proposed transformation[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 phenomenon. 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); see 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.'" (A24). 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

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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

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