UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ASSOCIATION FOR MOLECULAR PATHOLOGY; AMERICAN COLLEGE OF MEDICAL GENETICS; AMERICAN SOCIETY FOR CLINICAL PATHOLOGY; COLLEGE OF AMERICAN PATHOLOGISTS; HAIG KAZAZIAN, MD; ARUPA GANGULY, PhD; WENDY CHUNG, MD, PhD; HARRY OSTRER, MD; DAVID LEDBETTER, PhD; STEPHEN WARREN, PhD; ELLEN MATLOFF, M.S.; ELSA REICH, M.S.; BREAST CANCER ACTION; BOSTON WOMEN'S HEALTH BOOK COLLECTIVE; LISBETH CERIANI; RUNI LIMARY; GENAE GIRARD; PATRICE FORTUNE; VICKY THOMASON; KATHLEEN RAKER, Plaintiffs, v. UNITED STATES PATENT AND TRADEMARK OFFICE; MYRIAD GENETICS; LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation, Defendants	Civil Action No. 09-4515 (RWS) **DECLARATION OF WAYNE W. GRODY, M.D., Ph.D.**

1. My name is Wayne W. Grody, M.D., Ph.D. I am a Professor in the Divisions of Medical Genetics and Molecular Pathology and the Departments of Pathology & Laboratory Medicine, Pediatrics, and Human Genetics at the UCLA School of Medicine.

2. I have been retained by the plaintiffs and their counsel as a consulting expert for this case. I have received no compensation for my services.

3. I received a B.A. in Biology from Johns Hopkins University in 1974. I received an M.D. in 1977 and a Ph.D in Cell Biology in 1981 from the Baylor College of Medicine, where I also held a postdoctoral fellowship in Cell Biology from 1979 to 1981. I was a Resident in Pathology and Laboratory Medicine at the UCLA School of Medicine from 1982 to 1987, where I was also a Fellow in Medical Genetics from 1984 to 1986. I first joined the faculty of the UCLA School of Medicine in 1987. I am a licensed physician in the State of California and a licensed clinical genetic molecular biologist. I am board-certified by the American Board of Pathology (Anatomic and Clinical Pathology, Molecular Genetic Pathology) and the American Board of Medical Genetics (Clinical Genetics, Molecular Genetics, and Biochemical Genetics). I have lectured and published widely on the subject of medical and molecular genetics. Articles I have authored or co-authored have appeared in the *American Journal of Medical Genetics*, *Genetics in Medicine*, *Journal of the American Medical Association*, *Human Genetics, Human Mutation,* and many others. I have served as an *ad hoc* reviewer for *Cancer*, *Journal of the American Medical Association*, the *New England Journal of Medicine*, and many others. I have also received many federal and foundation research grants to do research in the areas of basic molecular genetics, genetic testing, and population-wide genetic screening. I am an officer or member of several professional societies, including the American College of Medical Genetics (of which I am president-elect), the Association for

Molecular Pathology and the College of American Pathologists, each of which are plaintiffs in this case. A copy of my curriculum vitae is attached hereto as Exhibit 1.

4. I currently perform limited *BRCA* genetic testing under a royalty-bearing license from Myriad Genetics, Inc. The license only allows me to perform single mutation tests and multiple mutation panels (up to three mutations) to allow for testing patients of Ashkenazi Jewish decent.

5. I have reviewed several documents, including: (i) U.S. Patents Nos. 5,747,282 ("the '282 patent"), 5,693,473 ("the '473 patent"), 5,709,999 ("the '999 patent"), 5,710,001 ("the '001 patent"), 5,753,441 ("the '441 patent"), 5,837,492 ("the '492 patent") and 6,033,857 ("the '857 patent") (collectively, "the patents in suit"); and, (ii) the prosecution/file history of each of the patents in suit. After reviewing these documents, I noticed that the '282, '473, '999, '001 and '441 patents all stem from the same patent application family, have substantially identical specifications and relate to the human gene known as *BRCA1*. Therefore, I may refer to these five patents as the "*BRCA1* patents." I also noticed that the '492 and '857 patents both stem from the same patent application family, have substantially identical specifications and relate to the human gene known as *BRCA2*. Therefore, I may refer to these two patents as the "*BRCA2* patents." Lastly, I also noticed that all seven of the patents in suit have specifications with substantial similarities, including with respect to the definition of certain terms.

