UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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ASSOCIATION FOR MOLECULAR PATHOLOGY; AMERICAN COLLEGE OF MEDICAL GENETICS; AMERICAN SOCIETY FOR CLINICAL PATHOLOGY; COLLEGE OF AMERICAN PATHOLOGISTS; HAIG KAZAZIAN, MD; ARUPA GANGULY, PhD; WENDY CHUNG, MD, PhD; HARRY OSTRER, MD; DAVID LEDBETTER, PhD; STEPHEN WARREN, PhD; ELLEN MATLOFF, M.S.; ELSA REICH, M.S.; BREAST CANCER ACTION; BOSTON WOMEN'S HEALTH BOOK COLLECTIVE; LISBETH CERIANI; RUNI LIMARY; GENAE GIRARD; PATRICE FORTUNE; VICKY THOMASON; KATHLEEN RAKER,

Plaintiffs,

v.

UNITED STATES PATENT AND TRADEMARK OFFICE; MYRIAD GENETICS; LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation,

Defendants.

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09 Civ. 4515 (RWS)

ECF Case

PLAINTIFFS' MEMORANDUM OF LAW IN SUPPORT OF MOTION FOR SUMMARY JUDGMENT

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INTRODUCTION AND STATEMENT OF FACTS

This case challenges the legality and constitutionality of certain patent claims that seek to patent natural ("wild type") human genes, mutations in those genes caused by nature, and correlations between those mutations and an increased risk of breast or ovarian cancer, a correlation also caused by nature.[1] These patent claims violate the Patent Act, 35 U.S.C. § 101, because they are not patentable subject matter. They also constitute patents on thought, knowledge, and ideas in violation of the First Amendment. Because they patent basic scientific principles, not inventions or discoveries, they have impeded rather than advanced science and thus also violate the U.S. Constitution, Article 1, Section 8, Clause 8 (the intellectual property clause).

Plaintiffs include four prominent, national organizations including pathologists, clinical laboratory scientists, other medical professionals, and researchers, with a combined membership of over 150,000 members. SMF ¶¶ 1-4.[2] Plaintiffs also include six of the nation's preeminent geneticists. SMF ¶¶ 5-10. In addition, two genetic counselors, two breast cancer and women's health advocacy organizations, and six individual women are plaintiffs. SMF ¶¶ 11-20.

Defendants include the U.S. Patent and Trademark Office ("USPTO"), which granted these patents pursuant to official written policies and practices permitting the patenting of natural human genes, naturally mutated genes, and the correlations created by nature between mutated genes and an increased risk of disease. Defendants also include Myriad Genetics and the University of Utah Research Foundation, the exclusive licensee and owner of the patents.

[1] The patent claims being challenged are identified in the Complaint ¶¶ 32, 55-80. The patents themselves are submitted with Plaintiffs' Motion for Summary Judgment.

[2] A complete list of all of the material facts is contained in the Statement of Material Facts (SMF) filed pursuant to Local Rule 56.1. As required by the Rule, each paragraph in the SMF includes a supporting citation to one or more declaration or other document, filed herewith.

Each defendant has moved to dismiss on procedural grounds, and plaintiffs have filed oppositions to those motions. This memorandum is filed in support of plaintiffs' separate motion for summary judgment. Summary judgment shall be granted if the papers show that "there is no genuine issue as to any material fact and that the movant is entitled to judgment as a matter of law." Fed. R. Civ. Pro. 56(c). "[F]acts must be viewed in the light most favorable to the nonmoving party only if there is a 'genuine' dispute as to those facts." *Scott v. Harris,* 550 U.S. 372, 380 (2007). "Where the record taken as a whole could not lead a rational trier of fact to find for the nonmoving party, there is no genuine issue for trial." *Matsushita Elec. Industrial Co. v. Zenith Radio Corp.,* 475 U.S. 574, 587 (1986) (internal quotation marks omitted).

Every human body contains genes that determine, in part, the structure and functions of the body. D. Sulston ¶¶ 10-11;[3] D. Mason ¶ 4; SMF ¶¶ 40-41. Genes are created by nature. D. Sulston ¶ 10; D. Mason ¶ 33; D. Chung ¶ 25; D. Ledbetter ¶ 27; D. Leonard ¶ 15. Through a natural process in the body, the genes instruct the body to create proteins and those proteins do the work of the body. D. Mason ¶¶ 7, 11-12; D. Sulston ¶ 17. Although every person has genes, and there is enormous similarity between the genes of one individual and another, sometimes genes become altered. SMF ¶ 51. These alterations can be inherited or can occur after birth, but in both instances it is nature that causes the alterations. D. Sulston ¶¶ 19, 27; D. Mason ¶¶ 14-17; D. Chung ¶ 10; D. Ledbetter ¶ 26; SMF ¶¶ 51-54, 60. Some of the alterations appear to be unimportant. Others correlate with an increased risk of disease or disorder and are called mutations. For others, the significance of the alteration is unknown ("variant of unknown significance"). D. Mason ¶ 19. The significance of the alteration is created entirely by nature. D. Sulston ¶ 27; D. Chung ¶ 10; D. Mason ¶ 20; D. Ledbetter ¶ 26.

[3] The designation "D. ____" refers to the declaration of the identified individual attached to Plaintiffs' Motion for Summary Judgment.

Because some alterations are of clinical significance, it is useful for pathologists, clinical laboratory scientists, other medical professionals, and researchers[4] to look at a particular person's genes to see if he or she has alterations known to be of clinical significance. D. Sulston ¶ 18; D. Mason ¶¶ 21, 23; D. Chung ¶ 10; D. Swisher ¶¶ 23-26; SMF ¶¶ 55-58. This process is called genetic testing. There are a variety of methods by which medical professionals and researchers can examine genes, including sequencing. D. Sulston ¶¶ 20-21, 23, 25; D. Mason ¶¶ 24-30; D. Chung ¶ 10; D. Swisher ¶¶ 23-24; D. Kant ¶ 5; D. Ledbetter ¶¶ 21-22. Thousands of medical professionals and researchers around the world sequence genes every day, and the processes by which gene sequencing is done are not at issue in this case. D. Sulston ¶¶ 21-22; D. Chung ¶¶ 10-11; D. Ostrer ¶¶ 4, 8-9; D. Hegde ¶¶ 6-7; D. Hubbard ¶¶ 3-6; D. Mason ¶¶ 22, 31; D. Ledbetter ¶¶ 9-10, 22.

At the end of the sequencing process, the medical professional or researcher has a long string of four letters (A, C, T, and G) that correspond to the four nucleotides (adenine, cytosine, thymine, and guanine) that form the basic elements of DNA and genes. D. Sulston ¶¶ 15-16; D. Mason ¶¶ 13, 23; D. Chung ¶ 10; SMF ¶ 55. For example, claim 2 of patent '282 is for DNA with "the nucleotide sequence set forth in SEQ ID No. 1." SEQ ID No. 1 consists of 5914 nucleotide base pairs and functionally begins with ATGGAT. This nucleotide sequence represents the human gene known as *BRCA1*. After sequencing, the clinician or scientist looks to see if there are variants. For example, claim 7 (a) of patent '282 claims the *BRCA1* gene in which there is a variant consisting of a "T at nucleotide position 4056." In SEQ ID. No. 1,

[4] Many professionals are affected by the patent claims at issue in this case. They include molecular pathologists, geneticists (molecular, biochemical, clinical, and cytogenic), genetic counselors, research doctors and scientists, physicians, medical technologists, laboratory professionals, and other health care professionals. Hereinafter, the phrase "medical professionals and researchers" is intended as a short-hand reference to encompass all of those who seek to take actions in their professional capacity but are prevented from doing so by the patent claims at issue in this case.

position 4056 is ordinarily a C. Nature sometimes causes that C to be changed to a T. The patent claim is over the DNA as changed by nature. D. Sulston ¶ 27; D. Chung ¶ 10; D. Mason ¶ 20; D. Ledbetter ¶ 26; SMF ¶¶ 86-100.

Several of the claims at issue in this case consist essentially of looking at genes. SMF ¶¶ 101-112. For example, claim 1 of patent '999 claims the act of looking at the patented gene. It does not specify or claim any particular method of looking at the gene. The only unique part of this claim is that the gene being looked at is the *BRCA1* gene. Claim 1 of patent '001 involves comparing a natural gene, such as that patented by claim 2 of '282, with a sample from a patient to see if variants exist. Again, the claim does not specify or claim any particular method of obtaining or comparing the sequences; it simply covers the act of looking at the two sequences and concluding they are the same or different. Claim 2 of patent '857 similarly involves comparing two gene sequences, but at the end, the person concludes not only that the sequences are different (if they are) but that the sequence does or does not correlate with an increased risk of breast and/or ovarian cancer.

