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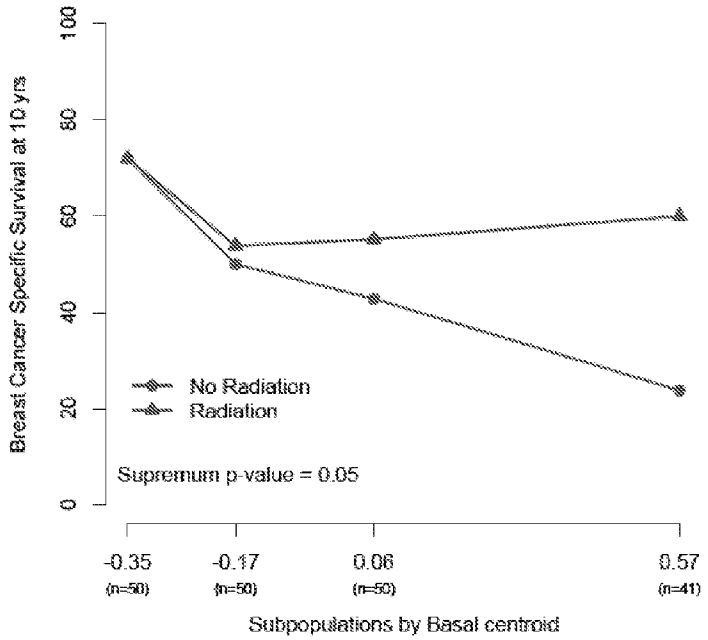
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[Continued on next page]

(54) Title: METHODS AND KITS FOR PREDICTING OUTCOME AND METHODS AND KITS FOR TREATING BREAST CANCER WITH RADIATION THERAPY

Figure 5



(57) Abstract: The application describes methods and kits for screening subjects with breast cancer to determine if the breast cancer will be responsive to a post-mastectomy breast cancer therapy including radiation. The application further describes methods and kits for treating subjects with post-mastectomy breast cancer by screening them for the likelihood of the effectiveness of treating the cancer with a therapy including radiation and administering the therapy in subjects when it is found that radiation is likely to be effective.

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METHODS AND KITS FOR PREDICTING OUTCOME AND METHODS AND KITS FOR TREATING BREAST CANCER WITH RADIATION THERAPY

CROSS-REFERENCE TO RELATED APPLICATIONS

[01] This application claims priority to U.S. Provisional Patent Application Serial No. 61/875,373 filed September 9, 2013 and to U.S. Provisional Patent Application Serial No. 61/990,948 filed May 9, 2014, the contents of which are herein incorporated by reference in their entirety.

FIELD OF THE INVENTION

[02] This disclosure relates generally to the field of cancer biology, and specifically, to the fields of detection and identification of specific cancer cell phenotypes and correlation with appropriate therapies.

INCORPORATION BY REFERENCE OF SEQUENCE LISTING

[03] The contents of the text file named "NATE-022001WO_ST25.txt", which was created on September 8, 2014 and is 328,667 bytes in size, are hereby incorporated by reference in their entireties

BACKGROUND OF THE INVENTION

[04] Radiation therapy (also known as radiotherapy or radiation oncology) is often utilized following lumpectomy or mastectomy to reduce or control malignant cancer cells that remain post-surgery, *i.e.*, as an adjuvant therapy, and is known to lower the chances of breast cancer recurrence and breast cancer death. Radiation is used after mastectomy to treat the chest wall and the lymph nodes around the collarbone and axillary nodes in the underarm area. However, there are various adverse side effects associated with radiation therapy, such as nausea and vomiting, intestinal discomfort, mouth, throat and stomach sores, damage to epithelial surfaces, edema, infertility, fibrosis, lymphedema, hypopituitarism and epilation. Thus, there is a need in the art to determine types of cancer and identifying subjects having such cancer types that respond best to radiation-based therapy and which types of cancer and subjects having such cancer types would be better treated with non-radiation-based therapy; accordingly, an optimal treatment is provided to the subject in need thereof. The present invention addresses these needs.

SUMMARY OF THE INVENTION

[05] The present invention provides a method of predicting local-regional relapse free, or breast cancer specific survival in a subject having a breast cancer including steps of: (a) obtaining a biological sample from the subject and (b) assaying the biological sample to determine whether the biological sample is classified as a Luminal A subtype, Luminal B subtype, Basal-like subtype, or HER2-enriched subtype, wherein the subtypes are determined using a measurement of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1, wherein (1) if the biological sample is classified as a Luminal A subtype or Basal-like subtype, a post-mastectomy breast cancer treatment including radiation is more likely to prolong local-regional relapse free survival or breast cancer specific survival of the subject or (2) if the biological sample is classified as a Luminal B subtype or HER2-enriched subtype, a post-mastectomy breast cancer treatment including radiation is not likely to prolong local-regional relapse free survival or breast cancer specific survival of the subject.

[06] The present invention also provides a method of screening for the likelihood of the effectiveness of a post-mastectomy breast cancer treatment including radiation in a subject in need thereof including steps of: (a) obtaining a biological sample from the subject and (b) assaying the biological sample to determine whether the biological sample is classified as a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype, wherein the subtype is determined using a measurement of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1, wherein (1) if the biological sample is classified as a Luminal A subtype or Basal-like subtype, the post-mastectomy breast cancer treatment including radiation is more likely to be effective in the subject or (2) if the biological sample is classified as a Luminal B subtype or HER2-enriched subtype, the post-mastectomy breast cancer treatment including radiation is not likely to be effective in the subject.

[07] The present invention also provides a method of treating breast cancer in a subject in need thereof including steps of: (a) obtaining a biological sample from the subject, (b) assaying the biological sample to determine whether the biological sample is classified as a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype, wherein the subtype is determined using a measurement of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1, and (c) administering a breast cancer treatment

to the subject, wherein (1) if the biological sample is classified as a Luminal A or Basal-like subtype, the subject is administered a post-mastectomy breast cancer treatment including radiation or (2) if the biological sample is a Luminal B or HER2-enriched subtype, the subject is administered a breast cancer treatment not including radiation, thereby treating breast cancer in the subject.

[08] In any of the above methods, preferably, the subtypes are determined using expression levels (*e.g.*, RNA expression levels) of at least 40 of the genes listed in Table 1, *e.g.*, 46 or 50 of the genes listed in Table 1. The step of assaying may include detecting expression levels of at the least the following 24 genes from the at least 40 of the genes listed in Table 1, *i.e.*, *FOXA1, MLPH, ESR1, FOXC1, CDC20, ANLN, MAPT, ORC6L, CEP55, MKI67, UBE2C, KNTC2, EXO1, PTTG1, MELK, BIRC5, GPR160, RRM2, SRFP1, NAT1, KIF2C, CXXC5, MIA* and *BCL2*. Expression levels of *CCNE1, CDC6, CDCA1, CENPF, TYMS*, and *UBE2T* may additionally be detected. In embodiments, expression level of each gene in the NANO46 gene set (which is all 50 genes in Table 1 with the exception of *MYBL2, BIRC5, GRB7* and *CCNB1*) is detected. Additionally, expression levels of housekeeping genes may be detected. Expression levels of the at least 40 genes as well as a plurality of (*e.g.*, eight or more) housekeeping genes can be detected in a single hybridization reaction. Expression levels of the at least 40 genes may be normalized to expression levels of the plurality of housekeeping genes. To control for any differences in the intact RNA amount in the reference sample, the levels of the at least 40 genes are normalized against the mean of the level of plurality of housekeeping genes.

[09] A synthetic RNA reference sample, comprising *in vitro* transcribed RNA targets from the at least 40 genes and the plurality of housekeeping genes, may be assayed and used as a control. Further, to control for any variation in the assay procedure, the above normalized expression levels for each of the at least 40 genes from a biological sample are then further normalized to the normalized levels from each of the at least 40 genes of the synthetic reference sample. The normalized gene expression levels are then log transformed and scaled using two scaling factors.

[10] The step of assaying may include one or more steps of generating a gene expression profile based on expression of the genes in the biological sample, comparing the gene expression profile for the biological sample to centroids constructed from gene expression data for the at least 40 of the genes listed in Table 1 for the Luminal A, Luminal B, HER2-enriched or Basal-like subtypes, utilizing a supervised algorithm and calculating the distance of the gene expression

profile for the biological sample to each of the centroids, and classifying the biological sample as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype based upon the nearest centroid. More specifically, a computational algorithm based on a Pearson's correlation compares the normalized and scaled gene expression profile of the entirety of the at least 40 genes from the biological sample to prototypical expression signatures (termed "centroids") which define each of the four breast cancer intrinsic subtypes, *e.g.*, derived from gene expression data deposited with the National Center for Biotechnology Information Gene Expression Omnibus (GEO) (as examples, with accession number GSE2845 or GSE10886). The Pearson's correlation calculation assigns the patient breast tumor sample to the intrinsic subtype with the most similar expression profile or centroid score across the at least 40 genes. The Pearson's correlation of the totality of the at least 40 genes to the four centroids results in four numerical values that each range from -1 to +1 where a value of +1 is a perfectly correlated expression profile, -1 is a perfectly anti-correlated profile and 0 is completely uncorrelated. Features of the above-mentioned steps are included in the "PAM50 classification model" or the "NANO46 classification model", as described below.

[11] At least one of the above described steps is performed on a computer or electronic computational device.

[12] In embodiments, assaying includes detecting expression levels of *HER2*.