6. I have been asked to provide my opinion on the construction of certain terms or phrases contained in certain claims of the patents in suit, including specifically: (i) claims 1, 2, 5, 6, 7 and 20 of the '282 patent; (ii) claim 1 of the '473 patent; (iii) claim 1 of the '999 patent; (iv) claim 1 of the '001 patent; (v) claim 1 of the 441 patent; (vi) claims 1, 6 and 7 of the '492 patent; and, (vii) claims 1 and 2 of the '857 patent. I understand that claims which refer to another claim are called dependent claims and incorporate by reference all of the terms and phrases in the claim to which they refer. For example, claim 6 of the '282 patent is dependent upon claim 2 of that patent, which is itself dependent upon claim 1. Thus, claim 6 of the '282 patent is read to include all of the terms and phrases of claims 2 and 1.

7. I have been asked to provide my opinion as to what a person having ordinary skill in the art would have understood at the time of application for the patents in suit, which I have been told to assume is approximately August 1994 for the five *BRCA1* patents and approximately December 1995 for the two BRCA2 patents.

8. Based on the foregoing and my professional experience in the field, I have formed the following opinions.

9. One of ordinary skill in the art at the time of application for the patents in suit would have been a graduate student or research assistant in the field of genetics with a couple years of experience isolating and analyzing human genes looking for genetic mutations. This is because methods for isolating human genes and analyzing their sequences were well known and considered basic in the art by the mid-1990's.

“DNA”, “DNA molecule”, “nucleotide sequence” (claims 1, 2, 5, 6 and 7 of the '282 patent; claim 1 of the '473 patent; and, claims 1, 6 and 7 of the '492 patent)

10. The ordinary or customary meaning of the term “DNA” to one of ordinary skill in the art at the time of application for the patents in suit would have been a sequence of nucleic acids, also known as nucleotides (there are only four possible nucleotides in DNA: A, C, T and G). Thus, “DNA” is made up of a “nucleotide sequence” and determining the precise nucleotide sequence (*i.e.,* the precise arrangement of A's, C's, T's and G's) is called “sequencing.” All DNA is a molecule, so the term “DNA molecule” is synonymous with just “DNA.” While the term “DNA” generally encompasses both double- or single-stranded DNA, one would assume it means double-stranded because that form of DNA was known to be more stable, which is helpful in sequencing, even though only one strand of DNA codes for a polypeptide.

11. I note that the specifications of the patents in suit each discuss DNA and nucleotide sequences (sometimes referred to as “polynucleotide sequences”) at length. However, I have found nothing in the specifications of the patents in suit that would contradict the ordinary or customary understanding of the terms.

12. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of these terms or that would alter my understanding of what they would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

“isolated DNA” (claims 1, 2, 5, 6 and 7 of the '282 patent; claim 1 of the '473 patent; and, claims 1, 6 and 7 of the '492 patent)

13. The ordinary or customary meaning of the term “isolated DNA” to one of ordinary skill in the art at the time of application for the patents in suit would have been a fragment of DNA that is separated enough from other cellular components and other DNA to sufficiently allow one to obtain a sequence of a specifically desired portion of DNA. This separation could have been accomplished through a number of well known techniques at the time, including restriction endonuclease digestion or polymerase chain reaction (PCR), and so I do not inherently interpret the phrase to be limited to any particular method of isolation.

