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

SUPPLEMENTAL DECLARATION OF CHRISTOPHER E. MASON

I, Christopher E. Mason, declare under penalty of perjury:

1. I previously submitted a declaration in this case on August 20, 2009. I am currently Assistant Professor of Computational Genomics at Weill Cornell Medical College in New York City. I also hold an appointment at the tri-institutional training program on computational biology and medicine between Rockefeller University, Memorial Sloan-Kettering Cancer Center, and Cornell University. I perform research, publish, and teach courses on whole genome

sequencing and methods for cataloguing and characterizing human genetic variants ranging from single cells to whole tissues, in normal development and in cancer.

2. I have read some of the submissions made by Myriad in this case. Specifically, I have read the Myriad brief, the declaration of Dr. Kay, and Myriad's Statement of Material Facts. I am submitting this supplemental declaration in response to those documents.

3. Naturally occurring genetic variants contribute to the phenotypic uniqueness of each individual and also create susceptibility to certain diseases, such as breast or ovarian cancer. These variations may be small, such as a single-nucleotide variant (SNV), such as changing an A to a G at one position. Also, genetic variants may be very large, such as the removal/insertion of hundreds of bases or the complete deletion/duplication of an entire gene. Consequently, genetic variants that can influence a person's susceptibility to disease may involve an extraordinarily large range of possibilities, and each individual is likely to harbor entirely novel (*de novo*) variants. As a result, a patent on a genetic sequence can include (and if it wishes to preclude sequencing of the gene, must include) *any* possible variants found by the patent applicants as well as claims on any *de novo* variations or fragments of the claimed sequence that might be found in the future. Recent research has shown variants at about one out of every 500 base pairs (bp), meaning that the BRCA1/BRCA2 genes are likely to hold dozens or hundreds of variants.

4. The natural variation inherent to the human genome makes patenting a specific locus of the human genome impossible, since any genomic locus is slightly different in every person, changes during a person's life and in each tissue, and changes within the human species throughout time. The very flexibility the defendants seek in their claims for cataloging all BRCA1/BRCA2 variants undermines their ability to claim a single molecule, since that molecule will vary from one individual to the next.

5. Among defendants' claims is claim 6 from patent '282.

1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.
2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.
6. An isolated DNA having at least 15 nucleotides of the DNA of claim 2.

6. Claim #6 is so broad that it includes at least 4% and as much as 100% of the genes in the human genome.

7. I used a Perl algorithm[1] to determine if any 15 contiguous nucleotides (15mer) present in the BRCA1 cDNA from claim 2 (SEQ ID NO:1) were also present in other genes' cDNAs. I used the NIH CCDS (National Institute of Health Consensus Coding Sequence) database, which maintains a well-defined set of cDNAs for 18,646 genes. I observed that 4% (716/18,646) of the cDNAs from genes in the human genome contain an exact match to one or more 15mer from SEQ ID NO:1, including, of course, BRCA1 (bold). These genes are the following:

ABCA10, ABCB4, ABCB7, ABCC1, ABCC5, ACCSL, ACER2, ACER3, ACSL3, ACSM3, ACTL6A, ACVR1B, ADAM22, AGAP2, AGAP3, AGFG1, AGGF1, AHNAK, AIM1L, AKAP9, AKR1B10, AKR1B15, ALPK1, ALS2, AMIGO2, ANKRD11, ANKRD13D, ANKRD31, ANKRD43, AP1S2, AP3M2, APOB, ARAP3, ARHGAP10, ARHGAP24, ARHGEF10L, ARHGEF12, ARHGEF15, ASB11, ASB16, ASPM, ATAD5, ATE1, ATG16L1, ATM, ATP1A1, ATP6V1D, ATR, B3GALTL, BAIAP2, BANK1, BAZ2B, BBS12, BCAT2, BCL9L, BCORL1, BDP1, BEND6, BEND7, BOD1L, **BRCA1**, BRD9, BRPF1, BRWD1, BTN1A1, BUB1, C10orf79, C10orf96, C14orf183, C14orf45, C16orf54, C16orf88, C17orf65, C17orf70, C18orf19, C18orf55, C1orf101, C1orf112, C1orf114, C1orf187, C1orf26, C1orf59, C1QTNF1, C20orf72, C2orf16, C2orf42, C2orf44, C2orf74, C3orf30, C5orf23, C6orf167, C6orf203, C7orf58, C7orf72, C8orf44, C8orf86, C9orf95, CABIN1, CABYR, CACNA1S, CAMTA2, CARKD, CASD1, CASK, CASP8, CCDC110, CCDC138, CCDC149, CCDC150, CCDC158, CCDC18, CCDC21, CCDC49, CCDC65, CCDC66, CCDC82, CCDC83, CCND3, CCT3, CD2BP2, CD59, CDC123, CDCP1, CDK2, CDR2L, CEACAM19, CECR5, CENPB, CENPE, CEP110, CEP152, CEP78, CHD7, CHIC1, CHRFAM7A, CHRNA7, CIC, CIZ1, CKAP4, CLCNKA, CLCNKB, CLK1, CLTC, CMBL, CMTM4, CNGA1, CNR1, CNTNAP2, COBLL1, COG1, COL15A1, COL4A2, COL4A6, COL7A1, CORO1A, COX7A2L, CPD, CRIM1, CRP, CSNK2A2, CSPP1, CTR9, CUL4B, CUX1, CXCL17, CYC1, CYP3A43, DAZ1, DAZ2, DAZ3, DCHS2, DCP1B, DCTN1, DDB1, DDX20, DDX46, DDX60L, DEK, DGKQ, DHX37, DIP2A, DIRAS3, DMRTC2, DMTF1, DNAH1, DNAH12, DNAH2, DNAH5,

[1] The algorithm utilized the the 5,914bp BRCA1 cDNA from the '282 patent and the CCDS latest release (January 3, 2010) from the NIH's site: ftp://ftp.ncbi.nih.gov/pub/CCDS/current_human.