[13] The breast cancer can be primary breast cancer, locally advanced breast cancer or metastatic breast cancer. The subject can be a mammal. Preferably, the subject is human. The subject may be a male or a female. The subject has been diagnosed by a skilled artisan as having a breast cancer and is included in a subpopulation of humans who currently have breast cancer or had breast cancer. The subject that has breast cancer can be pre-mastectomy or post-mastectomy. Preferably the subject is post-mastectomy. The subject may have undergone breast-conserving therapy. The subject that has breast cancer may have been previously been treated with an anti-cancer or chemotherapeutic agent. Preferably the subject has not been previously treated with an anti-cancer agent or chemotherapeutic agent. The subject may have been previously been treated with radiation. Preferably the subject has not been previously treated with radiation. The subject can be pre-menopausal or post-menopausal. Preferably, the subject is pre-menopausal. The subject can have node-positive breast cancer. Preferably, the subject has node-positive breast cancer. The subject can have estrogen receptor positive or estrogen receptor negative breast

cancer. The subject that has estrogen receptor positive breast cancer may also undergo or be subjected to oophorectomy, alone or in addition to other breast cancer treatments. The subject may have Stage I or II, lymph node-negative, breast cancer or Stage II, lymph node positive, breast cancer.

[14] The breast cancer treatment that includes radiation can also include one or more anti-cancer or chemotherapeutic agents. Classes of anti-cancer or chemotherapeutic agents can include anthracycline agents, alkylating agents, nucleoside analogs, platinum agents, taxanes, vinca agents, anti-estrogen drugs, aromatase inhibitors, ovarian suppression agents, endocrine/hormonal agents, bisphophonate therapy agents and targeted biological therapy agents. Specific anti-cancer or chemotherapeutic agents include cyclophosphamide, fluorouracil (or 5-fluorouracil or 5-FU), methotrexate, thiotepa, carboplatin, cisplatin, gemcitabine, anthracycline, taxanes, paclitaxel, protein-bound paclitaxel, docetaxel, vinorelbine, tamoxifen, raloxifene, toremifene, fulvestrant, irinotecan, ixabepilone, temozolmide, topotecan, vincristine, vinblastine, eribulin, mutamycin, capecitabine, capecitabine, anastrozole, exemestane, letrozole, leuprolide, abarelix, buserlin, goserelin, megestrol acetate, risedronate, pamidronate, ibandronate, alendronate, denosumab, zoledronate, trastuzumab, tykerb or bevacizumab, or combinations thereof. Preferably, the treatment that includes radiation also includes cyclophosphamide, fluorouracil (or 5-fluorouracil or 5-FU), methotrexate, or combinations thereof; one such combination is CMF which includes cyclophosphamide, methotrexate, and fluorouracil.

[15] The assaying of the biological sample to determine whether the biological sample is classified as either a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype cancer is performed using RNA expression profiling, immunohistochemistry (IHC) or fluorescence *in situ* hybridization (FISH). Preferably, the assay is RNA expression profiling. The expression of the members of the gene list of Table 1 can be determined using a nanoreporter and the nanoreporter code system (nCounter® Analysis system; NanoString Technologies, Seattle, WA). Preferably, expression of the members of the gene list of Table 1 can be determined using a reporter probe and capture probe for the detection of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1. In particular, expression of the "NANO46" set of genes is determined (which is by determining the expression of all 50 genes in Table 1 with the exception of determining the expression of *MYBL2*, *BIRC5*, *GRB7* and *CCNB1*). Preferably, there is only one reporter probe/capture probe pair for any one gene of

Table 1 to be detected.

[16] The biological sample can be a cell, a tissue or a bodily fluid. The tissue can be sampled from a biopsy or smear. The biological sample can be a tumor. The tumor can be an estrogen receptor positive tumor or an estrogen receptor negative tumor. The sample can also be a sampling of bodily fluids. The bodily fluid can include blood, lymph, urine, saliva, nipple aspirates and gynecological fluids. The biological sample can be a formalin fixed paraffin embedded tissues (FFPE) sample.

[17] When a biological sample is classified as either a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype cancer, the subject from which the biological sample is obtained is classified as having, respectively, a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype cancer. A subject is assigned to a recommended treatment group based on his/her classified cancer subtype. Finally, a recommend treatment to be provided to a subject depends on the group to which the subject is assigned.

[18] In embodiments, a computational algorithm then calculates a Risk of Recurrence (ROR) score. In embodiments, the ROR score is calculated using coefficients from a Cox model that includes (1) Pearson's correlation of the expression profiles of the at least 40 genes (*e.g.*, the NANO46 gene set) in the biological sample with the expected profiles for the four intrinsic subtypes (*as described above*), (2) a proliferation score (determined from the mean gene expression of a subset of 18 proliferation genes of the at least 40 genes (*as described below*) and (3) gross tumor size of the subject's tumor. The variables are multiplied by the corresponding coefficients from the Cox Model to generate the score, which is then adjusted to a 0-100 scale. The 0-100 ROR score is correlated with the probability of distant recurrence at ten years (Distant Recurrence-Free Survival (DRFS) at 10 years). Risk categories (low, intermediate, or high) are also calculated based on cut-offs for risk of recurrence score determined in a clinical validation study.

[19] In embodiments, a risk of recurrence (ROR) score of 0 to 40 is a low risk of recurrence for a node-negative cancer, a ROR score of 0 to 15 is a low risk of recurrence for a node-positive cancer, a ROR score of 61 to 100 is a high risk of recurrence for a node-negative cancer, and a ROR score of 41 to 100 is a high risk of recurrence for a node-positive cancer.

[20] As used herein a ROR score can be calculated using any method or formula known in the art. Exemplary formulae include Equations 1 to 6, *as described herein*.

[21] The at least 40 genes set contains many genes that are known markers for proliferation. The methods and kits of the present invention provide for the determination of subsets of genes that provide a proliferation signature. The methods and kits of the present invention can include steps and reagents for determining the expression of at least one of, a combination of, or each of, a 18-gene subset of the intrinsic genes of Table 1 selected from *ANLN*, *CCNE1*, *CDC20*, *CDC6*, *CDCA1*, *CENPF*, *CEP55*, *EXO1*, *KIF2C*, *KNTC2*, *MELK*, *MKI67*, *ORC6L*, *PTTG1*, *RRM2*, *TYMS*, *UBE2C* and/or *UBE2T*. Preferably, the expression of each of the 18-gene subset of the gene set of Table 1 is determined to provide a proliferation score. The expression of one or more of these genes may be determined and a proliferation signature index can be generated by averaging the normalized expression estimates of one or more of these genes in a sample. The sample can be assigned a high proliferation signature, a moderate/intermediate proliferation signature, a low proliferation signature or an ultra-low proliferation signature. Methods of determining a proliferation signature from a biological sample are as described in Nielsen *et al. Clin. Cancer Res.*, 16(21):5222-5232 (2009) and supplemental online material.

[22] The present invention provides a kit for predicting local-regional relapse free or breast cancer specific survival in a subject having a breast cancer including reagents (*e.g.*, sets of reporter/capture probes and/or primers) sufficient for detecting expression of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; instructions for performing an assay to classify a biological sample from the subject as a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype, by using the reagents to detect or measure expression of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; instructions providing information allowing a user to classify whether the biological sample from the subject is a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype by using the reagents to detect or measure expression at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; and instructions for obtaining a prediction whether a treatment including radiation is more likely or not likely to prolong local-regional relapse free or breast cancer specific survival in the subject based on the classified cancer subtype, wherein (a) if the biological sample is classified as a Luminal A subtype or Basal-like, a post-mastectomy breast cancer treatment including radiation is more likely to prolong local-regional relapse free survival or breast cancer specific survival of the subject and (b) if the

biological sample is classified as a Luminal B or HER2-enriched subtype, a post-mastectomy breast cancer treatment including radiation is not likely to prolong local-regional relapse free survival or breast cancer specific survival of the subject. The instructions may provide a recommended treatment for the subject based on the obtained prediction. The instructions may further specify how to determine a proliferation score/signature, how to utilize clinicopathological variables in calculations, and how to calculate risk of recurrence (ROR) scores/signatures, *e.g.*, which may be based in part of expression data of the NANO46 set of genes. The kit may also contain reagents sufficient to facilitate detection and/or quantitation of *HER2*, in order to classify cells as *HER2+*. The kit may include a positive and/or negative control reference sample(s). The kit may include reagents for detecting expression of one or more housekeeping genes, DNA Repair genes, and/or tumor suppressor genes (*e.g., RB1*). The kit may further comprise a non-transitory computer readable medium including, at least, any of the above-described instructions. The kit may comprise an array. The kit may include reagents and instructions for determining a VEGF-signature score (*as described below, including Table 7*).

[23] The present invention also provides a kit for screening for the likelihood of the effectiveness of a post-mastectomy breast cancer treatment including radiation in a subject in need thereof including reagents (*e.g.*, sets of reporter/capture probes and/or primers) sufficient for detecting expression of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; instructions for performing an assay to classify a biological sample from the subject as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype, by using the reagents to detect or measure expression of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; instructions providing information allowing a user to classify whether the biological sample from the subject is a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype by using the reagents to detect or measure expression of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; and instructions for determining the likelihood of the effectiveness of a post-mastectomy breast cancer treatment including radiation in the subject based on the classified cancer subtype, wherein (a) if the biological sample is classified as a Luminal A or Basal-like subtype, a post-mastectomy breast cancer treatment including radiation is more likely to be effective in the subject or (b) if the biological sample is classified as a Luminal B or HER2-enriched subtype, a

post-mastectomy breast cancer treatment including radiation is not likely to be effective in the subject. The instructions provide a recommended treatment based on the determined likelihood of effectiveness. The instructions may further specify how to determine a proliferation score/signature, how to utilize clinicopathological variables in calculations, and how to calculate risk of recurrence (ROR) scores/signatures, *e.g.*, which may be based in part of expression data of the NANO46 set of genes. The kit may also contain reagents sufficient to facilitate detection and/or quantitation of *HER2,* in order to classify cells as *HER2+*. The kit may include a positive and/or negative control reference sample(s). The kit may include reagents for detecting expression of one or more housekeeping genes, DNA Repair genes, and/or tumor suppressor genes (*e.g., RB1*). The kit may further comprise a non-transitory computer readable medium including, at least, any of the above-described instructions. The kit may comprise an array. The kit may include reagents and instructions for determining a VEGF-signature score.