14. I note that the specification of the patents in suit each contain significant discussion of the term “isolated.” For example, the '282 patent states, “An 'isolated' ... nucleic acid (e.g., an RNA, DNA or a mixed polymer) is one which is substantially separated from other cellular components which naturally accompany a native human sequence or protein, e.g., ribosomes, polymerases, many other human genome sequences and proteins,” and “[t]he terms 'isolated', 'substantially pure', and 'substantially homogeneous' are used interchangeably to describe a protein or polypeptide which has been separated from components which accompany it in its natural state.” '282 patent, col. 19, ll. 8-18 and col. 23, ll. 31-34. Identical language is contained in each of the patents in suit. This comports with the ordinary or

customary meaning of the term and I have found nothing in the specifications of the patents in suit that would contradict that understanding.

15. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"coding for", "encoding" (claims 1, 2, 5 and 6 of the '282 patent; and, claims 1, 6 and 7 of the '492 patent)

16. The ordinary or customary meaning of the term "coding for" with respect to DNA to one of ordinary skill in the art at the time of application for the patents in suit would have meant DNA that translates into amino acids according to the well known genetic code elucidated by Crick, Nirenberg, Leder and Khorana in the 1960s. "Coding for" is synonymous with "encoding." It is known that any three particular nucleotides (each of the three can be either A, C, T or G) form a codon and that each codon translates into one of twenty standard amino acids. As proteins are synthesized according to the genetic code, successive amino acids are chemically joined together to form peptides and, as such, a more lengthy string of amino acids is known as a polypeptide. It was well known in the art (since the 1960s) which codons "code for" which amino acids. As such, one of ordinary skill in the art, given a specific DNA, which is just a sequence of nucleotides that could be divided into tri-nucleotide codons, could determine the sequence of amino acids, or peptides, that such DNA

"codes for" or "encodes." It should be noted, though, that it was known that not all portions of DNA necessarily code for a polypeptide. Specifically, there are portions of DNA called introns (otherwise referred to as non-coding regions) that do not translate into amino acids.

17. I note that the specification of the patents in suit each contain significant discussion of this term. For example, the '282 patent states, "A polynucleotide is said to 'encode' a polypeptide if, in its native state or when manipulated by methods well known to those skilled in the art, it can be transcribed and/or translated to produce ... the polypeptide or a fragment thereof." '282 patent, col. 19, ll. 1-5. Identical language is contained in each of the patents in suit. This definition comports with the ordinary or customary meaning of the term and I have found nothing in the specifications of the patents in suit that would contradict that understanding.

18. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"BRCA1", "BRCA1 gene" (claims 1, 2, 5, 6 and 20 of the '282 patent; claim 1 of the '473 patent; claim 1 of the '999 patent; claim 1 of the 001 patent; and, claim 1 of the '441 patent)

19. *BRCA1* was known at the time of the application for the *BRCA1* patents to refer to a particular portion of DNA found on chromosome 17 that related to a person's

predisposition to develop breast and ovarian cancer. This particular portion of DNA is referred to as "the *BRCA1* gene."

20. I note that the specification of the five *BRCA1* patents each contain discussion of this term. For example, the '282 patent states, "a human breast and ovarian cancer predisposing gene (BRCA1)," and "'BRCA1 Gene,' 'BRCA1 Nucleic Acids' or 'BRCA1 Polynucleotide' each refer to polynucleotides, all of which are in the BRCA*1* region, that are likely to be expressed in normal tissue, certain alleles of which predispose an individual to develop breast, ovarian, colorectal and prostate cancers." '282 patent, col 1, ll 21-22 and col 19, ll 25-30. Identical language is contained in each of the five *BRCA1* patents. This definition comports with the ordinary or customary meaning of the term and I have found nothing in the specifications of the five *BRCA1* patents that would contradict that understanding.

21. I did not find anything in the prosecution/file history of any of the five *BRCA1* patent relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"BRCA2", "BRCA2 gene" (claims 1, 6 and 7 of the '492 patent; and, claims 1 and 2 of the '857 patent)

22. As the specification of the two *BRCA2* patents explains, "A second locus, *BRCA2*, has recently been mapped to chromosome 13 (Wooster et al., 1994) and appears to account for a proportion of early-onset breast cancer roughly equal to

BRCA1." '492 patent, col. 2, ll. 60-64. Thus, *BRCA2* was known at the time of the application for the *BRCA2* patents to refer to a particular portion of DNA found on chromosome 13 that related to a person's predisposition to develop breast cancer. This particular portion of DNA is referred to as "the BRCA2 gene."