Although the sequences are dictated by nature, the variants are dictated by nature, and the significance of the variants is dictated by nature, the USPTO has a policy and practice of issuing such patents. Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001). For patents on the genes themselves, the USPTO's theory is that the genes involved have been "isolated," by which the USPTO means that they have been removed from the body and separated from surrounding cellular material. *Id.* The claims in this case describe the gene being patented as "isolated" and the gene patents in this case were granted pursuant to the USPTO's policy.

"Isolation" means nothing more than a gene that has been removed from the body and separated from surrounding cellular material, and such a gene is functionally and informationally

identical to that in the body. D. Sulston ¶¶ 16-17, 26-27; D. Mason ¶¶ 23, 29, 32, 33; D. Chung ¶ 10; SMF ¶¶ 64-65. For example, claim 1 of patent '282 is for "isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID No. 2." But the gene as it exists in the body codes for (creates) the exact same BRCA1 polypeptide (protein). D. Sulston ¶¶ 11, 14-15; D. Mason ¶¶ 7, 11-12. Isolating the gene does not change its function. SMF ¶¶ 95-96.

For some of the patent claims, defendants may assert additionally that they have transformed the gene from DNA into cDNA (complementary DNA) and it is thus a new thing. For example, SEQ ID No. 1, referred to in claim 2 of patent '282 claims cDNA. cDNA is functionally and informationally identical to DNA. D. Sulston ¶¶ 16-18, 26-27; D. Mason ¶¶ 29, 32-33; D. Chung ¶ 10. Although there are certain structural differences, such as removal of the regions that are not used in creating the protein, the cDNA structure simply mirrors the RNA structure in the body, both of which are dictated by nature. D. Mason ¶¶ 29, 32. Moreover, the structural differences are irrelevant to the function of the gene in the body or in the lab or when used by medical professionals or researchers to determine if the gene has variants of clinical significance. *Id.*[5]

The patent claims in this case have had a negative impact on both breast and ovarian cancer research and clinical practice. D. Sulston ¶ 37-38; D. Cho ¶ 24. The patent claims permit defendants to preclude all research into genes known to correlate with an increased risk of breast and/or ovarian cancer. The patent claims have deterred research into this area critical for women's health. *Id.* The patent claims have also prevented other labs from looking at the genes

[5] Additional details concerning genes, gene variants and mutations, gene sequencing, and gene analysis are contained in SMF ¶¶ 40-85 and the declarations cited therein. Additional details concerning the patent claims at issue in this case and their scope are contained in SMF ¶¶ 86-124, the declarations cited therein, and in section I.B. below.

involved. *See, e.g.*, D. Kazazian ¶¶ 4-7; D. Ganguly ¶¶ 4-11; D. Chung ¶ 15; D. Hegde ¶ 10; D. Matloff ¶ 5; D. Ostrer ¶¶ 4-7, 9; D. Swisher ¶ 28; D. Hubbard ¶¶ 7-8; D. Kant ¶ 6; D. Ledbetter ¶¶ 13, 18; D. Reich ¶¶ 3, 5.[6] In some instances, the effect has been devastating, as defendants utilized methods of looking at the genes over a period of years that failed to identify all variants of clinical significance and advised women that no deleterious mutations were found, when other methods could have been utilized that could have found additional mutations. *See* D. Limary ¶ 7; D. Thomason ¶ 6; D. Raker ¶¶ 7-8; D. Swisher ¶¶ 25-27. Defendants do not share the data gathered as a result of their monopoly with other researchers, which means that advances in understanding the significance of variants, advances that could save women's lives, have been slowed. D. Swisher ¶¶ 15-21; D. Chung ¶¶ 20-22; D. Ostrer ¶¶ 12-13; D. Limary ¶ 8; D. Sulston ¶¶ 36, 38; D. Matloff ¶ 9; D. Ledbetter ¶ 20.

Clinical practice has also been harmed. Many women cannot afford the tests. D. Ceriani ¶¶ 5-7; D. Fortune ¶¶ 4-5; D. Thomason ¶ 8; D. Raker ¶¶ 7-11; D. Reich ¶¶ 6, 8, 10, 13; D. Kazazian ¶ 8; D. Matloff ¶¶ 7, 12, 14; D. Ostrer ¶ 8. Further, women cannot get a second opinion to confirm the accuracy of the testing or the meaning of the results. D. Girard ¶¶ 5-9; D. Ceriani ¶¶ 9, 11; D. Fortune ¶ 7; D. Ostrer ¶ 11; D. Swisher ¶¶ 32-33. No other diagnosticians can evaluate or ensure the quality of the testing done by defendants by attempting to replicate it. D. Chung ¶ 23; D. Ledbetter ¶ 23; D. Reich ¶ 9; D. Ostrer ¶ 11. In addition, Myriad refuses to do some critical tests. D. Chung ¶ 24. Labs have been deterred from developing new tests as a result of the patent. D. Cho ¶ 10; D. Ledbetter ¶¶ 14-15.[7]

[6]Additional details concerning the enforcement of the patents are contained in SMF ¶¶ 125-141 and the declarations cited therein.

[7] Additional details concerning the harms caused by these patent claims are contained in SMF ¶¶ 142-210 and the declarations cited therein.

The patent claims in this case cover products of nature, laws of nature, and abstract ideas, knowledge and even thought. These patents should never have been granted. The effect has been harmful for science, medicine, and women's health. The patents should be declared invalid.

ARGUMENT

I. CLAIM CONSTRUCTION OF THE PATENT CLAIMS IN SUIT

A. The Legal Framework

Patent analysis involves two steps. "In the first step the court determines the proper construction of the patent claims by establishing the scope and boundaries of the subject matter that is patented, as a matter of law, and in the second step the trier of fact determines issues of validity…." *WeddingChannel.com, Inc. v. Knot, Inc.*, 66 Fed. R. Evid. Serv. (Callaghan) 375, 2005 WL 165286, at *1 (S.D.N.Y. 2005) (citing *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370, 384-85 (1996)).

"A claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using, or selling the protected invention." *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989). The purpose of construing patent claims is to define the scope of the coverage of the claim by interpreting the words and terms of art used as they would be understood at the time the claim was made by one reasonably skilled in the relevant art. Claim construction is "the judicial statement of what is and is not covered by the technical terms and other words of the claims." *Netword, LLC v. Centraal Corp.*, 242 F.3d 1347, 1352 (Fed. Cir. 2001); *see also United States Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997), *cert. denied*, 522 U.S. 950 (1997).

In determining the proper construction of a claim, courts generally rely on two broad categories of evidence:

> (1) intrinsic evidence (*i.e.*, the patent claims, the patent specifications, and the prosecution history), and (2) extrinsic evidence (*i.e.*, expert and inventor testimony, dictionaries, treatises, and all other evidence external to the text of the patent and the prosecution history.)

2005 WL 165286 at *2; *See Markman*, 52 F.3d at 979-80. A court should examine the intrinsic evidence first, as it is "the most significant source of the legally operative meaning of disputed claim language." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). A court should look to extrinsic evidence only where necessary to resolve any ambiguities in a disputed claim term, and where the court requires assistance in understanding the technical aspects of the relevant art. *See DeMarini Sports, Inc. v. Worth, Inc.*, 239 F.3d 1314, 1323 (Fed. Cir. 2001) (citing *Mantech Envtl. Servs., Inc. v. Hudson Envtl. Serv., Inc.*, 152 F.3d 1368, 1373 (Fed. Cir. 1998); *EMI Group N. Am., Inc. v. Intel Corp.*, 157 F.3d 887, 892 (Fed. Cir. 1998)).

In examining the intrinsic evidence, a court should look first to the plain language of the claim itself. *WeddingChannel.com, Inc.*, 2005 WL 165286 at *3 (citing, *e.g.*, *Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 55 F.3d 615, 619-20 (Fed. Cir. 1995)). "Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history." *Vitronics*, 90 F.3d at 1582 (citing *Hoechst Celanese Corp. v. BP Chems. Ltd.*, 78 F.3d 1575, 1578 (Fed. Cir. 1996); *Hormone Research Found., Inc. v. Genentech, Inc.*, 904 F.2d 1558, 1563 (Fed. Cir. 1990)). As a result, "it is always necessary to review the specification to determine whether the inventor has used any terms in a manner inconsistent with their ordinary meaning." *Vitronics*, 90 F.3d at 1582; *see also Markman*, 52

F.3d at 979 (stating that "the description may act as a sort of dictionary, which explains the invention and may define terms used in the claims"). Shortly after this Court issued its *WeddingChannel.com* opinion, an *en banc* Federal Circuit confirmed this legal framework for claim construction. *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc).