[24] The present invention also provides a kit for treating breast cancer in a subject in need thereof including reagents (*e.g.*, sets of reporter/capture probes and/or primers) sufficient for detecting expression of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; instructions for performing an assay to classify a biological sample from the subject as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype, by using the reagents to detect or measure expression of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; instructions providing information allowing a user to classify whether the biological sample from the subject is a Luminal A, Luminal B, HER2-enriched, or Basal-like subtype by using the reagents to measure at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1; and instructions for administering a post-mastectomy breast cancer treatment including radiation if the biological sample is classified as a Luminal A or Basal-like subtype and instructions for administering a post-mastectomy breast cancer treatment not including radiation if the biological sample is classified as a Luminal B or HER2-enriched subtype. The instructions may further specify how to determine a proliferation score/signature, how to utilize clinicopathological variables in calculations, and how to calculate risk of recurrence (ROR) scores/signatures, *e.g.*, which may be based in part of expression data of the NANO46 set of genes. The kit may also contain reagents sufficient to facilitate detection and/or quantitation of *HER2,* in order to classify cells as *HER2+*.

The kit may include a positive and/or negative control reference sample(s). The kit may include reagents for detecting expression of one or more housekeeping genes, DNA Repair genes, and/or tumor suppressor genes (*e.g.*, *RB1*). The kit may further comprise a non-transitory computer readable medium including, at least, any of the above-described instructions. The kit may comprise an array. The kit may include reagents and instructions for determining a VEGF-signature score.

[25] Preferably, the kit provides reagents sufficient for the detection of at least 40 of the genes listed in Table 1. Preferably, the kit provides reagents sufficient for the detection of at least 45 of the genes listed in Table 1, *i.e.*, 46 of the genes listed in Table 1. The reagents sufficient for the detection of the at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1 can include an array (*e.g.*, a microarray) or a microfluidic device. Preferably, the reagents include a reporter probe and capture probe for the detection of at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 of the genes listed in Table 1. Preferably, the kit includes reagents sufficient to detect one or more housekeeping genes, DNA Repair genes, and/or tumor suppressor genes (*e.g.*, *RB1*). Preferably, there is only one reporter probe/capture probe pair for any one gene of Table 1 to be detected or only one housekeeping gene. Preferably, the kit includes reagents sufficient to facilitate detection and/or quantitation of HER2. Preferably, the kit includes reagents sufficient to determine a VEGF-signature score. Preferably, the kit includes instructions for utilizing the reagents and for performing any of the methods provided in the instant invention.

[26] The term "likely" as used herein has the meaning commonly understood by a person skilled in the art to which this invention belongs. For example, if a subject is "more likely" to benefit from a therapy, it would be recommended for a health care provider to select the therapy for the subject.

[27] The term "measurement" as used herein includes obtaining, measuring, or detecting a numeric value of a quantifiable property, *e.g.*, expression level of a gene, and also includes calculations using the value, *e.g.*, the deviation of a gene's expression level in a test sample relative to a control sample, a correlation, and a statistic.

[28] Any of the above aspects and embodiments can be combined with any other aspect or embodiment.

[29] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. In the specification, the singular forms also include the plural unless the context clearly dictates otherwise; as examples, the terms "a," "an," and "the" are understood to be singular or plural and the term "or" is understood to be inclusive. By way of example, "an element" means one or more element. Throughout the specification the word "comprising," or variations such as "comprises" or "comprising," will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps. About can be understood as within 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.1%, 0.05%, or 0.01% of the stated value. Unless otherwise clear from the context, all numerical values provided herein are modified by the term "about."

[30] Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. The references cited herein are not admitted to be prior art to the claimed invention. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and are not intended to be limiting. Other features and advantages of the invention will be apparent from the following detailed description and claim.

Brief Description of the Drawings

[31] The above and further features will be more clearly appreciated from the following detailed description when taken in conjunction with the accompanying drawings.

[32] Figures 1A and 1B show loco-regional relapse and breast cancer specific survival (BCSS), respectively, for subjects whose tumor samples are classified as Luminal A, with or without radiation therapy.

[33] Figures 2A and 2B show loco-regional free survival and BCSS, respectively, for subjects whose tumor samples are classified as Luminal B, with or without radiation therapy.

[34] Figures 3A and 3B show loco-regional free survival and BCSS, respectively, for subjects whose tumor samples are classified as HER2-enriched, with or without radiation therapy.

[35] Figures 4A and 4B show loco-regional free survival and BCSS, respectively, for subjects whose tumor samples are classified as Basal-like, with or without radiation therapy.

[36] Figure 5 shows 10-year BCSS for subpopulations of Basal-like tumors, with or without radiation therapy.

[37] Figures 6A and 6B show loco-regional free survival and BCSS, respectively, for subjects who are classified as low risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy.

[38] Figures 7A and 7B show loco-regional free survival and BCSS, respectively, for subjects who are classified as moderate/intermediate risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy.

[39] Figures 8A and 8B show loco-regional free survival and BCSS, respectively, for subjects who are classified as high risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy.

[40] Figure 9 is a schematic of the Breast Cancer Intrinsic Subtyping test.

[41] Figure 10 is a schematic of an algorithm process.

Detailed Description of the Invention

[42] The present invention provides a method of determining whether a post-mastectomy breast cancer treatment comprising radiation is optimal for administration to a patient suffering from breast cancer. Determining whether a breast cancer patient should receive a treatment including radiation includes classifying the subtype of the breast cancer using a gene expression set. The disclosure also provides a method of treating breast cancer by determining whether a post-mastectomy breast cancer patient should receive a treatment including radiation and then administering the optimal breast cancer treatment to the patient based on that determination.

[43] Intrinsic genes are statistically selected to have low variation in expression between biological sample replicates from the same individual and high variation in expression across samples from different individuals. Thus, intrinsic genes are used as classifier genes for breast cancer classification. Although clinical information was not used to derive the breast cancer intrinsic subtypes, this classification has proved to have prognostic significance. Intrinsic gene screening can be used to classify breast cancers into various subtypes. The major intrinsic subtypes of breast cancer are referred to as Luminal A (LumA), Luminal B (LumB), HER2-

enriched (Her-2-E), Basal-like, and Normal-like (Perou *et al. Nature*, 406(6797):747-52 (2000); Sorlie *et al. PNAS*, 98(19):10869-74 (2001)).

[44] The PAM50 gene expression assay, as described herein, is able to identify intrinsic subtype from standard formalin fixed paraffin embedded tumor tissue (also *see*, Parker *et al. J Clin Oncol.*, 27(8):1160-7 (2009) and U.S. Patent Application Publication No. 2011/0145176). The methods utilize a supervised algorithm to classify subject samples according to breast cancer intrinsic subtype. This algorithm, referred to herein as the "PAM50 classification model", is based on the gene expression profile of a defined subset of intrinsic genes that has been identified herein as superior for classifying breast cancer intrinsic subtypes. *See*, U.S. Patent Application Publication No. 2011/0145176. The subset of genes, along with exemplary primers specific for their detection, is provided in Table 1. The subset of genes, along with exemplary probes specific for their detection, is provided in Table 2. The exemplary primers and target specific probe sequences are merely representative and not meant to limit the invention. The skilled artisan can utilize any primer and/or target sequence-specific probe for detecting any of (or each of) the genes in Table 1.

[45] Table 1. PAM50 Intrinsic Gene List

[46] **Table 1**

GENE NAME	REPRESENTATIVE GENBANK ACCESSION NUMBER	FORWARD PRIMER	SEQ ID NO:	REVERSE PRIMER	SEQ ID NO:
ACTR3B	NM_020445 NM_001040135	AAAGATTCCTGGGA CCTGA	1	TGGGGCAGTTCTGTA TTACTTC	51
ANLN	NM_018685	ACAGCCACTTTCAG AAGCAAG	2	CGATGGTTTTGTACA AGATTTCTC	52
BAG1	NM_004323	CTGGAAGAGTTGAA TAAAGAGC	3	GCAAATCCTTGGGC AGA	53
BCL2	NM_000633	TACCTGAACCGGCA CCTG	4	GCCGTACAGTTCCAC AAAGG	54
BIRC5	NM_001012271	GCACAAAGCCATTC TAAGTC	5	GACGCTTCCTATCAC TCTATTC	55
BLVRA	BX647539	GCTGGCTGAGCAGA AAG	6	TTCCTCCATCAAGAG TTCAACA	56
CCNB1	NM_031966	CTTTCGCCTGAGCCT ATTT	7	GGGCACATCCAGAT GTTT	57