23. I note that the specification of the two *BRCA2* patents each contain significant discussion of this term. For example, the '492 patent states, "a human breast cancer predisposing gene (BRCA2)," and "'BRCA2 Locus,' 'BRCA2 Gene,' 'BRCA2 Nucleic Acids' or 'BRCA2 Polynucleotide' each refer to polynucleotides, all of which are in the BRCA2 region, that are likely to be expressed in normal tissue, certain alleles of which predispose an individual to develop breast, ovarian and stomach cancers." '492 patent, abstract and col. 18, ll. 12-17. Identical language is contained in both of the *BRCA2* patents. This definition comports with the ordinary or customary meaning of the term and I have found nothing in the specifications of the two *BRCA2* patents that would contradict that understanding.

24. I did not find anything in the prosecution/file history of either of the two *BRCA2* patents relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

“polypeptide”, “amino acid sequence” (claims 1, 2, 5 and 6 of the '282 patent; and, claims 1, 6 and 7 of the '492 patent)

25. The ordinary or customary meaning of the term “polypeptide” to one of ordinary skill in the art at the time of application for the patents in suit would have meant a string of several amino acids or even an entire protein. Two or more amino acids form a sequence of amino acids, or an “amino acid sequence.”

26. I note that the specification of the patents in suit each contain significant discussion of this term. For example, the '282 patent states, “The term 'polypeptide' refers to a polymer of amino acids and its equivalent and does not refer to a specific length of the product.” '282 patent, col. 21, ll 3-5. Identical language is contained in each of the patents in suit. This definition comports with the customary and ordinary meaning of the term and I have found nothing in the specifications of the patents in suit that would contradict that understanding.

27. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of these terms or that would alter my understanding of what they would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

“having the [] sequence” (claims 1, 2, 5, 6 and 7 of the '282 patent)

28. The ordinary or customary meaning of the phrase “having the [] sequence” to one of ordinary skill in the art at the time of application for the patents in suit would have

inherently meant "having *all of but no more than* the [] sequence," because construing that phrase any differently would be either over-inclusive (including additional unidentified sequence) or under-inclusive (excluding portions of the identified sequence). Thus, with respect to claim 1 of the '282 patent, for example, a "polypeptide *having the* amino acid *sequence* set forth in X" means a polypeptide that has all of but no more than the amino acid sequence set forth in X. If the phrase were to be construed to allow for more than just the identified amino acid sequence, then it could encompass up to the entire human genome, which would obviously 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 of the identified sequence, which could have substantial functional effects, as a partial polynucleotide or polypeptide sequence can indeed function much differently (or not at all) compared to the complete sequence from which it derives.

29. I note that the specification of the patents in suit each contain significant discussion relevant to this phrase. For example, the '282 patent states, "The nucleic acids of the present invention will possess a sequence which is either derived from, or substantially similar to a natural BRCA1-encoding gene or one having substantial homology with a natural BRCA1-encoding gene or a portion thereof." '282 patent, col. 19, ll. 43-47. Identical language is contained in each of the patents in suit (except that the *BRCA2* patents reference *BRCA2*, not *BRCA1*). This statement comports with the ordinary or customary understanding of the phrase and I have found nothing in the specifications of the patents in suit that would contradict that understanding.

30. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this phrase or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"SEQ ID NO:[X]" (claims 1, 2, 5, 6 and 7 of the '282 patent; claim 1 of the '473 patent; claim 1 of the '999 patent; and, claims 1, 6 and 7 of the '492 patent)

31. There is no ordinary or customary meaning for the phrase "SEQ ID NO:[X]." This is a generic phrase used to make reference to a specific sequence provided elsewhere within the document making the reference. Without such identification elsewhere in the patents in suit, one of ordinary skill in the art at the time of the application for the patents in suit would not have known what those sequences contained. Thus, the phrase "SEQ ID NO:2", for example, could mean different things depending upon what the supporting document identifies as the sequence with identification number 2.