B. The Claim Language

At issue in this case are 15 claims across 7 patents. The claims can be organized into two groups: (i) composition of matter claims for "isolated DNA," and (2) method claims for "comparing" or "analyzing." The table below sets forth all of the claims in suit divided into these two groups. The discussion below is based on what the claim terms would have meant to one of ordinary skill in the art at the time of application for the patents (presumed to be August 1994 for the '282, '473, '999, '001 and '441 patents and December 1995 for the '492 and '857 patents). D. Grody ¶¶ 6-7; D. Leonard ¶¶ 26-27.

U.S. Patent No.	Composition Claims	Method Claims
5,747,282 ("the '282 patent")	1, 2, 5, 6, 7	20
5,693,473 ("the '473 patent")	1	
5,709,999 ("the '999 patent")		1
5,710,001 ("the '001 patent")		1
5,753,441 ("the '441 patent")		1
5,837,492 ("the '492 patent")	1, 6, 7	
6,033,857 ("the '857 patent")		1, 2

1. Claims to *"isolated DNA"* ('282 patent claims 1, 2, 5, 6 and 7; '473 patent claim 1; and '492 patent claims 1, 6 and 7)

Claim 1 of the '282 patent is representative of the group of composition of matter claims and reads:

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

Several of the terms found in this claim merit discussion.

"DNA" The term "DNA" means a sequence of nucleic acids, also referred to as nucleotides. Each nucleotide is one of four possibilities: A, C, T or G. "DNA" is, thus, a "nucleotide sequence" or a "polynucleotide," although DNA is not synonymous with those terms, as not all polynucleotides are DNA, but all DNA is a polynucleotide. Determining the precise arrangement of A's, C's, T's and G's in a polynucleotide, such as DNA, is called "sequencing." D. Grody ¶¶ 1-12; D. Leonard ¶¶ 33-35.

"isolated"; "isolated DNA" The term "isolated DNA" means a fragment of DNA substantially separated from other cellular components and other DNA. There were several known techniques for performing such separation at the time, so this term is not inherently limited to any particular method of "isolation." The specification of the '282 patent adopts this definition. '282 patent, col. 19, ll. 8-18. D. Grody ¶¶ 13-15; D. Leonard ¶¶ 33-35.

"coding for" The term "coding for" means DNA that naturally translates into amino acids according to the well known genetic code. "Coding for" is synonymous with "encodes." A set of three nucleotides is known as a "codon" and individual codons naturally translate into one of twenty standard amino acids. A string of amino acides is called a "polypeptide." Nature determines which codons translate into which amino acids and when this genetic code was cracked it was heralded as a monumental scientific breakthrough. Thus, a DNA "codes for" a

certain polypeptide when it has a nucleotide sequence that will naturally translate into that polypeptide sequence. It is known that multiple codons translate into the same amino acid, so there can be multiple versions of DNA that "code for" the same polypeptide. It is also known that some portions of nucleotide sequences do not actually code for any amino acid. The specification of the '282 patent adopts this definition. '282 patent, col. 19, ll. 1-5. D. Grody ¶¶ 16-18; D. Leonard ¶¶ 36-38.

"BRCA1" The term "*BRCA1*" refers to a particular fragment of DNA found on chromosome 17 that relates to a person's predisposition to develop breast and ovarian cancer. This particular fragment of DNA is referred to as "the *BRCA1* gene." The specification of the '282 patent adopts this definition. '282 patent, col. 1, ll. 21-22. D. Grody ¶¶ 19-21; D. Leonard ¶¶ 39-41.

"polypeptide"; "amino acid sequence" The term "polypeptide" means a string of amino acids. Thus, the terms "polypeptide" and "amino acid sequence" are synonymous. The specification of the '282 patent adopts this definition. '282 patent, col. 21, ll 3-5. D. Grody ¶¶ 25-27; D. Leonard ¶¶ 45-47.

"having the amino acid sequence" The phrase "having the amino acid sequence" inherently means "having *all of but no more than* the amino acid sequence," because interpreting that phrase to allow for more than just the identified amino acid sequence would result in it encompassing up to an entire human genome, which would defeat the purpose of identifying the specific sequence. Similarly, to construe the phrase to include less than the entire identified sequence would potentially leave out important components, which could have substantial functional effects, as a partial amino acid sequence can – and usually does – function much differently than the complete sequence from which it is taken. D. Grody ¶¶ 28-30; D. Leonard

¶¶ 48-50.

"SEQ ID NO:2" This term has no ordinary meaning. Rather, it is a generic phrase that refers to a specific sequence given elsewhere, usually somewhere in the document making the reference. The specification of the '282 patent sets forth what is identified as "SEQ ID NO:2" in a "Sequence Listing" section in the back. '282 patent, cols. 79-90. The sequence is an "amino acid" (i.e. polypeptide) sequence having a total of 1863 amino acids. D. Grody ¶¶ 31-33; D. Leonard ¶¶ 51-53.

Claim 2 of the '282 patent depends from claim 1 and adds the limitation "wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1." As discussed above, it is possible for there to be several DNA polynucleotide sequences that code for the same amino acid / polypeptide sequence. As such, claim 1 could cover a number of isolated DNA's, because it is only limited to DNA that codes for a particularly given amino acid sequence. Claim 2, on the other hand, depends from claim 1 and identifies a specific DNA polynucleotide sequence. Therefore, there is only one polynucleotide sequence that is covered by claim 2 and it is identified in the claim as SEQ ID NO:1, which is set forth in the "Sequence Listing" section in the back of the specification. '282 patent, col. 67-80. The sequence is a "nucleic acid" sequence having 5,914 nucleotides (the patent uses the term "base pairs", which is synonymous with nucleotide for double stranded sequences like SEQ ID NO:1).

Claims 5 and 6 of the '282 patent claim an "isolated DNA having at least 15 nucleotides of the DNA of" claims 1 and 2 respectively. As discussed above, claim 1 is directed to an isolated DNA that codes for an amino acid sequence having 1863 amino acids. Because it takes three nucleotides to code for an amino acid, the isolated DNA of claim 1 must have at least 5,589 nucleotides. Thus, claim 5, directed to "isolated DNA having at least 15 nucleotides of the DNA

of claim 1" means any 15+ nucleotide portion of an isolated DNA that satisfies claim 1. These portions could have 15, 16, 17, etc. nucleotides and, thus, claim 5 is a much broader claim than claim 1, because there are a large number of portions of DNA satisfying claim 1 that could have at least 15 nucleotides. Similarly, claim 6, directed to "isolated DNA having at least 15 nucleotides of the DNA of claim 2," would also be much broader, because there are a large number of portions of that polynucleotide sequence that have at least 15 nucleotides, because the DNA of claim 2 has 5,914 nucleotides.

Claim 7 of the '282 patent is an independent claim directed to isolated DNA that contains the polynucleotide sequence set forth in SEQ ID NO:1 except for having one of a set of identified differences (a substitution of one nucleotide for another at a particular location, an additional nucleotide at a particular location, or a deletion of certain nucleotides at a particular location). In essence, the isolated DNA in this claim is exactly the same as that claimed in claim 2, except for having one of four identified differences.

Claim 1 of the '473 patent is an independent claim and reads:

> 1. An isolated DNA comprising an altered *BRCA1* DNA having at least one of the alterations set forth in Tables 12A, 14, 18 or 19 with the proviso that the alteration is not a deletion of four nucleotides corresponding to base numbers 4184-4187 in SEQ. ID. NO:1.

"altered"; "alterations" This term means being different from the most common form. With respect to DNA, the most common form of a gene is known as the "wild-type." Any persons who have differences in their genes from the "wild-type" are said to have "alterations" or "an altered gene." D. Grody ¶¶ 37-39; D. Leonard ¶¶ 57-59.

Thus, claim 1 of the '473 patent is directed to isolated *BRCA1* DNA that has at least one of a list of specified differences from the normal or "wild-type" *BRCA1* DNA. Those differences are set forth in the specification of the '473 patent in the cited tables. '473 patent, col. 61, ll. 1-5

(Table 12A), col. 66, ln.15 – col.67, ln. 20 (Table 14), col. 69, ll. 1-51 (Tables 18 and 19). While the claim does not expressly identify a sequence listing to define the term "*BRCA1* DNA," the specification of the '473 patent states that, "the coding sequence for a *BRCA1* polypeptide is shown in SEQ ID NO:1." '473 patent, col. 19, ll. 43-44. Thus, claim 1 of the '473 is virtually identical to claim 7 and the '282 patent, except for listing a different set of genetic alterations (claim 7 of the '282 patent identifies four alterations, while claim 1 of the '473 patent identifies several tables that each contain a number of alterations).

Claim 1 of the '492 patent is an independent claim that is virtually identical to claim 1 of the '282 patent discussed above. The only differences are that claim 1 of the '492 is directed to "*BRCA2*," not "*BRCA1*," and the amino acid sequence set forth as SEQ ID NO:2 in the '492 patent is not the same as that set forth in the '282 patent (this is because *BRCA1* and *BRCA2* are completely different genes existing at entirely different places on our chromosomes).