CCNE1	BC035498	GGCCAAAATCGACAGGAC	8	GGGTCTGCACAGACTGCAT	58
CDC20	BG256659	CTGTCTGAGTGCCGTGGAT	9	TCCTTGTAATGGGGAGACCA	59
CDC6	NM_001254	GTAAATCACCTTCTGAGCCT	10	ACTTGGGATATGTGAATAAGACC	60
CDCA1	NM_031423	GGAGGCGGAAGAAACCAG	11	GGGGAAAGACAAAGTTTCCA	61
CDH3	BC041846	GACAAGGAGAATCAAAAGATCAGC	12	ACTGTCTGGGTCCATGGCTA	62
CENPF	NM_016343	GTGGCAGCAGATCACAA	13	GGATTTCGTGGTGGGTTC	63
CEP55	AB091343	CCTCACGAATTGCTGAACTT	14	CCACAGTCTGTGATAAACGG	64
CXXC5	BC006428	CATGAAATAGTGCATAGTTTGCC	15	CCATCAACATTCTCTTTATGAACG	65
EGFR	NM_005228	ACACAGAATCTATACCCACCAGAGT	16	ATCAACTCCCAAACGGTCAC	66
ERBB2	NM_001005862	GCTGGCTCTCACACTGATAG	17	GCCCTTACACATCGGAGAAC	67
ESR1	NM_001122742	GCAGGGAGAGGAGTTTGT	18	GACTTCAGGGTGCTGGAC	68
EXO1	NM_130398	CCCATCCATGTGAGGAAGTATAA	19	TGTGAAGCCAGCAATATGTATC	69
FGFR4	AB209631	CTTCTTGGACCTTGGCG	20	TATTGGGAGGCAGGAGGTTTA	70
FOXA1	NM_004496	GCTACTACGCAGACACG	21	CTGAGTTCATGTTGCTGACC	71
FOXC1	NM_001453	GATGTTCGAGTCACAGAGG	22	GACAGCTACTATTCCCGTT	72
GPR160	AJ249248	TTCGGCTGGAAGGAACC	23	TATGTGAGTAAGCTCGGAGAC	73
GRB7	NM_005310	CGTGGCAGATGTGAACGA	24	AGTGGGCATCCCGTAGA	74
HSPC150 (UBE2T)	NM_014176	GGAGATCCGTCAACTCCAAA	25	AGTGGACATGCGAGTGGAG	75
KIF2C	NM_006845	TGGGTCGTGTCAGGAAAC	26	CACCGCTGGAAACTGAAC	76
KNTC2	NM_006101	CGCAGTCATCCAGAGATGTG	27	CGTGCACATCCATGACCTT	77
KRT14	BC042437	ACTCAGTACAAGAAAGAACCG	28	GAGGAGATGACCTTGCC	78
KRT17	AK095281	GTTGGACCAGTCAACATCTCTG	29	GCCATAGCCACTGCCACT	79
KRT5	M21389	TGTGGCTCATTAGGCAAC	30	CTTCGACTGGACTCTGT	80
MAPT	NM_001123066	GACTCCAAGCGCGAAAAC	31	CAGACATGTTGGTATTGCACATT	81

MDM2	M92424	CCACAAAATATTCA TGGTTCTTG	32	AGGCGATCCTGGGA AATTAT	82
MELK	NM_014791	CCAGTAGCATTGTC CGAG	33	CCCATTTGTCTGTCT TCAC	83
MIA	BG765502	GTCTCTGGTAATGC ACACT	34	CTGATGGTTGAGGCT GTT	84
MKI67	NM_002417	GTGGAATGCCTGCT GACC	35	CGCACTCCAGCACCT AGAC	85
MLPH	NM_024101	AGGGGTGCCCTCTG AGAT	36	TCACAGGGTCAAAC TTCCAGT	86
MMP11	NM_005940	CGAGATCGCCAAGA TGTT	37	GATGGTAGAGTTCC AGTGATT	87
MYBL2	BX647151	AGGCGAACACACAA CGTC	38	TCTGGTCACGCAGG GCAA	88
MYC	NM_002467	AGCCTCGAACAATT GAAGA	39	ACACAGATGATGGA GATGTC	89
NAT1	BC013732	ATCGACTGTGTAAA CAACTAGAGAAGA	40	AGTAGCTACATCTCC AGGTTCTCTG	90
ORC6L	NM_014321	TTTAAGAGGGCAAA TGGAAGG	41	CGGATTTTATCAACG ATGCAG	91
PGR	NM_000926	TGCCGCAGAACTCA CTTG	42	CATTTGCCGTCCTTC ATCG	92
PHGDH	AK093306	CCTCAGATGATGCC TATCCA	43	GCAGGTCAAAACTC TCAAAG	93
PTTG1	BE904476	CAGCAAGCGATGGC ATAGT	44	AGCGGGCTTCTGTAA TCTGA	94
RRM2	AK123010	AATGCCACCGAAGC CTC	45	GCCTCAGATTTCAAC TCGT	95
SFRP1	BC036503	TCGAACTGAAGGCT ATTTACGAG	46	CTGCTGAGAATCAA AGTGGGA	96
SLC39A6	NM_012319	GTCGAAGCCGCAAT TAGG	47	GGAACAAACTGCTC TGCCA	97
TMEM45B	AK098106	CAAACGTGTGTTCT GGAGG	48	ACAGCTCTTTAGCAT TTGTGGA	98
TYMS	BQ56428	TGCCCTGTATGATGT CAGGA	49	GGGACTATCAATGTT GGGTTCTC	99
UBE2C	BC032677	GTGAGGGGTGTCAG CTCAGT	50	CACACAGTTCACTGC TCCACA	100

[47] Table 2. Exemplary Probes for detecting NANO46 genes

[48] **Table 2**

Gene Name	**Ref Seq Accession**	**Target Sequence**	**SEQ ID NO:**
ACTR3B	NM_001040135.1	CCAGAAGAAGTTTGTTATAGACGTTGGTTACGAA AGATTCCTGGGACCTGAAATATTCTTTCACCCGGA	101

		GTTTGCCAACCCAGACTTTATGGAGTCCATC	
ANLN	NM_018685.2	CGTGCCAGGCGAGAGAATCTTCAGAGAAAAATGG CTGAGAGGCCCACAGCAGCTCCAAGGTCTATGAC TCATGCTAAGCGAGCTAGACAGCCACTTTCAG	102
BAG1	NM_004323.3	CTTCATGTTACCTCCCAGCAGGGCAGCAGTGAAC CAGTTGTCCAAGACCTGGCCCAGGTTGTTGAAGA GGTCATAGGGGTTCCACAGTCTTTTCAGAAAC	103
BCL2	NM_000633.2	CCAAGCACCGCTTCGTGTGGCTCCACCTGGATGTT CTGTGCCTGTAAACATAGATTCGCTTTCCATGTTG TTGGCCGGATCACCATCTGAAGAGCAGACG	104
BLVRA	NM_000712.3	TTCCTGAAAAAAGAAGTGGTGGGGAAAGACCTGC TGAAAGGGTCGCTCCTCTTCACAGCTGGCCCGTTG GAAGAAGAGCGGTTTGGCTTCCCTGCATTCA	105
CCNE1	NM_001238.1	GAGAACTGTGTCAAGTGGATGGTTCCATTTGCCA TGGTTATAAGGGAGACGGGGAGCTCAAAACTGAA GCACTTCAGGGGCGTCGCTGATGAAGATGCAC	106
CDC20	NM_001255.1	CCCGAGTGGGCTCCCTAAGCTGGAACAGCTATAT CCTGTCCAGTGGTTCACGTTCTGGCCACATCCACC ACCATGATGTTCGGGTAGCAGAACACCATGT	107
CDC6	NM_001254.3	GGGGAAGTTATATGAAGCCTACAGTAAAGTCTGT CGCAAACAGCAGGTGGCGGCTGTGGACCAGTCAG AGTGTTTGTCACTTTCAGGGCTCTTGGAAGCC	108
CDCA1	NM_145697.1	GCCTGGCGGTGTTTTCGTCGTGCTCAGCGGTGGG AGGAGGCGGAAGAAACCAGAGCCTGGGAGATTA ACAGGAAACTTCCAAGATGGAAACTTTGTCTTT	109
CDH3	NM_001793.3	CCCTCGACCGTGAGGATGAGCAGTTTGTGAGGAA CAACATCTATGAAGTCATGGTCTTGGCCATGGAC AATGGAAGCCCTCCCACCACTGGCACGGGAAC	110
CENPF	NM_016343.3	AGAAAATCTTGCAGAGTCCTCCAAACCAACAGCT GGTGGCAGCAGATCACAAAAGGTCAAAGTTGCTC AGCGGAGCCCAGTAGATTCAGGCACCATCCTC	111
CEP55	NM_018131.3	GTACTACCGCATTGCTTGAACAGCTGGAAGAGAC AACGAGAGAAGGAGAAAGGAGGGAGCAGGTGTT GAAAGCCTTATCTGAAGAGAAAGACGTATTGAA	112
CXXC5	NM_016463.5	AGCTGCCCTCTCCGTGCAATGTCACTGCTCGTGTG GTCTCCAGCAAGGGATTCGGGCGAAGACAAACGG ATGCACCCGTCTTTAGAACCAAAAATATTCT	113
EGFR	NM_005228.3	GCAGCCAGGAACGTACTGGTGAAAACACCGCAGC ATGTCAAGATCACAGATTTTGGGCTGGCCAAACT GCTGGGTGCGGAAGAGAAAGAATACCATGCAG	114
ERBB2	NM_004448.2	TGAAGGTGCTTGGATCTGGCGCTTTTGGCACAGTC TACAAGGGCATCTGGATCCCTGATGGGGAGAATG TGAAAATTCCAGTGGCCATCAAAGTGTTGAG	115
ESR1	NM_000125.2	AGGAACCAGGGAAAATGTGTAGAGGGCATGGTG GAGATCTTCGACATGCTGCTGGCTACATCATCTCG GTTCCGCATGATGAATCTGCAGGGAGAGGAGT	116
EXO1	NM_006027.3	TGGCCCACAAAGTAATTAAAGCTGCCCGGTCTCA GGGGGTAGATTGCCTCGTGGCTCCCTATGAAGCT GATGCGCAGTTGGCCTATCTTAACAAAGCGGG	117
FGFR4	NM_002011.3	CCCACATCCAGTGGCTGAAGCACATCGTCATCAA CGGCAGCAGCTTCGGAGCCGACGGTTTCCCCTAT GTGCAAGTCCTAAAGACTGCAGACATCAATAG	118
FOXA1	NM_004496.2	TGGATGGTTGTATTGGGCAGGGTGGCTCCAGGAT GTTAGGAACTGTGAAGATGGAAGGGCATGAAACC	119