32. The specifications of the patents in suit each provide a specific sequence for each SEQ ID NO. referenced in the claims. For example, the '282 patent states, "The coding sequence for a BRCA1 polypeptide is shown in SEQ ID NO:1, with the amino acid sequence shown in SEQ ID NO:2," and then continues to specifically set forth those sequences in a "Sequence Listing" section in the back of the specification. '282 patent, col. 19, ll. 47-49 and cols. 67-90. The identical sequences are identified in each of the *BRCA1* patents. Similarly, the '492 patent specifically sets forth the

sequences identified in it as “SEQ ID NO:1” and “SEQ ID NO:2” in the “Sequence Listing” section of its specification. '492 patent, cols. 59-100. The identical sequences are identified in both of the *BRCA2* patents. Thus, when the claims make references to a “SEQ ID NO:1” or “SEQ ID NO:2”, one of ordinary skill in the art at the time of the application for the patents in suit would have known to refer to those sequences set forth in the specifications and identified as such.

33. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

“transformed eukaryotic host cell” (claim 20 of the '282 patent)

34. The ordinary or customary meaning of the term “transformed eukaryotic host cell” to one of ordinary skill in the art at the time of application for the patents in suit would have been a cell with a distinct nucleus that has had something done to it to make the cell malignant or cancerous or immortal in culture. For example, a cell can be exposed to carcinogenic chemicals or viruses to accomplish this result. The purpose of such cells is to be used in studying cancer cell biology and testing potential treatments for cancer or genetic diseases.

35. I note that the specifications of the patents in suit each contains a discussion of this term. For example, the '282 patent says, “A further technique for drug screening involves the use of host eukaryotic cell lines or cells (such as described above) which

have a nonfunctional BRCA1 gene. These host cell lines or cells are defective at the BRCA1 polypeptide level. The host cell lines or cells are grown in the presence of drug compound. The rate of growth of the host cells is measured to determine if the compound is capable of regulating the growth of BRCA1 defective cells." '282 patent, col. 31, ll 46-53. Identical language is contained in each of the patents in suit. This description comports with the ordinary or customary meaning of the term and I have found nothing in the specifications of the patents in suit that would contradict that understanding.

36. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"altered", "alterations" (claim 20 of the '282 patent; claim 1 of the '473 patent; claim 1 of the '999 patent; claim 1 of the '001 patent; claim 1 of the '441 patent; and, claim 2 of the '857 patent)

37. The ordinary or customary meaning of the term "altered" or "alteration" to one of ordinary skill in the art at the time of application for the patents in suit would have been being different from the most common typical version. And while it is true that alterations can sometimes be created by man, generally speaking, and specifically in the context of the patents in suit, the terms "altered" and "alterations" inherently mean made by nature. Thus, with respect to claim 20 of the '282 patent, for example,

the phrase "altered BRCA1 gene" means a *BRCA1* gene that nature has caused to be different than the typical *BRCA1* gene found naturally in most humans. Such a difference could be as minor as a difference in a single nucleotide, or could include more differences, and either case may be disease-causing.

38. I note that the specifications of the patents in suit each contains a discussion of this term. For example, the '282 patent says, "'Alteration of a wild-type gene' encompasses all forms of mutations including deletions, insertions and point mutations in the coding and noncoding regions." '282 patent, col. 12, ll 31-33. Identical language is contained in each of the patents in suit. This definition comports with the ordinary or customary meaning of the term and I have found nothing in the specifications of the patents in suit that would contradict that understanding.

39. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"comparing" (claim 20 of the '282 patent; claim 1 of the '001 patent; claim 1 of the '441 patent; and, claims 1 and 2 of the '857 patent)

40. The ordinary or customary meaning of the term "comparing" to one of ordinary skill in the art at the time of application for the patents in suit would have been looking at two or more things to determine if there is a difference between them. In

the context of claim 1 of the '001 patent, claim 1 of the '441 patent, and claims 1 and 2 of the '857 patent, the term is used to mean looking at two or more nucleotide sequences to see if there is a difference between them. This act of "looking" could be performed by any of a number of available methods and it inherently presumes that such sequences are already provided.

41. I have found nothing in the specifications of the patents in suit that would contradict the ordinary or customary understanding of the term.

42. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"analyzing" (claim 1 of the '999 patent)

43. The ordinary or customary meaning of the term "analyzing" to one of ordinary skill in the art at the time of application for the patents in suit would have been looking at a thing to determine its characteristics. In the context of claim 1 of the '999 patent, the term is used to mean looking at a nucleotide sequence to see if it contains one of a particular known set of alterations. This act of "looking" could be performed by any method and inherently presumes that the sequence is already provided.

44. I have found nothing in the specifications of the patents in suit that would contradict the ordinary or customary understanding of the term.

45. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"wild-type", "mutated" (claim 1 of the '441 patent; claims 6 and 7 of the '492 patent; and, claims 1 and 2 of the '857 patent)

46. The ordinary or customary meaning of the phrase "wild-type" to one of ordinary skill in the art at the time of application for the patents in suit would have meant the most common typical version of, for example, a gene. The opposite of "wild-type" is generally "altered", but some in the art would also use the term "mutated." Thus, with respect to claim 1 of the '441 patent, for example, the phrase "wild-type BRCA1 gene" means the normal *BRCA1* gene found naturally in the vast majority of human beings and that does not have an "alteration" or "mutation." And while it is true that mutations can sometimes be created by man, generally speaking, and specifically in the context of the patents in suit, the terms "mutated" and "mutation" inherently mean made by nature and usually inherited from a parent.

47. I note that the specification of the patents in suit each contain significant discussion of these terms. For example, the '282 patent states, "It has been discovered that individuals with the wild-type BRCA1 gene do not have cancer which results

from the BRCA1 allele. However, mutations which interfere with the function of the BRCA1 protein are involved in the pathogenesis of cancer. Thus, the presence of an altered (or a mutant) BRCA1 gene which produces a protein having a loss of function, or altered function, directly correlates to an increased risk of cancer." '282 patent, col. 16, ll. 57-64. Identical language is contained in each of the patents in suit (except that the *BRCA2* patents reference *BRCA2*, not *BRCA1*). This definition comports with the customary and ordinary meaning of the terms and I have found nothing in the specification that would contradict that understanding.

48. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of these terms or that would alter my understanding of what they would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"germline", "germline alteration", "germline sequence" (claim 1 of the '999 patent; claim 1 of the '441 patent; and, claim 2 of the '857 patent)

49. The ordinary or customary meaning of the term "germline" to one of ordinary skill in the art at the time of application for the patents in suit would have been hereditary, or that which is passed down to an individual from his or her genetic parents. Therefore, a "germline alteration" is an alteration that was inherited by a person from his or her parents and a "germline sequence" is a sequence that was inherited by a person from his or her parents.

50. I note that the specifications of the patents in suit each contains a discussion of this term. For example, the '999 patent says, "Germline mutations can be found in any of a body's tissues and are inherited." '999 patent, col. 12, ll. 40-42. Identical language is contained in each of the patents in suit. This definition comports with the ordinary or customary meaning of the term and I have found nothing in the specifications of the patents in suit that would contradict that understanding.

51. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"RNA" (claim 1 of the '999 patent; claim 1 of the '001 patent; and, claim 1 of the '441 patent)

52. The ordinary or customary meaning of the term "RNA" to one of ordinary skill in the art at the time of application for the patents in suit would have been a polynucleotide sequence that is naturally transcribed from DNA, but yet which is only single-stranded. RNA will have the same (*i.e.*, complementary) nucleotide sequence as the DNA from which it is transcribed.