DNAH6, DNAJC10, DNAJC13, DNAJC2, DNTTIP2, DOCK11, DOCK4, DOCK6, DOK1, DOPEY2, DPEP1, DPYD, DRG1, DSC3, DST, DYNC2H1, DYTN, E2F1, EFEMP2, EFHA2, EIF2AK3, EIF2S1, EIF2S2, ELF1, ELMO3, ELOVL2, ELOVL3, ELP2, EMILIN2, EMILIN3, ENG, ENOX1, ENPP3, ENPP6, EPHX2, ERLEC1, ESCO2, ETAA1, EXOC3L, EXOG, EXPH5, EYA3, EYS, F13B, FAAH, FAM102B, FAM116A, FAM123B, FAM135B, FAM13A, FAM151B, FAM160B2, FAM161A, FAM179B, FAM185A, FAM186A, FAM193B, FAM22F, FAM22G, FAM57B, FAM5B, FAM82A2, FAM9A, FANCG, FAT2, FBXO21, FBXO38, FBXO42, FBXW5, FCGBP, FCN3, FCRL5, FER1L6, FHOD3, FIS1, FLJ23834, FLJ32810, FNDC7, FOS, FRYL, FSIP1, FUT9, GAL3ST4, GALC, GAPDH, GDF10, GEMIN5, GMIP, GNPAT, GOLGA3, GOLGA4, GOLGA8E, GOLGA8F, GOLGA8G, GOLGB1, GPAM, GPATCH1, GPATCH4, GPR56, GPR98, GRAMD2, GRIA2, GRK4, GSTCD, GTF2A1, GTF3C4, HABP2, HCLS1, HDLBP, HEATR5B, HEPHL1, HERC2, HERC6, HGF, HHAT, HIP1, HIST4H4, HLX, HMCN1, HNRNPA2B1, HNRNPC, HNRNPCL1, HSCB, HSP90AA1, HSPA8, IFI16, IGDCC4, IGF1, IGFBP4, IGSF21, IGSF9, IKZF3, IMMP1L, IMPG2, INTS6, INTS8, IPO8, IQCD, IQCF2, ITGA1, ITGA4, ITIH4, ITSN1, IVNS1ABP, JRKL, KBTBD7, KCND1, KCNJ6, KCNK1, KCNQ1, KCNQ5, KCTD20, KDM4A, KIAA0652, KIAA1009, KIAA1109, KIAA1244, KIAA1267, KIAA1429, KIAA1549, KIAA1683, KIAA1731, KIAA2026, KIDINS220, KIF15, KIF16B, KIF21A, KIF5B, KIR3DL2, KRI1, KRT8, LAMA4, LAMB3, LARP1B, LARP7, LCP1, LDHB, LEO1, LHCGR, LIG1, LPGAT1, LRP1B, LRRC45, LRRC8D, LSG1, LYPD6B, MAGEB10, MAN2A2, MAP1A, MAP3K12, MAP3K2, MAP3K7IP1, MAP7D2, MAP9, MASP1, MAST4, MCCC1, MDN1, MED12L, MED13, MED7, MET, METAP2, MIA2, MICALCL, MICALL2, MIER3, MINK1, MKL2, MLH3, MRPL55, MRPS10, MRPS25, MS4A8B, MTERF, MTIF2, MTUS2, MUC15, MUC6, MYCN, MYH1, MYH15, MYH3, MYLK, MYO15A, MYO1B, MYO3B, MYO5C, N4BP2, NAGPA, NAP1L2, NAT10, NAV1, NBEAL1, NCOR1, NDE1, NDEL1, NEK1, NFATC2IP, NFKBIL2, NFXL1, NGDN, NGFR, NIN, NKAPL, NKTR, NLRP13, NLRP2, NLRP9, NMBR, NOC3L, NPAS4, NR3C2, NT5C1B, NTRK3, NUDT5, NUP153, NUP85, ODZ3, OFD1, OR13F1, OR2A1, OR2A12, OR2A14, OR2A5, OR2M2, OR2M7, OR2T1, OR2T6, OR4C3, OR4F16, OR4F21, OR4F29, OR4F3, OR5B21, OSBPL3, OTOF, PABPC1, PADI1, PAK1, PAN2, PCDHA10, PCDHA11, PCDHA12, PCDHA13, PCDHA6, PCDHAC1, PCDHAC2, PCDHB15, PCLO, PDCD4, PDCD6IP, PDE6C, PDS5A, PDZD2, PDZD4, PGK1, PHEX, PHF20, PHF23, PHKA1, PIGN, PIH1D2, PIK3AP1, PIK3C2A, PIKFYVE, PITPNM3, PKD1L2, PLB1, PLCZ1, PLEKHM1, PNMA5, POLQ, PPP1R10, PPP1R3A, PPP1R3B, PPP2R3C, PRDM5, PRKAG2, PRODH2, PROX1, PRPF40A, PRPS1, PSPH, PTDSS2, PTK7, PTPDC1, PTPRN, PUS3, RAB11FIP5, RANBP2, RASAL1, RAVER1, RBM20, RBM25, REV3L, RGN, RGS3, RIMBP3, RIMBP3B, RIMBP3C, RNF14, RNF20, RNPC3, ROD1, ROR1, RORB, RPGRIP1, RPL13A, RPS6KA1, RRBP1, RSPRY1, RXFP3, SAMD4A, SAPS1, SBNO1, SCAND3, SCG3, SDK1, SEBOX, SECISBP2, SEMA5A, SEMA6C, SENP7, SERPINB5, SERPIND1, SERPINH1, SESN1, SETD5, SF3A1, SFRS18, SFRS4, SGCB, SGCG, SGOL2, SH2D3A, SH3D19, SHPRH, SIGLEC10, SIM2, SIN3B, SIPA1, SKAP1, SLC15A4, SLC1A6, SLC30A2, SLC38A4, SLC39A10, SLC3A1, SLC43A2, SLC5A3, SLC8A3, SLCO2A1, SLIT3, SLU7, SMC4, SMC5, SMYD3, SNAPC4, SNX6, SON, SORBS3, SOX6, SP100, SP140, SPAG16, SPATA16, SPPL2A, SRCAP, SRP54, SRPK2, SRRM2, SRRM4, SSBP2, STAG2, STIM1, STK10, STK35, STOX1, STOX2, STRADA, SUV420H2, SVIL, SYNE2, SYNGAP1, SYNRG, SYT1, SYT13, TAF3, TANC2, TAOK3, TARS, TARS2, TAS1R1, TBC1D8B, TCOF1, TDRD6, TESC, TET3, TEX2, TFAP2B, TFB1M, TFE3, TGS1, THUMPD2, TIGD1, TLR6, TMC4, TMEM161B,