		AGCGACTGGAACAGCTACTACGCAGACACGCA	
FOXC1	NM_001453.1	TTCGAGTCACAGAGGATCGGCTTGAACAACTCTC CAGTGAACGGGAATAGTAGCTGTCAAATGGCCTT CCCTTCCAGCCAGTCTCTGTACCGCACGTCCG	120
GPR160	NM_014373.1	GGATTTCAGTCCTTGCTTATGTTTTGGGAGACCCA GCCATCTACCAAAGCCTGAAGGCACAGAATGCTT ATTCTCGTCACTGTCCTTTCTATGTCAGCAT	121
UBE2T	NM_014176.1	GTGTCAGCTCAGTGCATCCCAGGCAGCTCTTAGT GTGGAGCAGTGAACTGTGTGTGGTTCCTTCTACTT GGGGATCATGCAGAGAGCTTCACGTCTGAAG	122
KIF2C	NM_006845.2	GTTGTCTACAGGTTCACAGCAAGGCCACTGGTAC AGACAATCTTTGAAGGTGGAAAAGCAACTTGTTT TGCATATGGCCAGACAGGAAGTGGCAAGACAC	123
KNTC2	NM_006101.1	AAAAGGTCATAAGCATGAAGCGCAGTTCAGTTTC CAGCGGTGGTGCTGGCCGCCTCTCCATGCAGGAG TTAAGATCCCAGGATGTAAATAAACAAGGCCT	124
KRT14	NM_000526.3	GCAGTCATCCAGAGATGTGACCTCCTCCAGCCGC CAAATCCGCACCAAGGTCATGGATGTGCACGATG GCAAGGTGGTGTCCACCCACGAGCAGGTCCTT	125
KRT17	NM_000422.1	CTGACTCAGTACAAGAAAGAACCGGTGACCACCC GTCAGGTGCGTACCATTGTGGAAGAGGTCCAGGA TGGCAAGGTCATCTCCTCCCGCGAGCAGGTCC	126
KRT5	NM_000424.2	CTGGTTCTCTTGCTCCACCAGGAACAAGCCACCAT GTCTCGCCAGTCAAGTGTGTCCTTCCGGAGCGGG GGCAGTCGTAGCTTCAGCACCGCCTCTGCCA	127
MAPT	NM_016835.3	GCCGGGTCCCTCAACTCAAAGCTCGCATGGTCAG TAAAAGCAAAGACGGGACTGGAAGCGATGACAA AAAAGCCAAGACATCCACACGTTCCTCTGCTAA	128
MDM2	NM_006878.2	GGTGAGGAGCAGGCAAATGTGCAATACCAACATG TCTGTACCTACTGATGGTGCTGTAACCACCTCACA GATTCCAGCTTCGGAACAAGAGACCCTGGTT	129
MELK	NM_014791.2	AGAGACAGCCAACAAAATATTCATGGTTCTTGAG TACTGCCCTGGAGGAGAGCTGTTTGACTATATAA TTTCCCAGGATCGCCTGTCAGAAGAGGAGACC	130
MIA	NM_006533.1	CCGGGGCCAAGTGGTGTATGTCTTCTCCAAGCTG AAGGGCCGTGGGCGGCTCTTCTGGGGAGGCAGCG TTCAGGGAGATTACTATGGAGATCTGGCTGCT	131
MKI67	NM_002417.2	GCTTCCAGCAGCAAATCTCAGACAGAGGTTCCTA AGAGAGGAGGAGAAAGAGTGGCAACCTGCCTTC AAAAGAGAGTGTCTATCAGCCGAAGTCAACATG	132
MLPH	NM_024101.4	GAGGAAGTCAAACCTCCCGATATTTCTCCCTCGA GTGGCTGGGAAACTTGGCAAGAGACCAGAGGAC CCAAATGCAGACCCTTCAAGTGAGGCCAAGGCA	133
MMP11	NM_005940.3	AGCAGCCAAGGCCCTGATGTCCGCCTTCTACACC TTTCGCTACCCACTGAGTCTCAGCCCAGATGACTG CAGGGGCGTTCAACACCTATATGGCCAGCCC	134
MYC	NM_002467.3	CACCGAGGAGAATGTCAAGAGGCGAACACACAA CGTCTTGGAGCGCCAGAGGAGGAACGAGCTAAA ACGGAGCTTTTTTGCCCTGCGTGACCAGATCCCG	135
NAT1	NM_000662.4	AGCACTTCCTCATAGACCTTGGATGTGGGAGGAT TGCATTCAGTCTAGTTCCTGGTTGCCGGCTGAAAT AACCTGAATTCAAGCCAGGAAGAAGCAGCAA	136
ORC6L	NM_014321.2	GACTGTGTAAACAACTAGAGAAGATTGGACAGCA GGTCGACAGAGAACCTGGAGATGTAGCTACTCCA	137

		CCACGGAAGAGAAAGAAGATAGTGGTTGAAGC	
PGR	NM_000926.2	GGGATGAAGCATCAGGCTGTCATTATGGTGTCCT TACCTGTGGGAGCTGTAAGGTCTTCTTTAAGAGG GCAATGGAAGGGCAGCACAACTACTTATGTGC	138
PHGDH	NM_006623.2	GCGACGGCTTCGATGAAGGACGGCAAATGGGAG CGGAAGAAGTTCATGGGAACAGAGCTGAATGGA AAGACCCTGGGAATTCTTGGCCTGGGCAGGATTG	139
PTTG1	NM_004219.2	CACCAGCCTTACCTAAAGCTACTAGAAAGGCTTT GGGAACTGTCAACAGAGCTACAGAAAAGTCTGTA AAGACCAAGGGACCCCTCAAACAAAAACAGCC	140
RRM2	NM_001034.1	TTCCTTTTGGACCGCCGAGGAGGTTGACCTCTCCA AGGACATTCAGCACTGGGAATCCCTGAAACCCGA GGAGAGATATTTTATATCCCATGTTCTGGCT	141
SFRP1	NM_003012.3	GTGGGTCACACACACGCACTGCGCCTGTCAGTAG TGGACATTGTAATCCAGTCGGCTTGTTCTTGCAGC ATTCCCGCTCCCTTCCCTCCATAGCCACGCT	142
SLC39A6	NM_012319.2	GATCGAACTGAAGGCTATTTACGAGCAGACTCAC AAGAGCCCTCCCACTTTGATTCTCAGCAGCCTGCA GTCTTGGAAGAAGAAGAGGTCATGATAGCTC	143
TMEM45B	NM_138788.3	CTGGCTGCCCTCAGCATTGTGGCCGTCAACTATTC TCTTGTTTACTGCCTTTTGACTCGGATGAAGAGAC ACGGAAGGGGAGAAATCATTGGAATTCAGA	144
TYMS	NM_001071.1	TGCTAAAGAGCTGTCTTCCAAGGGAGTGAAAATC TGGGATGCCAATGGATCCCGAGACTTTTTGGACA GCCTGGGATTCTCCACCAGAGAAGAAGGGGAC	145
UBE2C	NM_007019.2	GTCTGCCCTGTATGATGTCAGGACCATTCTGCTCT CCATCCAGAGCCTTCTAGGAGAACCCAACATTGA TAGTCCCTTGAACACACATGCTGCCGAGCTC	146

[49] Table 3 provides select sequences for the PAM50 genes of Table 1.

[50] **Table 3**

GENBANK ACCESSION NUMBER	SEQUENCE	SEQ ID NO:
NM_020445	CAGCGGCGCTGCGGCGGCTCGCGGGAGACGCTGCGCGCGGGGCTAGCG GGCGGCGGAGCGGACGGCGACGGGGCGCTCTCGGGCTGCCGGCGGGGC CGAGCGCCGCGCGTCCCGAGCATGGCAGGCTCCCTGCCTCCCTGCGTGG TGGACTGTGGCACCGGGTATACCAAGCTTGGCTACGCAGGCAACACTG AGCCCCAGTTCATTATTCCTTCATGTATTGCCATCAGAGAGTCAGCAAA GGTAGTTGACCAAGCTCAAAGGAGAGTGTTGAGGGGAGTTGATGACCT TGACTTTTTCATAGGAGATGAAGCCATCGATAAACCTACATATGCTACA AAGTGGCCGATACGACATGGAATCATTGAAGACTGGGATCTTATGGAA AGGTTCATGGAGCAAGTGGTTTTTAAATATCTTCGAGCTGAACCTGAGG ACCATTATTTTTTAATGACAGAACCTCCACTCAATACACCAGAAAACAG AGAGTATCTTGCAGAAATTATGTTTGAATCATTTAACGTACCAGGACTC TACATTGCAGTTCAGGCAGTGCTGGCCTTGGCGGCATCTTGGACATCTC GACAAGTGGGTGAACGTACGTTAACGGGGATAGTCATTGACAGCGGAG ATGGAGTCACCCATGTTATCCCAGTGGCAGAAGGTTATGTAATTGGAAG	147