53. I note that the specification of the patents in suit each discuss RNA at length. However, I have found nothing in the specifications of the patents in suit that would contradict the ordinary or customary understanding of the term.

54. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"cDNA", "mRNA", "cDNA made from mRNA" (claim 1 of the '999 patent; claim 1 of the '001 patent; claim 1 of the '441 patent; and, claim 2 of the '857 patent)

55. The ordinary or customary meaning of the term "cDNA" to one of ordinary skill in the art at the time of application for the patents in suit would have been complementary DNA, which is synthesized from mRNA using the enzyme reverse transcriptase. The ordinary or customary meaning of the term "mRNA" to one of ordinary skill in the art at the time of application for the patents in suit would have been messenger RNA, which is RNA that has had all of its introns, or non-coding regions, removed. So, in a step by step fashion, double stranded DNA transcribes single stranded RNA, the single stranded RNA is then reduced to mRNA by removing all of the non-coding regions, and then the mRNA is reverse-transcribed into cDNA. Thus, the coding produced by a cDNA is the same as that produced by the original DNA from which is it ultimately derived despite having a different sequence (the cDNA will not include the non-functional regions that were part of the DNA). Thus, the phrase "cDNA made from mRNA" means a purely functional polynucleotide sequence that is produced from RNA that has had all of its non-coding regions (called introns) removed.

56. I note that the specification of the patents in suit each discuss cDNA and mRNA at length. However, I have found nothing in the specifications of the patents in suit that would contradict the ordinary or customary understanding of the term.

57. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

"somatic", "somatic alteration" (claim 1 of the '001 patent)

58. The ordinary or customary meaning of the term "somatic" to one of ordinary skill in the art at the time of application for the patents in suit would refer to something having been created or altered within a peripheral tissue of the body, and not inherited. "Somatic" is the opposite of germline. Thus, a "somatic alteration" is one that occurred within a tissue or organ of a person's body, and was not inherited by them from one of their parents (inherited alterations would typically be present in *all* cells and tissues of the body). Somatic alterations of genes can result from viruses, radiation or other environmental conditions to which a human cell is exposed.

59. I note that the specifications of the patents in suit each contains a discussion of this term. For example, the '001 patent says, "Somatic mutations are those which occur only in certain tissues, e.g., in the tumor tissue, and are not inherited in the germline." '001 patent, col. 12, ll. 40-42. Identical language is contained in each of the patents in suit. This definition comports with the ordinary or customary meaning

of the term and I have found nothing in the specifications of the patents in suit that would contradict that understanding.

60. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

“allele”, “mutant allele” (claim 1 of the '857 patent)

61. The ordinary or customary meaning of the term “allele” to one of ordinary skill in the art at the time of application for the patents in suit would have been one member of a pair of genes at a specific location on a chromosome. Every nucleated human cell (except for germ cells: sperm and oocytes) has two alleles at each location (one on each of the pair of chromosomes originally inherited from mother and father). Thus, a cell could have a mutated allele and a wild-type allele on opposite chromosomes but at the same genomic location. If the mutation is recessive, the disease is only expressed if both alleles (maternal and paternal) are mutated; if only one is mutated and the other is wild-type, the individual is an asymptomatic carrier. On the other hand, if the mutation is dominant, as is the case for mutations in the *BRCA1* and *BRCA2* genes, then only a single mutant allele, inherited from either parent, is sufficient to cause the disease.

62. I note that the specification of the patents in suit each use the term "allele" at length. However, I have found nothing in the specifications of the patents in suit that would contradict the ordinary or customary understanding of the term.

63. I did not find anything in the prosecution/file history of any of the patents in suit relevant to the construction of this term or that would alter my understanding of what it would have meant to a person of ordinary skill in the art at the time of application for the patents in suit.

I declare, pursuant to 28 U.S.C. §1746, under penalty of perjury under the laws of the United States, that the foregoing is true and correct to the best of my knowledge and belief.

Wayne W. Grody, M.D., Ph.D.

Executed on August 24 2009