"BRCA2" The term "*BRCA2*" was known at the time to refer to a particular fragment of DNA found on chromosome 13 that related to a person's predisposition to develop breast and ovarian cancer. This particular fragment of DNA is referred to as "the *BRCA2* gene." The specification of the '492 patent adopts this definition. '492 patent, abstract. D. Grody ¶¶ 22-24; D. Leonard ¶¶ 42-44.

Claim 6 of the '492 patent is an independent claim and reads:

> 6. An isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide set forth in SEQ ID NO:2, wherein said mutated form of the BRCA2 polypeptide is associated with susceptibility to cancer.

"mutated"; "mutation" This term means an alteration or altered substance that causes or results in a meaningful (typically harmful) effect. Many alterations are benign and have no effect on the operation of the cell within which they exist. Other alterations do have an effect

(usually harmful) on the operation of the cell within which they exist. These types of alterations are typically called "mutations." Mutations can exist in either a nucleotide sequence or an amino acid sequence. D. Grody ¶¶ 46-48; D. Leonard ¶¶ 66-68.

Claim 6 of the '492 patent, therefore, broadly claims any and all nucleotide sequences that would translate into any *BRCA2* amino acid sequence that correlates to a greater likelihood of getting cancer because, unlike the claims discussed above, this claim is not limited to any particular list of alterations.

Claim 7 of the '492 patent depends from claim 6 and adds the limitation, "wherein the DNA molecule comprises a mutated nucleotide sequence set forth in SEQ ID NO:1." Because multiple DNA polynucleotide sequences can code for the same amino acid sequence, claim 6 could cover multiple DNA nucleotide sequences. Claim 7 limits that range to just one specific nucleotide sequence, that set forth in the '492 patent as SEQ ID NO:1. However, there are multiple ways in which that nucleotide sequence can be "mutated" and still code for a mutated form of *BRCA2* polypeptide. Thus, claim 7 is not limited to a single mutated form of that nucleotide sequence.

2. Claims to methods of "comparing" or "analyzing" ('282 patent claim 20; '999 patent claim 1; '001 patent claim 1; '441 patent claim 1; and '857 patent claims 1 and 2)

Claim 1 of the '999 patent is representative of the group of "method" claims. It is independent and reads:

> 1. 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 12A, 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.

This claim relates to a method for determining whether there is an alteration in a *BRCA1* gene and includes only one step: "analyzing a sequence." This is because a *BRCA1* gene, a *BRCA1* RNA from a human sample, and a *BRCA1* cDNA made from mRNA from said human sample all have the same polynucleotide sequence. D. Grody ¶¶ 52-57; D. Leonard ¶¶ 72-77. The "analyzing" performed in this claim merely requires one to look at the sequence and see if it contains one of the identified alterations. D. Grody ¶¶ 43-45; D. Leonard ¶¶ 63-65. This claim presumes that the sequence is already provided, as it does not include a step of first sequencing the gene before "analyzing" it. The tables referenced in the claim are all set forth in the specification of the '999 patent and contain lists of alterations. '999 patent, col. 61, ll. 36-51 (Table 12A), col. 66, ln.32 – col.67, ln. 38 (Table 14), col. 69, ln. 31 – col. 70, ln. 22 (Tables 18 and 19).

"germline" This term means hereditary, or received from genetic parents. D. Grody ¶¶ 49-51; D. Leonard ¶¶ 69-71.

Thus, claim 1 of the '999 patent is nothing more than a method for detecting whether a particular *BRCA1* gene has an inherited alteration that is listed in one of the referenced tables.

Claim 1 of the '001 patent is a similar independent claim. It relates to a method for determining whether a tumor sample from a human contains a *BRCA1* alteration and includes only one step: "comparing a first sequence ... with a second sequence" to see if there is a difference between them and, if there is, then concluding that such "indicates a somatic alteration" in the tumor sample. The "comparing" performed in this claim merely requires one to look at the two sequences, see if there is a difference between them and then conclude that a difference means there is an alteration. D. Grody ¶¶ 40-42; D. Leonard ¶¶ 60-62. This claim presumes the sequences are already provided, as it does not include a step of first "sequencing"

the *BRCA1* gene, *BRCA1* RNA, or cDNA made from mRNA, or otherwise acquiring the nucleotide sequences. D.

"somatic" This term means created within the body, not inherited. D. Grody ¶¶ 58-60; D. Leonard ¶¶ 78-80. It is the opposite of "germline." Somatic alterations are created within the body at a particular place, and often lead to tumors at that location. As such, other parts of the body will not have the somatic alteration.

Thus, claim 1 of the '001 patent is nothing more than a method for detecting if a tumor sample from a human contains an altered *BRCA1* gene that was created within the body, not inherited, by comparing the *BRCA1* sequence from the tumor with the *BRCA1* sequence from a non-tumor sample from the same person.

Claim 1 of the '441 patent and Claim 1 of the '857 patents are similar independent claims, differing only as to *BRCA1* ('441) or *BRCA2* ('857). They relate to a method for determining whether a human has an inherited *BRCA1* genetic alteration and include only one step: "comparing" a nucleotide sequence from the human to what is known to be the "wild-type" nucleotide sequence. D. Grody ¶¶ 46-48; D. Leonard ¶¶ 66-68. The "comparing" performed in these claims merely requires one to look at the two sequences, see if there is a difference between them and then conclude that a difference means there is an alteration. These claims presume the sequences are already provided, as they do not include a step of first "sequencing" the *BRCA1/2* gene, *BRCA1/2* RNA, or cDNA made from mRNA, or otherwise acquiring the nucleotide sequences. Thus, claim 1 of the '441 patent and claim 1 of the '857 patent are nothing more than a method for determining if a person has an altered *BRCA1* or *BRCA2* gene by comparing his or her inherited *BRCA1* or *BRCA2* gene to that which is previously known to be the normal or most common typical version of the gene.

"allele" This term means one member of a pair of genes at a specific location on a chromosome. Double stranded DNA has one allele on each strand at each location. Thus, a DNA could have a wild-type allele and a mutated allele at the same location. When this occurs, one of the alleles may be dominant while the other is recessive. Thus, for the purposes of the patents in suit, the term "allele" and the term "gene" are practically synonymous. D. Grody ¶¶ 46-48, 61-63; D. Leonard ¶¶ 66-68, 81-83.

Claim 2 of the '857 patent is a similar independent claim. It relates to a method for determining if a human is predisposed to getting breast cancer and has only one step: "comparing" the *BRCA2* nucleotide sequence from the human with the known nucleotide sequence for the normal, most-typical version of the *BRCA2* gene and concluding that a difference between them means the human has an alteration that predisposes him or her to breast cancer. The "comparing" performed in this claim merely requires one to look at the two sequences, see if there is a difference between them and then conclude that the person has an alteration that predisposes him or her to breast cancer. This claim presumes the sequences are already provided, as it does not include a step of first "sequencing" the *BRCA2* gene or its mRNA, or otherwise acquiring the nucleotide sequences.

Claim 20 of the '282 patent is an independent claim that relates to a method for determining whether a potential cancer therapeutic actually is a cancer therapeutic and includes only four steps: (i) growing a cell containing an altered *BRCA1* gene that is known to predispose the cell to cancer in the presence of the potential therapeutic; (ii) growing the same cell in the absence of the potential therapeutic; (iii) calculating the respective growth rates of those two cells; and, (iv) concluding that a slower growth rate for the cell in the presence of the potential therapeutic indicates the compound is indeed a cancer therapeutic. The growth of cells in the

presence or absence of a potential therapeutic is a natural process and does not result in a transformation of the cells in any way that would not occur naturally. Determining the growth rate of such cells is a simple task. The final step is a purely mental conclusion of comparing two growth rates to determine if they are different and then concluding that it was the presence of the potential therapeutic that caused any such difference. D. Grody ¶¶ 34-36; D. Leonard ¶¶ 54-56.

II. HUMAN GENETIC SEQUENCES AND THE SCIENTIFIC INQUIRY OF LOOKING AT A GENE OR COMPARING TWO HUMAN GENES CONSTITUTE NATURAL PHENOMENA, LAWS OF NATURE, AND ABSTRACT IDEAS AND THUS ARE NOT PATENTABLE SUBJECT MATTER UNDER 35 U.S.C. § 101.

The patenting of human genes, the concept of looking at or comparing human genes, and correlations found in nature between mutated genes and an increased risk of breast and/or ovarian cancer violates long-established Supreme Court precedent that prohibits the patenting of laws of nature, physical phenomena, and abstract ideas. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (citations omitted). The Court has explained repeatedly that products and laws of nature and abstract ideas cannot meet the threshold for qualifying as "inventions patentable" under 35 U.S.C. § 101 because "[s]uch discoveries are 'manifestations of . . . nature, free to all men and reserved exclusively to none.'" *Id.* quoting *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948). "[T]he 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." *Laboratory Corp. of America Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 126-27 (2006) (J. Breyer, dissenting).