	CTGCATCAAACACATCCCGATTGCAGGTAGAGATATTACGTATTTCATT CAACAGCTGCTAAGGGAGAGGGAGGTGGGAATCCCTCCTGAGCAGTCA CTGGAGACCGCAAAAGCCATTAAGGAGAAATACTGTTACATTTGCCCC GATATAGTCAAGGAATTTGCCAAGTATGATGTGGATCCCCGGAAGTGG ATCAAACAGTACACGGGTATCAATGCGATCAACCAGAAGAAGTTTGTT ATAGACGTTGGTTACGAAAGATTCCTGGGACCTGAAATATTCTTTCACC CGGAGTTTGCCAACCCAGACTTTATGGAGTCCATCTCAGATGTTGTTGA TGAAGTAATACAGAACTGCCCCATCGATGTGCGGCGCCCGCTGTATAAG AATGTCGTACTCTCAGGAGGCTCCACCATGTTCAGGGATTTCGGACGCC GACTGCAGAGGGATTTGAAGAGAGTGGTGGATGCTAGGCTGAGGCTCA GCGAGGAGCTCAGCGGCGGGAGGATCAAGCCGAAGCCTGTGGAGGTCC AGGTGGTCACGCATCACATGCAGCGCTACGCCGTGTGGTTCGGAGGCTC CATGCTGGCCTCGACTCCCGAGTTCTTTCAGGTCTGCCACACCAAGAAG GACTATGAAGAGTACGGGCCCAGCATCTGCCGCCACAACCCCGTCTTTG GAGTCATGTCCTAGTGTCTGCCTGAACGCGTCGTTCGATGGTGTCACGT TGGGGAACAAGTGTCCTTCAGAACCCAGAGAAGGCCGCCGTTCTGTAA ATAGCGACGTCGGTGTTGCTGCCCAGCAGCGTGCTTGCATTGCCGGTGC ATGAGGCGCGGCGCGGGCCCTTCAGTAAAAGCCATTTATCCGTGTGCCG ACCGCTGTCTGCCAGCCTCCTCCTTCTCCCGCCCTCCTCACCCTCGCTCT CCCTCCTCCTCCTCCTCCGAGCTGCTAGCTGACAAATACAATTCTGAAG GAATCCAAATGTGACTTTGAAAATTGTTAGAGAAAACAACATTAGAAA ATGGCGCAAAATCGTTAGGTCCCAGGAGAGAATGTGGGGGCGCAAACC CTTTTCCTCCCAGCCTATTTTTGTAAATAAAATGTTTAAACTTGAAATAC AAATCGATGTTTATATTTCCTATCATTTTGTATTTTATGGTATTTGGTAC AACTGGCTGATACTAAGCACGAATAGATATTGATGTTATGGAGTGCTGT AATCCAAAGTTTTTAATTGTGAGGCATGTTCTGATATGTTTATAGGCAA ACAAATAAAACAGCAAACTTTTTTGCCACATGTTTGCTAGAAAATGATT ATACTTTATTGGAGTGACATGAAGTTTGAACACTAAACAGTAATGTATG AGAATTACTACAGATACATGTATCTTTTAGTTTTTTTTGTTTGAACTTTC TGGAGCTGTTTTATAGAAGATGATGGTTTGTTGTCGGTGAGTGTTGGAT GAAATACTTCCTTGCACCATTGTAATAAAAGCTGTTAGAATATTTGTAA ATATC	
NM_001040135	CAGCGGCGCTGCGGCGGCTCGCGGGAGACGCTGCGCGCGGGGCTAGCG GGCGGCGGAGCGGACGGCGACGGGGCGCTCTCGGGCTGCCGGCGGGGC CGAGCGCCGCGCGTCCCGAGCATGGCAGGCTCCCTGCCTCCCTGCGTGG TGGACTGTGGCACCGGGTATACCAAGCTTGGCTACGCAGGCAACACTG AGCCCCAGTTCATTATTCCTTCATGTATTGCCATCAGAGAGTCAGCAAA GGTAGTTGACCAAGCTCAAAGGAGAGTGTTGAGGGGAGTTGATGACCT TGACTTTTTCATAGGAGATGAAGCCATCGATAAACCTACATATGCTACA AAGTGGCCGATACGACATGGAATCATTGAAGACTGGGATCTTATGGAA AGGTTCATGGAGCAAGTGGTTTTTAAATATCTTCGAGCTGAACCTGAGG ACCATTATTTTTTAATGACAGAACCTCCACTCAATACACCAGAAAACAG AGAGTATCTTGCAGAAATTATGTTTGAATCATTTAACGTACCAGGACTC TACATTGCAGTTCAGGCAGTGCTGGCCTTGGCGGCATCTTGGACATCTC GACAAGTGGGTGAACGTACGTTAACGGGGATAGTCATTGACAGCGGAG ATGGAGTCACCCATGTTATCCCAGTGGCAGAAGGTTATGTAATTGGAAG CTGCATCAAACACATCCCGATTGCAGGTAGAGATATTACGTATTTCATT CAACAGCTGCTAAGGGAGAGGGAGGTGGGAATCCCTCCTGAGCAGTCA CTGGAGACCGCAAAAGCCATTAAGGAGAAATACTGTTACATTTGCCCC GATATAGTCAAGGAATTTGCCAAGTATGATGTGGATCCCCGGAAGTGG ATCAAACAGTACACGGGTATCAATGCGATCAACCAGAAGAAGTTTGTT ATAGACGTTGGTTACGAAAGATTCCTGGGACCTGAAATATTCTTTCACC CGGAGTTTGCCAACCCAGACTTTATGGAGTCCATCTCAGATGTTGTTGA TGAAGTAATACAGAACTGCCCCATCGATGTGCGGCGCCCGCTGTATAAG CCCGAGTTCTTTCAGGTCTGCCACACCAAGAAGGACTATGAAGAGTACG GGCCCAGCATCTGCCGCCACAACCCCGTCTTTGGAGTCATGTCCTAGTG	148

	TCTGCCTGAACGCGTCGTTCGATGGTGTCACGTTGGGGAACAAGTGTCC TTCAGAACCCAGAGAAGGCCGCCGTTCTGTAAATAGCGACGTCGGTGTT GCTGCCCAGCAGCGTGCTTGCATTGCCGGTGCATGAGGCGCGGCGCGG GCCCTTCAGTAAAAGCCATTTATCCGTGTGCCGACCGCTGTCTGCCAGC CTCCTCCTTCTCCCGCCCTCCTCACCCTCGCTCTCCCTCCTCCTCCTCCTC CGAGCTGCTAGCTGACAAATACAATTCTGAAGGAATCCAAATGTGACTT TGAAAATTGTTAGAGAAAACAACATTAGAAAATGGCGCAAAATCGTTA GGTCCCAGGAGAGAATGTGGGGGCGCAAACCCTTTTCCTCCCAGCCTAT TTTTGTAAATAAAATGTTTAAACTTGAAATACAAATCGATGTTTATATTT CCTATCATTTTGTATTTTATGGTATTTGGTACAACTGGCTGATACTAAGC ACGAATAGATATTGATGTTATGGAGTGCTGTAATCCAAAGTTTTTAATT GTGAGGCATGTTCTGATATGTTTATAGGCAAACAAATAAAACAGCAAA CTTTTTTGCCACATGTTTGCTAGAAAATGATTATACTTTATTGGAGTGAC ATGAAGTTTGAACACTAAACAGTAATGTATGAGAATTACTACAGATAC ATGTATCTTTTAGTTTTTTTTGTTTGAACTTTCTGGAGCTGTTTTATAGAA GATGATGGTTTGTTGTCGGTGAGTGTTGGATGAAATACTTCCTTGCACC ATTGTAATAAAAGCTGTTAGAATATTTGTAAATATC	
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	GCCGAGGCGGGCGGATCACGAGAGAGGAACATAAAAAGCATTCGTCCG GTTGCGCTTTCCTTTCTGTCAAGAAGCAGTTTGAAGAATTAACCCTTGGT GAATTTTTGAAACTGGACAGAGAAAGAGCCAAGAACAAAATTGCAAAG GAAACCAACAATAAGAAGAAAGAATTTGAGGAAACTGCGGAGAAAGT GCGCCGTGCCATCGAGCAGCTGGCTGCCATGGATTGAGGCCTCTGGCCG GAGCTGCCTGGTCCCAGAGTGGCTGCACCACTTCCAGGGTTTATTCCCT GGTGCCACCAGCCTTCCTGTGGGCCCCTTAGCAATGTCTTAGGAAAGGA GATCAACATTTTCAAATTAGATGTTTCAACTGTGCTCTTGTTTTGTCTTG AAAGTGGCACCAGAGGTGCTTCTGCCTGTGCAGCGGGTGCTGCTGGTAA CAGTGGCTGCTTCTCTCTCTCTCTCTCTTTTTTGGGGGCTCATTTTTGCTG TTTTGATTCCCGGGCTTACCAGGTGAGAAGTGAGGGAGGAAGAAGGCA GTGTCCCTTTTGCTAGAGCTGACAGCTTTGTTCGCGTGGGCAGAGCCTT CCACAGTGAATGTGTCTGGACCTCATGTTGTTGAGGCTGTCACAGTCCT GAGTGTGGACTTGGCAGGTGCCTGTTGAATCTGAGCTGCAGGTTCCTTA TCTGTCACACCTGTGCCTCCTCAGAGGACAGTTTTTTTGTTGTTGTGTTT TTTTGTTTTTTTTTTTTTTGGTAGATGCATGACTTGTGTGTGATGAGAGAA TGGAGACAGAGTCCCTGGCTCCTCTACTGTTTAACAACATGGCTTTCTT ATTTTGTTTGAATTGTTAATTCACAGAATAGCACAAACTACAATTAAAA CTAAGCACAAAGCCATTCTAAGTCATTGGGGAAACGGGGTGAACTTCA GGTGGATGAGGAGACAGAATAGAGTGATAGGAAGCGTCTGGCAGATAC TCCTTTTGCCACTGCTGTGTGATTAGACAGGCCCAGTGAGCCGCGGGGC ACATGCTGGCCGCTCCTCCCTCAGAAAAAGGCAGTGGCCTAAATCCTTT TTAAATGACTTGGCTCGATGCTGTGGGGGACTGGCTGGGCTGCTGCAGG CCGTGTGTCTGTCAGCCCAACCTTCACATCTGTCACGTTCTCCACACGG GGGAGAGACGCAGTCCGCCCAGGTCCCCGCTTTCTTTGGAGGCAGCAG CTCCCGCAGGGCTGAAGTCTGGCGTAAGATGATGGATTTGATTCGCCCT CCTCCCTGTCATAGAGCTGCAGGGTGGATTGTTACAGCTTCGCTGGAAA CCTCTGGAGGTCATCTCGGCTGTTCCTGAGAAATAAAAAGCCTGTCATT TCAAACACTGCTGTGGACCCTACTGGGTTTTTAAAATATTGTCAGTTTTT CATCGTCGTCCCTAGCCTGCCAACAGCCATCTGCCCAGACAGCCGCAGT GAGGATGAGCGTCCTGGCAGAGACGCAGTTGTCTCTGGGCGCTTGCCA GAGCCACGAACCCCAGACCTGTTTGTATCATCCGGGCTCCTTCCGGGCA GAAACAACTGAAAATGCACTTCAGACCCACTTATTTCTGCCACATCTGA GTCGGCCTGAGATAGACTTTTCCCTCTAAACTGGGAGAATATCACAGTG GTTTTTGTTAGCAGAAAATGCACTCCAGCCTCTGTACTCATCTAAGCTG CTTATTTTTGATATTTGTGTCAGTCTGTAAATGGATACTTCACTTTAATA ACTGTTGCTTAGTAATTGGCTTTGTAGAGAAGCTGGAAAAAAATGGTTT TGTCTTCAACTCCTTTGCATGCCAGGCGGTGATGTGGATCTCGGCTTCTG TGAGCCTGTGCTGTGGGCAGGGCTGAGCTGGAGCCGCCCCTCTCAGCCC GCCTGCCACGGCCTTTCCTTAAAGGCCATCCTTAAAACCAGACCCTCAT GGCTACCAGCACCTGAAAGCTTCCTCGACATCTGTTAATAAAGCCGTAG GCCCTTGTCTAAGTGCAACCGCCTAGACTTTCTTTCAGATACATGTCCAC ATGTCCATTTTTCAGGTTCTCTAAGTTGGAGTGGAGTCTGGGAAGGGTT GTGAATGAGGCTTCTGGGCTATGGGTGAGGTTCCAATGGCAGGTTAGA GCCCCTCGGGCCAACTGCCATCCTGGAAAGTAGAGACAGCAGTGCCCG CTGCCCAGAAGAGACCAGCAAGCCAAACTGGAGCCCCCATTGCAGGCT GTCGCCATGTGGAAAGAGTAACTCACAATTGCCAATAAAGTCTCATGTG GTTTTATCTAAAAAAAAAAAAAAAAAAAAAAAAA	
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NM_001254	GAGCGCGGCTGGAGTTTGCTGCTGCCGCTGTGCAGTTTGTTCAGGGGCT TGTGGTGGTGAGTCCGAGAGGCTGCGTGTGAGAGACGTGAGAAGGATC CTGCACTGAGGAGGTGGAAAGAAGAGGATTGCTCGAGGAGGCCTGGGG TCTGTGAGGCAGCGGAGCTGGGTGAAGGCTGCGGGTTCCGGCGAGGCC TGAGCTGTGCTGTCGTCATGCCTCAAACCCGATCCCAGGCACAGGCTAC AATCAGTTTTCCAAAAAGGAAGCTGTCTCGGGCATTGAACAAAGCTAA AAACTCCAGTGATGCCAAACTAGAACCAACAAATGTCCAAACCGTAAC	157