TMEM168, TMEM176B, TMEM232, TMEM99, TMF1, TMPRSS11E, TMPRSS7, TNRC6B, TP53TG5, TPST2, TPX2, TRAF6, TREM2, TRIM33, TRIM60, TRIM61, TRNT1, TRPC1, TRPM3, TSPAN12, TSPAN13, TSPAN3, TTC28, TTLL7, TWF1, TWISTNB, UBAP2, UBR3, UEVLD, ULBP1, UROD, USP39, USP42, UTP14A, UTP20, VASN, VCPIP1, VPS8, VSX1, VWF, WDR33, WDR54, WDR75, WDR87, XRN1, ZADH2, ZBTB32, ZBTB34, ZC3H12B, ZC3HAV1, ZCCHC17, ZCCHC6, ZDBF2, ZDHHC12, ZEB1, ZFC3H1, ZFHX4, ZFP1, ZMYM4, ZMYM6, ZNF133, ZNF195, ZNF238, ZNF25, ZNF322B, ZNF34, ZNF407, ZNF438, ZNF469, ZNF521, ZNF530, ZNF546, ZNF655, ZNF709, ZNF732, ZNF772, ZNF804B, ZNF84, ZSWIM4.

8. Since the definition of the BRCA locus from '282 is broad enough to include the entire gene, I then used the same Perl algorithm (see Paragraph 7) to determine if any 15 contiguous nucleotides (15mer) present in the BRCA1 cDNA from claim 2 (SEQ ID NO:1) were present in any gene in the genome. Using the '282 definition of a genetic locus and the University of California Santa Cruz Genome Browser (http://genome.ucsc.edu/) database, I extracted all full-length genetic loci from any known gene (UCSC official genes) in the human genome (build 37), including one kilobase of upstream sequence to represent regulatory regions. I observed that 99.999% (66,794/66,803) of the genes in the human genome contain an exact match to one or more 15mer from SEQ ID NO:1, including BRCA1. On average, each gene contains 595.3 instances of one of the 15mers listed in SEQ ID NO:1. The only nine genes without any of the 15mer sequences were: uc002tlg, uc003arw, uc002ahy, uc003wbc, uc002bsc, uc002btr, uc003vzz, and uc002vvu.

9. Claim #6 does not appear to be limited to 15 *consecutive* nucleotides. Re-running the analysis for any 15 nucleodides from SEQ ID #1 in any order results in every gene in the human genome (100%) being covered by claim #6.

10. Claim #1 and #2 of '282 are so broad that they can include up to 100% of the genes in the human genome. Because fragments of the BRCA1 gene can also be informative about

susceptibility to disease, the defendants also sought claims on DNA molecules or fragments of DNA molecules with 'substantial homology.' See patent '282 (19:26-50) (emphasis added):

> "BRCA1 Locus," "BRCA1 Gene," "BRCA1 Nucleic Acids" or "BRCA1 Polynucleotide" each refer to polynucleotides, all of which are in the BRCA1 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. Mutations at the BRCA1 locus may be involved in the initiation and/or progression of other types of tumors. The locus is indicated in part by mutations that predispose individuals to develop cancer. These mutations fall within the BRCA1 region described infra. The BRCA1 locus is intended to include coding sequences, intervening sequences and regulatory elements controlling transcription and/or translation. The BRCA1 locus is intended to include all allelic variations of the DNA sequence.
>
> These terms, when applied to a nucleic acid, refer to a nucleic acid which encodes a BRCA1 polypeptide, fragment, homolog or variant, including, e.g., protein fusions or deletions. 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**. 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.