Relying on this principle, the Supreme Court has rejected patent claims even when the purported invention was highly beneficial or novel, or the research and work that went into identifying it was costly or time-consuming. "The obligation to determine what type of

discovery is sought to be patented must precede the determination of whether that discovery is, in fact, new or obvious." *Parker v. Flook*, 437 U.S. 584, 593 (1978). While the Court has not yet considered the patentability of human genes, its precedents support only one conclusion: *BRCA1/2* gene sequences and the thought of comparing genes are so fundamental to human nature and scientific inquiry that these patent claims cannot pass muster under section 101.[8]

A. The *BRCA1/2* genes and their mutations are natural phenomena, products of nature, and manifestations of laws of nature.

This case challenges claims over *BRCA1/2* wild-type (or normal) genetic sequences and *BRCA1/2* genetic sequences containing naturally-occurring mutations [collectively, "the composition claims" or "the gene sequence claims"]. Some of these claims are over genes in the exact same structure as they exist in the human body, and other claims may be limited to DNA without their non-coding sections – DNA that has the exact same function and informational content as the genes as they exist in the body. All of these claims embody products and laws of nature. D. Sulston ¶¶ 10, 16-17, 19, 27; D. Ostrer ¶ 14; D. Chung ¶¶ 10, 25; D. Mason ¶¶ 20, 29, 32-33; D. Ledbetter ¶¶ 26-27; D. Leonard ¶ 15.

1. The claimed gene sequences are products of nature.

Supreme Court precedent establishes that merely extracting, purifying, or changing a natural product does not render that product patent-eligible, unless a fundamentally new product is created. Because the composition claims patent genes that simply have been removed from

[8] Some lower courts have looked at gene patents without examining the patentable subject matter question under section 101. A Federal Circuit case looking at patents on the DNA sequence that encodes human erythropoietin (EPO) assumed that isolated and purified genes were patentable. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200 (Fed. Cir. 1991). *Amgen* did not engage in a section 101 analysis, but merely upheld the gene sequence claims against prior art and best mode challenges. A more recent case concluded that claims on DNA molecules encoding for a protein known as "NAIL," thought to help activate cells that can play a major role in fighting tumors, were obvious. *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009). The court held that it was "obvious to try" to identify the gene sequences given the previous disclosure of a protein identical to NAIL and a method for obtaining the DNA sequence for NAIL. *Id.* at 1361. Neither of these cases dealt with whether genes are patentable subject matter.

other cellular materials or genes whose non-coding sections have been removed, this case law mandates the invalidation of these claims. In 1931, the Court rejected the patenting of a fruit, the skin or rind of which carried mold-resistant borax. *American Fruit Growers, Inc. v. Brodgex Co.*, 283 U.S. 1 (1931). Although the "complete article is not found in nature," and despite the "treatment, labor and manipulation" that went into producing the fruit, the Court held that the fruit did not become an "article of manufacture" unless it "possesses a new or distinctive form, quality, or property" distinct from nature. *Id.* at 11.

In 1948, the Court concluded that a mixture of several naturally-occurring species of bacteria was not patentable, despite the special commercial utility shown by the combination. *Funk Bros. Seed Co.*, 333 U.S. at 128-31. Each species of bacteria in the mixture could extract nitrogen from the air for plant usage. While the patent holder had created a mixture by selecting and testing for strains of bacteria that did not mutually inhibit one another, the Court concluded that the patent holder did "not create a state of inhibition or of non-inhibition in the bacteria. Their qualities are the work of nature. Those qualities are of course not patentable." *Id.* at 130. Just as the fruit and the bacteria strains were works of nature, so, too, are the genes in this case. D. Jackson ¶ 34.

Fully consistent with this precedent, the Court recognized the patentability of genetically-engineered bacterium capable of breaking down crude oil in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980). There, 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." *Id.* at 310. Unlike the gene sequences at issue here, the *Chakrabarty* bacterium

was a product that was engineered by man to serve an entirely innovative function. D. Jackson ¶ 41.

Chakrabarty often has been cited for the proposition that "anything under the sun that is made by man" is patentable, *id.* at 309, but that phrase cannot support the notion that anything created by human effort survives section 101 scrutiny. The legislative history of the Patent Act of 1952, from which *Chakrabarty* only partially quotes, clearly acknowledges the statutory limitations. "A person may have 'invented' a *machine or a manufacture*, which may include anything under the sun made by man, but it is not necessarily patentable under section 101 unless the conditions of the title are fulfilled." H.R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952) (emphasis added). In this case, the claimed gene sequences and mutations are neither machine nor manufacture. *Chakrabarty* itself reaffirms that the case does not "suggest that § 101 has no limits or that it embraces every discovery . . . a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter." 447 U.S. at 309. *Funk Brothers* and *Chakrabarty* teach that the conditions of section 101 cannot be satisfied by naturally-occurring products, even when human ingenuity led to their packaging in a more useful form whose function is identical to that found in nature.

"Purification" also does not make a product of nature into something patentable. Starting as early as 1894, the Supreme Court recognized that simply purifying a natural substance is insufficient to create a "new composition of matter." In *American Wood Paper Co. v. Fibre Disintegrating Co.*, the Court held that refined cellulose, consisting of purified pulp derived from wood and vegetable, was unpatentable because it was "an extract obtained by the decomposition or disintegration of material substance." 90 U.S. 566, 570 (1874).

> There are many things well known and valuable in medicine or in the arts which may be extracted from divers 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.

Id. at 593-94. D. Jackson ¶¶ 17-25. The principle that one cannot patent a purified product of nature was further explained in *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884). There, the Court rejected a patent on an artificial version of a natural red dye called alizarine that was produced by manipulating another compound through acid, heat, water, or distillation. *Id.* Although the artificial version of the dye was of brighter hue than observed in nature and prepared through a new, man-made process, it was unpatentable because of its similarity to the natural product. D. Jackson ¶¶ 7-16.

This precedent has been applied to prohibit patents on naturally-occurring products that have been extracted, distilled, or purified. In *Ex Parte Latimer*, the Patent Commissioner refused to allow a patent on pine needle fibers that were better suited for textile production, even though it was necessary to remove the needle from its sheath and other resinous material. 1889 Dec. Comm'r Pat. 123, 125 (1889)("Nature made them so and not the process by which they are taken from the leaf or needle"). Similarly, the Third Circuit held that a patent applicant named Coolidge could not patent "substantially pure tungsten having ductility and high tensile strength," despite the superiority of purified tungsten over its naturally-occurring, brittle form. *General Electric Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d Cir. 1928).

> Naturally we inquire who created pure tungsten. Coolidge? No. It existed in nature and doubtless has existed there for centuries. The fact that no one before Coolidge found it there does not negative its origin or existence.
>
> The second part of the claim reads: 'Having ductility and high tensile strength.' Did Coolidge give those qualities to 'substantially pure tungsten'? We think not for it is now conceded that tungsten pure is ductile cold. If it possesses that quality now it is certain that it possessed it always.

Id. at 643; D. Jackson ¶¶ 38-40. *General Electric* confirms that a naturally-occurring substance does not transform into a synthetic product when isolated and purified, as the characteristics of a purified substance are inherent to nature rather than created by the researcher. *See also In re Marden*, 18 C.C.P.A. 1046 (C.C.P.A. 1931) (rejecting patent on purified uranium); *In re Marden*, 18 C.C.P.A. 1057 (C.C.P.A. 1931) (rejecting patent on purified vanadium); *In re Merz*, 25 C.C.P.A. 1314 (C.C.P.A. 1935) (rejecting patent on purified ultramarine). "[M]ere purification of known materials does not result in a patentable product," unless "the product obtained in such a case had properties and characteristics which were different in kind from those of the known product rather than in degree." *Merz*, 25 C.C.P.A. at 1316.

The USPTO's policy of treating genes as patentable misses this important distinction. The USPTO policy allows patents on "isolated and purified" DNA that has the same sequence as a naturally occurring gene because 1) "the DNA molecule does not occur in that isolated form in nature" and 2) the purified state of synthetic DNA preparations "is different from the naturally occurring compound." 2001 Utility Guidelines at 1093. Thus, according to the PTO, one can patent a "gene excised from the natural chromosome," *id.*, although that would simply entail removing the gene from its natural environment. If this erroneous analysis had been applied in the Supreme Court cases discussed above, then the cellulose at issue in *Wood Paper*, the dye of *Cochrane*, the fruit of *American Fruit Growers*, and the combination of bacteria species of *Funk Brothers* could have been patented because they did not occur in nature in their claimed form.