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AB091343	GGCACGAGGGGCCGACGCGAGCGCCGCGCTTCGCTTCAGCTGCTAGCT GGCCCAAGGGAGGCGACCGCGGAGGGTGGCGAGGGGCGGCCAGGACC CGCAGCCCCGGGGCCGGGCCGGTCCGGACCGCCAGGGAGGGCAGGTCA GTGGGCAGATCGCGTCCGCGGGATTCAATCTCTGCCCGCTCTGATAACA GTCCTTTTCCCTGGCGCTCACTTCGTGCCTGGCACCCGGCTGGGCGCCTC AAGACCGTTGTCTCTTCGATCGCTTCTTTGGACTTGGCGACCATTTCAGA GATGTCTTCCAGAAGTACCAAAGATTTAATTAAAAGTAAGTGGGGATC GAAGCCTAGTAACTCCAAATCCGAAACTACATTAGAAAAATTAAAGGG	161

	AGAAATTGCACACTTAAAGACATCAGTGGATGAAATCACAAGTGGGAA AGGAAAGCTGACTGATAAAGAGAGACACAGACTTTTGGAGAAAATTCG AGTCCTTGAGGCTGAGAAGGAGAAGAATGCTTATCAACTCACAGAGAA GGACAAAGAAATACAGCGACTGAGAGACCAACTGAAGGCCAGATATA GTACTACCGCATTGCTTGAACAGCTGGAAGAGACAACGAGAGAAGGAG AAAGGAGGGAGCAGGTGTTGAAAGCCTTATCTGAAGAGAAAGACGTAT TGAAACAACAGTTGTCTGCTGCAACCTCACGAATTGCTGAACTTGAAAG CAAAACCAATACACTCCGTTTATCACAGACTGTGGCTCCAAACTGCTTC AACTCATCAATAAATAATATTCATGAAATGGAAATACAGCTGAAAGAT GCTCTGGAGAAAAATCAGCAGTGGCTCGTGTATGATCAGCAGCGGGAA GTCTATGTAAAAGGACTTTTAGCAAAGATCTTTGAGTTGGAAAAGAAA ACGGAAACAGCTGCTCATTCACTCCCACAGCAGACAAAAAAGCCTGAA TCAGAAGGTTATCTTCAAGAAGAGAAGCAGAAATGTTACAACGATCTC TTGGCAAGTGCAAAAAAAGATCTTGAGGTTGAACGACAAACCATAACT CAGCTGAGTTTTGAACTGAGTGAATTTCGAAGAAAATATGAAGAAACC CAAAAAGAAGTTCACAATTTAAATCAGCTGTTGTATTCACAAAGAAGG GCAGATGTGCAACATCTGGAAGATGATAGGCATAAAACAGAGAAGATA CAAAAACTCAGGGAAGAGAATGATATTGCTAGGGGAAAACTTGAAGAA GAGAAGAAGAGATCCGAAGAGCTCTTATCTCAGGTCCAGTTTCTTTACA CATCTCTGCTAAAGCAGCAAGAAGAACAAACAAGGGTAGCTCTGTTGG AACAACAGATGCAGGCATGTACTTTAGACTTTGAAAATGAAAAACTCG ACCGTCAACATGTGCAGCATCAATTGCATGTAATTCTTAAGGAGCTCCG AAAAGCAAGAAATCAAATAACACAGTTGGAATCCTTGAAACAGCTTCA TGAGTTTGCCATCACAGAGCCATTAGTCACTTTCCAAGGAGAGACTGAA AACAGAGAAAAAGTTGCCGCCTCACCAAAAAGTCCCACTGCTGCACTC AATGAAAGCCTGGTGGAATGTCCCAAGTGCAATATACAGTATCCAGCC ACTGAGCATCGCGATCTGCTTGTCCATGTGGAATACTGTTCAAAGTAGC AAAATAAGTATTTGTTTTGATATTAAAAGATTCAATACTGTATTTTCTGT TAGCTTGTGGGCATTTTGAATTATATATTTCACATTTTGCATAAAACTGC CTATCTACCTTTGACACTCCAGCATGCTAGTGAATCATGTATCTTTTAGG CTGCTGTGCATTTCTCTTGGCAGTGATACCTCCCTGACATGGTTCATCAT CAGGCTGCAATGACAGAATGTGGTGAGCAGCGTCTACTGAGACTACTA ACATTTTGCACTGTCAAAATACTTGGTGAGGAAAAGATAGCTCAGGTTA TTGCTAATGGGTTAATGCACCAGCAAGCAAAATATTTTATGTTTTGGGG GTTTGAAAAATCAAAGATAATTAACCAAGGATCTTAACTGTGTTCGCAT TTTTTATCCAAGCACTTAGAAAACCTACAATCCTAATTTTGATGTCCATT GTTAAGAGGTGGTGATAGATACTATTTTTTTTTTCATATTGTATAGCGGT TATTAGAAAAGTTGGGGATTTTCTTGATCTTTATTGCTGCTTACCATTGA AACTTAACCCAGCTGTGTTCCCCAACTCTGTTCTGCGCACGAAACAGTA TCTGTTTGAGGCATAATCTTAAGTGGCCACACACAATGTTTTCTCTTATG TTATCTGGCAGTAACTGTAACTTGAATTACATTAGCACATTCTGCTTAGC TAAAATTGTTAAAATAAACTTTAATAAACCCATGTAGCCCTCTCATTTG ATTGACAGTATTTTAGTTATTTTTGGCATTCTTAAAGCTGGGCAATGTAA TGATCAGATCTTTGTTTGTCTGAACAGGTATTTTTATACATGCTTTTTGT AAACCAAAAACTTTTAAATTTCTTCAGGTTTTCTAACATGCTTACCACTG GGCTACTGTAAATGAGAAAAGAATAAAATTATTTAATGTTTTAAAAAA AAAAAAAAA	
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	CGGCCTCGCGGCGACGGCGGCGGTGGCGGCTTGGACGACTCGGAGAGC CGAGTGAAGACATTTCCACCTGGACACCTGACCATGTGCCTGCCCTGAG CAGCGAGGCCCACCAGGCATCTCTGTTGTGGGCAGCAGGGCCAGGTCC TGGTCTGTGGACCCTCGGCAGTTGGCAGGCTCCCTCTGCAGTGGGGTCT GGGCCTCGGCCCCACCATGTCGAGCCTCGGCGGTGGCTCCCAGGATGCC GGCGGCAGTAGCAGCAGCAGCACCAATGGCAGCGGTGGCAGTGGCAGC AGTGGCCCAAAGGCAGGAGCAGCAGACAAGAGTGCAGTGGTGGCTGCC GCCGCACCAGCCTCAGTGGCAGATGACACACCACCCCCCGAGCGTCGG AACAAGAGCGGTATCATCAGTGAGCCCCTCAACAAGAGCCTGCGCCGC TCCCGCCCGCTCTCCCACTACTCTTCTTTTGGCAGCAGTGGTGGTAGTGG CGGTGGCAGCATGATGGGCGGAGAGTCTGCTGACAAGGCCACTGCGGC TGCAGCCGCTGCCTCCCTGTTGGCCAATGGGCATGACCTGGCGGCGGCC ATGGCGGTGGACAAAAGCAACCCTACCTCAAAGCACAAAAGTGGTGCT GTGGCCAGCCTGCTGAGCAAGGCAGAGCGGGCCACGGAGCTGGCAGCC GAGGGACAGCTGACGCTGCAGCAGTTTGCGCAGTCCACAGAGATGCTG AAGCGCGTGGTGCAGGAGCATCTCCCGCTGATGAGCGAGGCGGGTGCT GGCCTGCCTGACATGGAGGCTGTGGCAGGTGCCGAAGCCCTCAATGGC CAGTCCGACTTCCCCTACCTGGGCGCTTTCCCCATCAACCCAGGCCTCTT CATTATGACCCCGGCAGGTGTGTTCCTGGCCGAGAGCGCGCTGCACATG GCGGGCCTGGCTGAGTACCCCATGCAGGGAGAGCTGGCCTCTGCCATC AGCTCCGGCAAGAAGAAGCGGAAACGCTGCGGCATGTGCGCGCCCTGC CGGCGGCGCATCAACTGCGAGCAGTGCAGCAGTTGTAGGAATCGAAAG ACTGGCCATCAGATTTGCAAATTCAGAAAATGTGAGGAACTCAAAAAG AAGCCTTCCGCTGCTCTGGAGAAGGTGATGCTTCCGACGGGAGCCGCCT TCCGGTGGTTTCAGTGACGGCGGCGGAACCCAAAGCTGCCCTCTCCGTG CAATGTCACTGCTCGTGTGGTCTCCAGCAAGGGATTCGGGCGAAGACA AACGGATGCACCCGTCTTTAGAACCAAAAATATTCTCTCACAGATTTCA TTCCTGTTTTTATATATATATTTTTTGTTGTCGTTTTAACATCTCCACGTC CCTAGCATAAAAAGAAAAAGAAAAAAATTTAAACTGCTTTTTCGGAAG AACAACAACAAAAAAGAGGTAAAGACGAATCTATAAAGTACCGAGACT TCCTGGGCAAAGAATGGACAATCAGTTTCCTTCCTGTGTCGATGTCGAT GTTGTCTGTGCAGGAGATGCAGTTTTTGTGTAGAGAATGTAAATTTTCT GTAACCTTTTGAAATCTAGTTACTAATAAGCACTACTGTAATTTAGCAC AGTTTAACTCCACCCTCATTTAAACTTCCTTTGATTCTTTCCGACCATGA AATAGTGCATAGTTTGCCTGGAGAATCCACTCACGTTCATAAAGAGAAT GTTGATGGCGCCGTGTAGAAGCCGCTCTGTATCCATCCACGCGTGCAGA GCTGCCAGCAGGGAGCTCACAGAAGGGGAGGGAGCACCAGGCCAGCT GAGCTGCACCCACAGTCCCGAGACTGGGATCCCCCACCCCAACAGTGA TTTTGGAAAAAAAAATGAAAGTTCTGTTCGTTTATCCATTGCGATCTGG GGAGCCCCATCTCGATATTTCCAATCCTGGCTACTTTTCTTAGAGAAAA TAAGTCCTTTTTTTTCTGGCCTTGCTAATGGCAACAGAAGAAAGGGCTTC TTTGCGTGGTCCCCTGCTGGTGGGGGTGGGTCCCCAGGGGGCCCCCTGC GGCCTGGGCCCCCCTGCCCACGGCCAGCTTCCTGCTGATGAACATGCTG TTTGTATTGTTTTAGGAAACCAGGCTGTTTTGTGAATAAAACGAATGCA TGTTTGTGTCACGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAA	
NM_005228	CCCCGGCGCAGCGCGGCCGCAGCAGCCTCCGCCCCCCGCACGGTGTGA GCGCCCGACGCGGCCGAGGCGGCCGGAGTCCCGAGCTAGCCCCGGCGG CCGCCGCCGCCCAGACCGGACGACAGGCCACCTCGTCGGCGTCCGCCC GAGTCCCCGCCTCGCCGCCAACGCCACAACCACCGCGCACGGCCCCCTG ACTCCGTCCAGTATTGATCGGGAGAGCCGGAGCGAGCTCTTCGGGGAG CAGCGATGCGACCCTCCGGGACGGCCGGGGCAGCGCTCCTGGCGCTGC TGGCTGCGCTCTGCCCGGCGAGTCGGGCTCTGGAGGAAAAGAAAGTTT GCCAAGGCACGAGTAACAAGCTCACGCAGTTGGGCACTTTTGAAGATC ATTTTCTCAGCCTCCAGAGGATGTTCAATAACTGTGAGGTGGTCCTTGG GAATTTGGAAATTACCTATGTGCAGAGGAATTATGATCTTTCCTTCTTA	163