11. The patent defines the terms bolded in the prior paragraph:

> "Substantial homology or similarity". A nucleic acid or fragment thereof is "substantially homologous" ("or substantially similar") to another if, when optimally aligned (with appropriate nucleotide insertions or deletions) with the other nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 60% of the nucleotide bases, usually at least about 70%, more usually at least about 80%, preferably at least about 90%, and more preferably at least about 95-98% of the nucleotide bases.
>
> Alternatively, substantial homology or (similarity) exists when a nucleic acid or fragment thereof will hybridize to another nucleic acid (or a complementary strand thereof) under selective hybridization conditions, to a strand, or to its complement. Selectivity of hybridization exists when hybridization which is substantially more selective than total lack of specificity occurs. Typically, selective hybridization will occur when there **is at least about 55% homology over a stretch of at least about 14 nucleotides**, preferably at least about 65%, more preferably at least about 75%, and most preferably at least about 90%. See, Kanehisa, 1984. The length of homology comparison, as described, may be over longer stretches, and in certain embodiments will often be over a stretch of at least about nine nucleotides, usually at least about 20 nucleotides, more usually at least about 24 nucleotides, typically at least about 28 nucleotides, more typically at least about 32 nucleotides, and preferably at least about 36 or more nucleotides.

12. Because of this low threshold of homology, any 55% homology of 14 nucleotides is now any 8 nucleotides from BRCA1 cDNA. Also, homology could include any 9-13 nucleotide sequence with insertions and deletions. Utilizing the same algorithm from above, the conclusion is that 100% of the genes in the human genome have at least one 8mer from the BRCA1 cDNA.

13. The patents define "isolated" DNA as something that encodes a BRCA1 protein or a fragment thereof. See patent '282, 19:5. If so defined, very small segments of DNA can encode a fragment of the BRCA1 protein.

14. The contention by the Myriad defendants that "isolated" DNA acquires new properties which are different in kind is erroneous. They claim isolated DNA can be used as a probe. They rely on the Alberts et al. text for several of their definitions. This text defines probe as follows: "a defined fragment of RNA or DNA, radioactively or chemically labeled, used to locate specific nucleic acid sequences by hybridization." (Alberts, Bruce, et al. Molecular biology of the Cell, 3rd ed. New York City: Garland Publishing. 1994. p. G-19). According to this definition, isolated DNA by itself cannot be used as a probe, as it requires subsequent chemical modifications, such as fluorescent or biotinylated tags, to allow the DNA to be visualized and therefore serve as a probe. If what defendants mean by a "probe" is any sequence of DNA or RNA that binds to a complementary sequence, then this would include every segment of the human genome in the cellular milieu or in an isolated state.

15. Also, for a DNA probe to actually "probe" another region of the genome, it utilizes the same functional and chemical properties as the native DNA, which is hybridization of the complementary base pairs through hydrogen bonds. For the probe to actually work, it is **necessary** that the isolated DNA still functions in the **exact** same capacity as the native DNA, wherein complementary bases can anneal, or hybridize, to each other.

16. Myriad claims isolated DNA can be used as a primer. This claim is incorrect. A portion of the isolated DNA may be used as a primer. I know of no instance in the scientific literature of a full length cDNA having been used as a primer. cDNA of the length specified in SEQ ID NO:1 would very likely fold into secondary structures and inhibit any reaction. Indeed, the patent itself recognizes the need to design a pair of short primers from the sequence itself. Patent '282, claim 16.

17. A primer is simply a short, single-stranded segment of DNA or RNA (usually 15-30 nucleotides) that is complementary to a given DNA sequence and that can be used to initiate a sequencing reaction or replication. A segment of native DNA can also be used as a primer for DNA replication to occur. In both the native and isolated state, the same functional and chemical properties of the DNA allow for these reactions to occur – namely, the binding of complementary sequences to initiate a reaction. This also occurs in the body (Figure 1).