Some lower courts have committed this same error by mistakenly focusing on novelty and utility rather than patentability. For example, in *In re Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970), the court upheld patents on purified prostaglandins as useful without citing to any case law supporting the rejection of the section 101 arguments. In *Merck & Co. v. Olin Mathieson*

Chemical Corp., 253 F.2d 156 (4th Cir. 1958), the court upheld a patent on the purified B-12 vitamin because the natural form "has no utility, therapeutically or commercially, until converted into compositions comparable to the patented products." Although apparently thinking utility the only relevant question, the *Merck* court did note that "[t]he claims of this patent do not reach pure, crystalline vitamin B(12)" or "vitamin B(12) compositions derived from liver or any source other than the specified fermentates." *Id.* at 160. It was thus interpreted not to reach all B-12, but only one type, manufactured from a single source. D. Jackson ¶¶ 35-37. All of the claims in this case reach genes from any source. Indeed, claims 6 and 7 of '492 encompass all the mutated forms of the *BRCA2* gene, without specifying mutation type or location, and whether discovered at the time of the patent or in the future, by Myriad or someone else. Some of the mutations claimed by Myriad were found by others. D. Sulston ¶¶ 30-32.

The court in *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95 (S.D.N.Y. 1911), also erroneously justified its finding that purified adrenaline was patentable based on its commercial utility. In reaching this conclusion, the court relied on *Kuehmsted v. Farbenfabriken of Elberfeld Co.*, 179 F. 701 (7th Cir. 1910), and *Union Carbide Co. v. American Carbide Co.*, 181 F. 104 (2d Cir. 1910), two inapposite cases, as both dealt with the purification of human-made chemicals that did not exist in nature. *Parke-Davis* also is unpersuasive in the gene patent context for scientific reasons. Whereas the human body does not possess a natural process for purifying adrenaline, the human body does possess a natural process for isolating and purifying genes. D. Jackson ¶¶ 26-29; D. Mason ¶¶ 11-12.

All four Supreme Court cases (*American Wood Paper*, *Cochrane*, *Funk Brothers*, and *Chakrabarty*) hold that patentability requires more than removing a natural product from its environment and purifying it. There must be a change in function. Genes are products of nature

and sequencing genes does not produce something with a new function. Indeed, sequencing is designed solely to reveal the functions of the gene dictated by nature. D. Mason ¶¶ 23, 29, 32, 33; D. Sulston ¶¶ 16-17, 18, 26-27; D. Chung ¶ 10.

2. The claimed gene sequences are a manifestation of laws of nature.

Patent law has long held that scientific truths and natural phenomena cannot be patented. "The Supreme Court has recognized that scientific principles and laws of nature, even when for the first time discovered, have existed throughout time, define the relationship of man to his environment, and, as a consequence, ought not to be the subject of exclusive rights to any one person." *In re Meyer*, 688 F.2d 789, 795 (C.C.P.A. 1982). "The rule that the discovery of a law of nature cannot be patented rests, not on the notion that natural phenomena are not processes, but rather on the more fundamental understanding that they are not the kind of 'discoveries' that the statute was enacted to protect." *Parker v. Flook*, 437 U.S. 584, 593 (1978). Examples of nonpatentable subject matter include Newton's law of gravity, Einstein's e=mc2, and the Arrhenius equation. *See Chakrabarty*, 447 U.S. at 309; *Diamond v. Diehr*, 450 U.S. 175 (1981).

The Supreme Court applied this doctrine in *Funk Bros.*, 333 U.S. at 130:

> The qualities of these bacteria like the heat of the sun, electricity, or the qualities of metals, 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. He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end.

The qualities of the bacteria in *Funk Brothers* were a manifestation of a law of nature – the law being that these six bacteria, when combined, could fix nitrogen in plants without inhibiting each other. That scientific principle was set, it was not created by man.

Just as genes – whether normal or containing naturally-occurring mutations – are products of nature, they also embody a naturally-occurring genetic code and act as a law of

nature. A gene is not simply a chemical compound. D. Jackson ¶¶ 12-16, 49. The critical aspect of a gene is the information it contains. *See* D. Sulston ¶¶ 16-17, 18, 26-27; D. Mason ¶¶ 23, 29, 32, 33; D. Chung ¶ 10. The same genetic information is transmitted in the body as is transmitted when a gene is sequenced and examined. D. Mason ¶¶ 11-12, 23, 29, 32, 33; D. Sulston ¶¶ 16-18, 26-27. The gene's instructions to the body are laws of nature. *E.g.* D. Chung ¶¶ 10; D. Mason ¶¶ 20; D. Sulston ¶ 27; D. Ledbetter ¶ 26. Because the gene sequence claims embody a law of nature, they encompass natural phenomena and cannot be patentable subject matter under section 101.

The Supreme Court has long excluded laws of nature from patentability to ensure that scientific principles and natural phenomena are not preempted. In *O'Reilly v. Morse*, the Court invalidated a patent on any use of electromagnetism to send signals over distance. 56 U.S. 62, 112-13 (1853). In *Gottschalk v. Benson,* 409 U.S. 63 (1972), a patent over a method of programming a general purpose computer to convert signals from binary-coded decimal form into pure binary form was rejected.

> It is conceded that one may not patent an idea. But in practical effect that would be the result if the formula for converting BCD numerals to pure binary numerals were patented in this case. The mathematical formula involved here has no substantial practical application except in connection with a digital computer, which means that if the judgment below is affirmed, the patent would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself.

Id. at 71-72. Preemption concerns also led the Court to conclude that the use of a new formula to update alarm limit values during the catalytic chemical conversion of hydrocarbons could not be patented because the method was a manifestation of a mathematical formula. *Flook,* 437 U.S. 584. On the other hand, a process utilizing the Arrhenius equation for adjusting temperature inside a rubber mold while curing rubber was upheld because the Court found that the claim did not foreclose others from using the equation. *Diehr,* 450 U.S. 175.

This Court has applied these principles. In *Nippon Electric Glass Co. v. Sheldon*, this Court invalidated claims to a television tube that was created according to the inventor's observation that radiation above a certain level is unhealthy. 539 F. Supp. 542 (S.D.N.Y. 1982). "He claimed to have discovered a phenomenon of nature, that X-radiation in excess of 0.04 mr/hr from televisions is harmful to human health and applied for a patent to privatize the benefits that would flow from his teaching. Such a monopoly on ideas is unavailable under the patent laws." *Id.* at 546.

Similarly, the gene sequence claims in effect patent any use of the *BRCA1/2* genes. The patents cover the genes themselves; because the function of the genes both in the body and in the defendant's lab is to convey information, they cover all of the information for all of its uses. They cover the normal and mutated forms. It does not matter whether a scientist analyzes the DNA from a blood sample or tissue sample, or uses traditional or new sequencing methods. D. Sulston ¶ 27. Any scientist who wants to analyze the entire genome, analyze the *BRCA1/2* genes for reasons other than for breast and/or ovarian cancer, or analyze the interaction of the genes with other critical genes will also face this obstacle. D. Chung ¶ 24; D. Ledbetter ¶¶ 24-25. The claims are not even restricted to the *BRCA1/2* genes as a whole, but also cover "[a]n isolated DNA having at least 15 nucleotides of the DNA" of claim 1 or 2, s*ee* '282 cls. 5 and 6, extending the patents' reach to even smaller stretches of genetic information. Because the gene sequence claims seek to monopolize laws of nature and natural phenomena, they are unpatentable.

Perhaps most egregiously, the defendants have gained critical scientific evidence of additional laws of nature (*i.e.* previously unknown alterations, including deleterious mutations) and have refused to allow others to search the genes for those laws of nature at least insofar as that searching is done in a clinical setting. D. Ganguly ¶ 14; D Chung ¶¶ 13, 17, 18; D. Ostrer ¶¶

6-8; D. Hegde ¶ 10; D. Swisher ¶¶ 34-35; D. Hubbard ¶ 9; D. Kant ¶ 6; D. Ledbetter ¶ 16; D. Reich ¶¶ 3, 5.

B. A claim over any method of looking for naturally-occurring mutations in human genes that does not specify any particular method of analysis is invalid under 35 U.S.C. § 101.

Claim 1 of '999 patents any method for analyzing a *BRCA1* gene for one of the specified alterations, without specifying a method of analysis or requiring a further action beyond the mental process of "analyzing" the sequence for an alteration. What is patented is the mere thought process of looking at a *BRCA1* sequence and noting whether or not the specified naturally-occurring alterations appear.