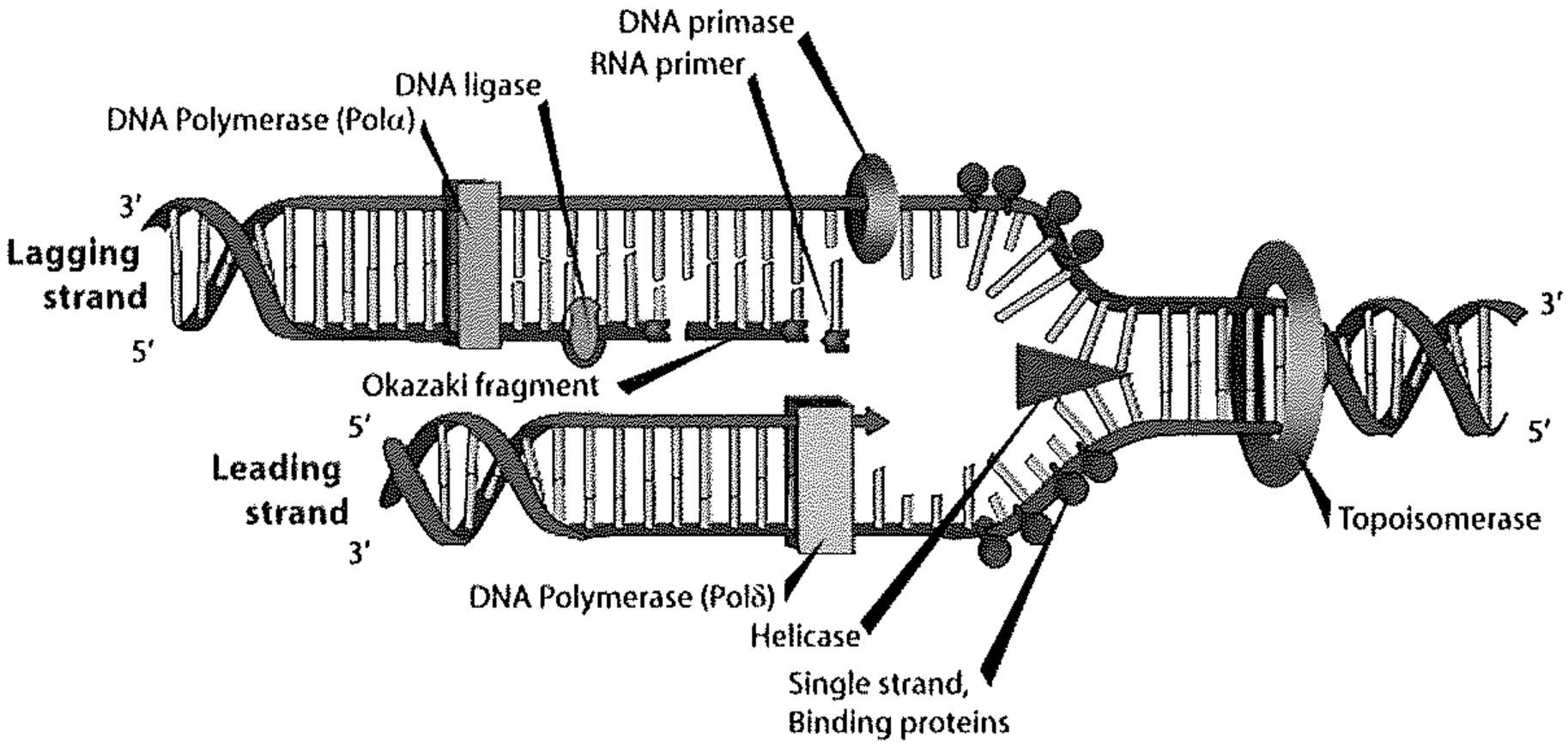

Figure 1 – DNA replication. The new DNA strand and Okazaki fragments serve as a primer for DNA replication. From Mariana Ruiz.