Because this patent claim is directed to an unpatentable abstract mental process, it cannot satisfy section 101. "Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Benson*, 409 U.S. at 67. The '999 claim is analogous to patenting a method for "analyzing" a page of text for certain typos, without stating what method to use. A person could infringe by looking letter-by-letter at the text backwards, or simply by reading the text. In a case that sought to patent a method of diagnosing an abnormal condition in an individual, the Federal Circuit rejected the method as unpatentable under section 101 because the "only physical step involves merely gathering data" for the algorithm that was applied to perform the diagnosis. *In re Grams*, 888 F.2d 835, 839 (Fed. Cir. 1989). Here, unlike *Grams*, there is not even a physical step to gather data. The claim assumes the sequence is present, and the only step is mentally analyzing the sequence for an alteration. What is claimed is the "idea" of looking for a specified alteration. That is forbidden under *Benson*, 409 U.S. at 71.[9]

[9] The recent holding in *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) *(en banc), cert. gr.* 129 S.Ct. 2735 (2009) confirms this conclusion. In *Bilski*, the *en banc* Federal Circuit held that a process is patentable if "(1) it is tied to a

C. Claims over comparing two genes monopolize laws of nature and abstract ideas and thus are not patentable processes under 35 U.S.C. § 101.

Four of the challenged claims involve "methods" for comparing two genes – claim 1 of '001, claim 1 of '441, and claims 1 and 2 of '857 [hereinafter, "claims on comparing genes"]. Just as claim 1 of '999 patented a mental process, the claims on comparing genes patent abstract thought: comparing two gene sequences for naturally-occurring differences. The similarities or differences between the two compared genes were not created by the inventor, and none of these claims is limited even to "isolated DNA." For example, claim 1 of '441 patents comparing the germline sequence of a *BRCA1* gene taken from a person with the germline sequence of wildtype *BRCA1*; a difference between the two indicates that the person has an alteration in his or her *BRCA1* gene. The claim does not require a researcher to sequence the *BRCA1* gene, only to compare two given sequences. *See* Claim Construction, *supra*. Nor does the claim require any particular mode of comparison or any action after an alteration has been identified. *Id.* The '001 claim and the '857 claims operate the same way – a person infringes by noting natural facts about whether two genes are the same or diverge. *Id.*

Claim 2 of '857 is doubly troubling because it patents the correlation between any alteration in the *BRCA2* sequence with a predisposition for breast cancer.[10] The fact that a *BRCA2* alteration "indicates a predisposition to said cancer" is a law of nature or scientific principle, not a relationship invented by the patent holder. Concern about the overreach of

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particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." *Id.* at 954. Neither of these conditions is satisfied by any of the method claims challenged in this case. The methods are not tied to a particular machine or apparatus for "analyzing" or "comparing" and do not transform a gene into a different state or thing.

[10] Although the claim states that any alteration of the *BRCA2* gene indicates a predisposition to cancer, even that observation is scientifically incorrect. Only some alterations of the *BRCA2* gene are considered harmful and indicative of a higher risk of cancer, SMF ¶¶ 54, 71, but the claim does not identify them. Thus, the claim illustrates a major problem with allowing a patent on a law of nature – that monopolizing a scientific principle prevents others from testing or further developing it. A scientist who wants to identify which alterations in fact indicate a predisposition to breast cancer will run afoul of the patent claim as soon as he or she compares two gene sequences and thinks about the significance of an alteration.

correlation claims was articulated by Justice Breyer, in his dissenting opinion in *Laboratory Corp. v. Metabolite Labs.*, 548 U.S. at 124. The Court had granted *certiorari* on the question of whether a patent claim over the relationship between the level of homocysteine in a person and vitamin deficiency monopolized a basic scientific relationship, but later dismissed the petition as improvidently granted because the petitioner had not raised a patentability argument. Discussing section 101 at some length, Justice Breyer noted that even when the correlation was framed as a process for "detection of a vitamin deficiency" with discrete testing and correlating steps, the process simply "instructs the user to (1) obtain test results and (2) think about them." *Id.* at 136. As for the '857 patent, the first step of obtaining test results is not even included; the claim merely commands one to "compare" genetic sequences.[11] The correlations in this case are natural phenomena and neither they nor the process of thinking about them are patentable.

D. Comparing the growth rates of two cells is not patentable subject matter.

Just as the claims on comparing genes patent mental thoughts, claim 20 of '282 patents the abstract idea of comparing growth rates of two cells and preempts a basic scientific principle: that a slower rate of cell growth in the presence of a compound may indicate that the compound is a cancer therapeutic. The claim does not seek to actually patent a particular cancer therapeutic or drug, only an elementary, non-patentable method for screening one. As in *Grams* and *Prometheus*, the physical step in claim 20 of "growing a transformed … cell" in the presence of a compound is a preparatory, data-gathering step. *Grams*, 888 F.2d at 840 (noting that "[t]he

[11] For that reason, the invalidity of claim 2 of '857 is even more apparent than the claim at issue in *Prometheus Labs. v. Mayo Collaborative Services*, where the district court invalidated a claim that correlated metabolite levels after the administration of a drug with therapeutic efficacy. 2008 WL 878910, No. 04 Civ. 1200 (S.D. Cal. Mar. 28, 2008), *argued*, No. 2008-1403 (Fed. Cir. 2008). In *Prometheus*, the patent holder argued that the correlation could not be a natural phenomenon because it only occurred after the intervention of human-made drugs. The court rejected this argument, finding that the correlation was not an invention and that the "inventors merely discovered the relationship between these naturally produced metabolites and therapeutic efficacy and toxicity." *Id.* at *9. With regard to claim 2 of '857, there are no physical steps and no human intervention involved in triggering the correlation.

presence of a physical step in the claim to derive data for the algorithm will not render the claim statutory"); *Prometheus*, 2008 WL 878910 at *6 (finding that "administering" a drug and "determining" the level "are merely necessary data-gathering steps for any use of the correlations").

When claim 20 of '282 is considered in its entirety, what is patented is the comparing of cell growth rates and, to quote the claim, observing that "a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic." This "process" is among the most basic in all of science. Although an actual therapeutic that works to slow the growth of a cell containing a *BRCA1* gene could be patented, claim 20 seeks to patent a simple train of thought (or indeed the essence of the basic scientific method itself) for determining whether a compound may slow cancer cell growth. As in *Flook*, where the "respondent's claim is, in effect, comparable to a claim that the formula 2 r can be usefully applied in determining the circumference of a wheel," 437 U.S. at 595, the claim here is comparable to applying a mental process of comparing cell growth rates to the *BRCA1* gene context. For that reason, it does not pass statutory muster.

III. THE PATENT CLAIMS ARE UNCONSTITUTIONAL UNDER THE FIRST AMENDMENT.

The structure of intellectual property is created by Article 1, section 8, clause 8 which covers copyrights and patents. It is clear that the First Amendment limits the reach of intellectual property laws. In copyright, where the potential conflict between copyright law and the First Amendment is more obvious, various doctrines, such as fair use, exist to accommodate the First Amendment's values. The copyright doctrine most relevant to this case is the distinction between ideas and their expression. The former is not copyrightable; the latter is. Although those doctrines are incorporated into the copyright statute, the Supreme Court has suggested that

these doctrines are required by the First Amendment. *Harper & Row v. Nation*, 471 U.S. 539, 555-560 (1985); *Eldred v. Ashcroft*, 537 U.S. 186, 219 (2003). *See also Salinger v. Colting*, 2009 U.S. Dist. LEXIS 56012, at *4-5 (S.D.N.Y. 2009); *Maxtone-Graham v. Buttchaell*, 631 F. Supp. 1432, 1435 (S.D.N.Y. 1986).

The doctrine of patent law that abstract ideas are not patentable is statutory and has not been previously described as compelled by the First Amendment. 35 U.S.C. § 101. However, there can be little doubt that patenting of abstract ideas or thought or an entire body of knowledge would violate the First Amendment.

The First Amendment's free speech protection prevents the government from limiting thought. In *Palko v. Connecticut*, 302 U.S. 319, 326-27 (1937), the Supreme Court, in discussing the First Amendment, referred to "… freedom of thought and speech. Of that freedom, one may say that it is the matrix, the indispensible condition of nearly every other form of freedom." *See also Stanley v. Georgia*, 394 U.S. 557, 566 (1969) ("Whatever the power of the state to control public dissemination of ideas inimical to public morality, it cannot constitutionally premise legislation on the desirability of controlling a person's private thoughts."); *Griswold v. Connecticut*, 381 U.S. 479, 482 (1965) ("The right to freedom of speech … includes not only the right to utter or to print, but the right to … freedom of inquiry, freedom of thought …"); *U.S. v. Reidel*, 402 U.S. 351, 355-56 (1971). More recently, in *Ashcroft v. Free Speech Coalition*, 535 U.S. 234, 256 (2002), the Court held, "First Amendment freedoms are most in danger when the government seeks to control thought or justify its laws for that impermissible end. The right to think is the beginning of freedom …."

The First Amendment also prevents the government from limiting knowledge. *Epperson v. Arkansas*, 393 U.S. 97, 100-101 (1968); *Griswold*, 381 U.S. at 482 ("the State may not,

consistently with the spirit of the First Amendment, contract the spectrum of available knowledge"); *Grosjean v. American Press*, 297 U.S. 233, 245-51 (1936).

Because the gene patents in this case directly limit thought and knowledge, they are unconstitutional. For First Amendment purposes, the claims can again be divided into two categories: claims for reaching conclusions about the genes, *see* Compl. ¶¶ 68-80, and the claims over the genes themselves, *see* Compl. ¶¶ 55-67.

Five of the patent claims challenged by the plaintiffs involve looking at one or more sequences and reaching some conclusion about the genes. That conclusion might be that the genes contain certain mutations. Compl. ¶¶ 68-70 (describing the '999 patent, claim 1). It might also be that the genes in a particular patient differ from the natural or "wild-type" gene. Compl. ¶¶ 72-74 (describing the '001 patent, claim 1, the '441 patent, claim 1, and the '857 patent, claim 1). It might also be that the two genes are different and that the difference indicates a predisposition to breast cancer. Compl. ¶ 75 (describing patent '857, claim 2). A sixth claim challenged involves the mental process of comparing growth rates of a cell with a mutated *BRCA* gene in the presence or absence of a potential treatment drug to see if it slows cell growth. Compl. ¶ 76 (describing patent '282, claim 20).

These six claims are not on the genes themselves (which are covered by other patent claims). Further, none of these claims purports to be over any particular process of sequencing a gene or looking at a gene or putting a gene into contact with a drug or any drugs themselves. The claims purport to apply regardless of the process or method by which the actions are taken. The only unique part of these claims is that at the end, the scientist or physician thinks, "They are the same" or "They are different" or "They are different in a way that is significant." In other words, it is the thought that is patented, not the process. A medical professional or researcher

who paid a fee to utilize the gene itself and then used unpatented methods to sequence the gene so that he or she could look at it, would infringe on these claims if, after looking at it, he or she thought any conclusions about it. Put another way, if the medical professional or researcher was given a piece of paper with both sequences and mentally compared them, that would constitute infringement. The USPTO may not give exclusive control over certain thoughts to a single company. That it has done so is a violation of the First Amendment.

The inability to compare genes in order to think about them also interferes with scientific inquiry. The framers of the Constitution discussed the sacred nature of scientific inquiry. Gary L. Francione, "Experimentation and the Marketplace Theory of the First Amendment," 136 U. Pa. L. Rev. 417, 428-29 (1987). Providing a private company a monopoly that has the effect of inhibiting, even completely preventing scientific inquiry, into a field of knowledge is not permissible under the First Amendment.

Claims over the genes themselves whether in the natural or wild-type form or mutated forms also violate the First Amendment. Genes are not like carburetors. The function of a gene is to convey information to the body. D. Mason ¶ 4; D. Sulston ¶¶ 10-11. Transcription and translation are the processes by which the gene acts in the body to convey information. D. Mason ¶¶ 11-12.

A genetic sequence is *biological information itself*. D. Sulston ¶ 16. A gene is represented by a series of letters. D. Mason ¶ 6; D. Sulston ¶ 14. Like strings of alphabetic text, the genetic sequences are the same regardless of whether the data reside in the DNA of an organism, a computer, or as letters on a printed page. D. Sulston ¶ 16. The physical form in which they occur is unimportant; what matters is the informational content. *Id.* The information in a gene sequenced in a lab is identical in function to that in the body. SMF ¶¶ 44-75.

The sole reason for sequencing a gene is to uncover that information. D. Sulston ¶¶ 16; D. Mason ¶¶ 13, 23; D. Chung ¶ 10. In that respect, sequencing can be compared to using a microscope to read small letters. D. Mason ¶ 23; D. Sulston ¶ 18. Alterations or mutations are recognized exactly as typographical errors are recognized, by a letter being seen as out of place. D. Sulston ¶ 18; D. Mason ¶ 16. The comparisons between two genes are done by comparing the letters, exactly like proof-reading a book. D. Mason ¶ 23; D. Sulston ¶ 18. Because of the informational aspect of genes, it is inaccurate to treat genes as if they were carburetors or chemicals. D. Jackson ¶¶ 12-16, 49. Thus, the patent claims in this case directly limit information in a manner far different from patents on true inventions, such as carburetors. They limit pure information.

One fundamental aspect of patent law is that in order to ensure that a patent fulfills its constitutional requirement of advancing the useful arts, it must be made public with sufficient specificity. 35 U.S.C. § 112. The purpose of this requirement is to ensure that the public benefits from the invention and that subsequent inventors can build upon the invention or, in patent law jargon, “invent around” it.

The doctrine that prevents the patenting of natural phenomena, abstract ideas, and products and laws of nature is premised, in part, on the obvious conclusion that it is impossible to invent around those things. For a typical invention, such as a carburetor, once the specifications of the patent are published, others can try to build a better carburetor using different materials or methods or structure. In contrast, if gravity were patented, no one could invent a new method of gravity. If oxygen were patented, no one could invent a new oxygen. Similarly, once a gene is patented, no one can invent a new gene with the same informational

content or function.[12] The *BRCA1* and *BRCA2* genes exist in nature as do the mutations on those genes. They cannot be invented around. The sequence of those genes exists in nature and cannot be invented around. The functions of those genes exist in nature. The effects of alterations in those genes are created by nature. The effect of the patents is to give control of all knowledge of those genes and the functions dictated by nature to the defendants. Indeed, rather than leading to a greater understanding or a better product, the patent claims challenged in this case inhibit research into and understanding of the genes. *E.g.* D. Sulston ¶ 37; D. Cho ¶ 24; D. Norsigian ¶ 7. The defendant USPTO has given entire control over a body of knowledge and over pure information to a private company. That, under the First Amendment, it cannot do.

IV. THE PATENT CLAIMS ARE INVALID UNDER ARTICLE 1, SECTION 8, CLAUSE 8 OF THE CONSTITUTION.

Article 1, Section 8, Clause 8 (hereinafter "the intellectual property clause") provides that Congress has the authority "To promote the Progress of Science and the useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." In exercising its authority, Congress is given wide deference. *Eldred v. Ashcroft*, 537 U.S. 186 (2003).

This deference is not absolute and the Second Circuit has suggested that some of the common exceptions to intellectual property laws, such as fair use or the idea/expression dichotomy, are not only required by the First Amendment, but also by the intellectual property clause. *Attia v. Society of the NY Hosp.*, 201 F.3d 50, 54 (2nd Cir. 1999) ("The purpose for which the Copyright Acts were adopted was to expand human knowledge for the general good …. As the law developed, however, it was adjudged that, if exclusive rights of ownership extended to ideas, the result would be to retard rather than advance the progress of knowledge….") (citations

[12] New genes can be invented, of course, that have never existed in nature and are created by recombinant methods. Such genes are not claimed by any of the patent claims in this case.

omitted); *Salinger*, 2009 U.S. Dist. LEXIS at 4 ("some opportunity for fair use of copyrighted materials has been thought necessary to fulfill copyright's very purpose ….").

For the reasons stated above, the patent claims in this case can be held as a matter of law to impede rather than promote the progress of science. The nature and range of the plaintiffs make clear that it is a widely held view of medical professionals and researchers that these patent claims impede the progress of science.

There is, additionally, factual evidence that these patent claims were not necessary for the *BRCA1* and *BRCA2* genes to have been identified and sequenced. Compl. ¶¶ 41-42, 44; D. Cho ¶ 23, 25. There is evidence that the patent claims were not necessary to induce physicians to sequence and analyze the *BRCA1* and *BRCA2* genes. Compl. ¶¶ 82, 84; D. Chung ¶¶ 11, 13, 17, 18; D. Hegde ¶10; D. Ostrer ¶¶ 6-8; D. Swisher ¶¶ 34-35; D. Hubbard ¶ 9; D. Kant ¶ 6; D. Ledbetter ¶ 16; D. Reich ¶¶ 3, 5. There is evidence that the effect of the patents has been to impede research and the clinical development of and quality assurance of genetic testing for *BRCA1* and *BRCA2*. Compl. ¶¶ 81-101; D. Chung ¶¶ 16, 19-24, D. Ostrer ¶¶ 11-13; D. Matloff ¶¶ 8-9; D. Swisher ¶¶ 15-21, 26, 32-35; D. Limary ¶ 7; D. Thomason ¶ 6; D. Raker ¶¶ 7-8; D. Sulston ¶ 36; D. Ledbetter ¶¶ 16, 19-20, 23-25; D. Cho ¶¶ 21-25; D. Reich ¶¶ 9, 11.

The patent claims in this case impede science and are unconstitutional under the intellectual property clause.

CONCLUSION

For the above reasons, plaintiffs respectfully ask that the motion in support of summary judgment be granted.

Respectfully submitted,

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