18. My prior declaration (paragraphs 27-29) discussed the process of making cDNA in a laboratory. cDNA can be generated in the laboratory using routine, standard techniques. Defendants assert that cDNA is different in kind from what exists in the body. This is incorrect. Both DNA and cDNA are described by the same series of nucleotide bases – these bases are the same chemical structure in both DNA and cDNA and in the same sequential order in both, much like the pages in a book are still in the same order even when one page is removed. Moreover, the same process for making cDNA in the laboratory, using the same enzyme, occurs naturally in the body. In the scientific literature, these naturally occurring cDNAs are created through a process called retrotransposition. In this process, a portion of a normal mRNA transcript from a gene is reverse transcribed back into DNA (naturally creating a cDNA) and is often re-inserted back into the genome. These converted, or retrotransposed, genes often create a cDNA copy of the mRNA, and as such, they are usually inserted back into the genome with a poly-A tail, no introns and no regulatory elements. These naturally occurring cDNAs are structurally, functionally, and chemically identical to cDNAs made in the laboratory. These cDNAs, if then inserted back into the genome, are called pseudogenes. Most importantly, a segment of the claimed cDNA already exists in the human genome, known as BRCA1 Psuedogene1 (also called BRCA1P1). These processes that generate pseudogenes are not done by scientists, but naturally occur inside the cells of living beings.

19. Defendants are correct that cDNA can be made in a laboratory. The methods for doing so are routine, standard methods. Those methods are utilized every day by scientists all over the world to make cDNA from other genes and other segments of DNA. There is also nothing unique in making BRCA1 or BRCA2 cDNA; the same standard methods are merely applied to that particular region of the DNA. When cDNA is made in a laboratory, the result is

usually fragments of cDNA that are not as long as a full gene. (Note, the same is true for naturally occurring cDNA – these often occur as fragments of the full length gene). But, contrary to defendants' implications, scientists sequencing the cDNA do not stick the fragments together. A simple computer program, used every day by scientists all over the world, can determine the sequence even though the cDNA is fragmented. Thus, the full cDNA sequence described in the patents would rarely exist as one intact chain in the laboratory. The same is true of isolated DNA.

20. Defendants argue that cDNA is different from "native DNA" because it does not contain regulatory regions. However, cDNAs may contain untranslated regions (UTRs) which contain regulatory structures that are targeted by cellular machinery to regulate the translation of the mRNA. As such, while cDNA generally does not contain all regulatory sequences or structures needed for transcription, it can contain some regulator elements.

21. DNA is not generally described according to the sugars and phosphates that make up its backbone. As the patents in this case make clear, DNA is described according to the sequence of nucleic acids, which contain all of the relevant information about the product that the gene creates. In this respect, its description is entirely different from H_2O as a description of water. For example, H_2O, HOH and OH_2 all describe and represent the exact same molecule; conversely TAA, ATA and AAT encode entirely different amino acids. TAA instructs the body to stop translation. ATA codes for isoleucine. AAT codes for asparagine.

22. The chemical structure of nucleotides outside the body is the same as the chemical structure of nucleotides inside the body. Defendants argue that DNA in the body can be methylated, i.e. that it can have additional chemical groups attached to it. That statement is true. However, DNA also appears in the body in a non-methylated state. Also, many isolation

techniques maintain the methylated state of the nucleotides after they have been removed from the body. Thus, both native DNA and isolated DNA can me methylated or un-methylated.

23. Defendants argue that DNA in the body is never "free floating." That argument is incorrect. During replication inside the body, a fragment of the DNA is free floating, with no proteins or other molecules attached to it. The body unwinds DNA and separates the strands when it duplicates the genes during mitosis and meiosis (Figure 1) and when it transcribes the genes during protein synthesis. At that time, segments of the DNA strands are free floating.

I declare pursuant to 42 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.

Christopher E. Mason

January 19, 2010