	AAGACCATCCAGGAGGTGGCTGGTTATGTCCTCATTGCCCTCAACACAG TGGAGCGAATTCCTTTGGAAAACCTGCAGATCATCAGAGGAAATATGT ACTACGAAAATTCCTATGCCTTAGCAGTCTTATCTAACTATGATGCAAA TAAAACCGGACTGAAGGAGCTGCCCATGAGAAATTTACAGGAAATCCT GCATGGCGCCGTGCGGTTCAGCAACAACCCTGCCCTGTGCAACGTGGA GAGCATCCAGTGGCGGGACATAGTCAGCAGTGACTTTCTCAGCAACAT GTCGATGGACTTCCAGAACCACCTGGGCAGCTGCCAAAAGTGTGATCC AAGCTGTCCCAATGGGAGCTGCTGGGGTGCAGGAGAGGAGAACTGCCA GAAACTGACCAAAATCATCTGTGCCCAGCAGTGCTCCGGGCGCTGCCGT GGCAAGTCCCCCAGTGACTGCTGCCACAACCAGTGTGCTGCAGGCTGCA CAGGCCCCCGGGAGAGCGACTGCCTGGTCTGCCGCAAATTCCGAGACG AAGCCACGTGCAAGGACACCTGCCCCCCACTCATGCTCTACAACCCCAC CACGTACCAGATGGATGTGAACCCCGAGGGCAAATACAGCTTTGGTGC CACCTGCGTGAAGAAGTGTCCCCGTAATTATGTGGTGACAGATCACGGC TCGTGCGTCCGAGCCTGTGGGGCCGACAGCTATGAGATGGAGGAAGAC GGCGTCCGCAAGTGTAAGAAGTGCGAAGGGCCTTGCCGCAAAGTGTGT AACGGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATAAATGCTA CGAATATTAAACACTTCAAAAACTGCACCTCCATCAGTGGCGATCTCCA CATCCTGCCGGTGGCATTTAGGGGTGACTCCTTCACACATACTCCTCCTC TGGATCCACAGGAACTGGATATTCTGAAAACCGTAAAGGAAATCACAG GGTTTTTGCTGATTCAGGCTTGGCCTGAAAACAGGACGGACCTCCATGC CTTTGAGAACCTAGAAATCATACGCGGCAGGACCAAGCAACATGGTCA GTTTTCTCTTGCAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCT CCCTCAAGGAGATAAGTGATGGAGATGTGATAATTTCAGGAAACAAAA ATTTGTGCTATGCAAATACAATAAACTGGAAAAAACTGTTTGGGACCTC CGGTCAGAAAACCAAAATTATAAGCAACAGAGGTGAAAACAGCTGCAA GGCCACAGGCCAGGTCTGCCATGCCTTGTGCTCCCCCGAGGGCTGCTGG GGCCCGGAGCCCAGGGACTGCGTCTCTTGCCGGAATGTCAGCCGAGGC AGGGAATGCGTGGACAAGTGCAACCTTCTGGAGGGTGAGCCAAGGGAG TTTGTGGAGAACTCTGAGTGCATACAGTGCCACCCAGAGTGCCTGCCTC AGGCCATGAACATCACCTGCACAGGACGGGGACCAGACAACTGTATCC AGTGTGCCCACTACATTGACGGCCCCCACTGCGTCAAGACCTGCCCGGC AGGAGTCATGGGAGAAAACAACACCCTGGTCTGGAAGTACGCAGACGC CGGCCATGTGTGCCACCTGTGCCATCCAAACTGCACCTACGGATGCACT GGGCCAGGTCTTGAAGGCTGTCCAACGAATGGGCCTAAGATCCCGTCC ATCGCCACTGGGATGGTGGGGGCCCTCCTCTTGCTGCTGGTGGTGGCCC TGGGGATCGGCCTCTTCATGCGAAGGCGCCACATCGTTCGGAAGCGCAC GCTGCGGAGGCTGCTGCAGGAGAGGGAGCTTGTGGAGCCTCTTACACC CAGTGGAGAAGCTCCCAACCAAGCTCTCTTGAGGATCTTGAAGGAAAC TGAATTCAAAAAGATCAAAGTGCTGGGCTCCGGTGCGTTCGGCACGGT GTATAAGGGACTCTGGATCCCAGAAGGTGAGAAAGTTAAAATTCCCGT CGCTATCAAGGAATTAAGAGAAGCAACATCTCCGAAAGCCAACAAGGA AATCCTCGATGAAGCCTACGTGATGGCCAGCGTGGACAACCCCCACGT GTGCCGCCTGCTGGGCATCTGCCTCACCTCCACCGTGCAGCTCATCACG CAGCTCATGCCCTTCGGCTGCCTCCTGGACTATGTCCGGGAACACAAAG ACAATATTGGCTCCCAGTACCTGCTCAACTGGTGTGTGCAGATCGCAAA GGGCATGAACTACTTGGAGGACCGTCGCTTGGTGCACCGCGACCTGGC AGCCAGGAACGTACTGGTGAAAACACCGCAGCATGTCAAGATCACAGA TTTTGGGCTGGCCAAACTGCTGGGTGCGGAAGAGAAAGAATACCATGC AGAAGGAGGCAAAGTGCCTATCAAGTGGATGGCATTGGAATCAATTTT ACACAGAATCTATACCCACCAGAGTGATGTCTGGAGCTACGGGGTGAC CGTTTGGGAGTTGATGACCTTTGGATCCAAGCCATATGACGGAATCCCT GCCAGCGAGATCTCCTCCATCCTGGAGAAAGGAGAACGCCTCCCTCAG CCACCCATATGTACCATCGATGTCTACATGATCATGGTCAAGTGCTGGA TGATAGACGCAGATAGTCGCCCAAAGTTCCGTGAGTTGATCATCGAATT CTCCAAAATGGCCCGAGACCCCCAGCGCTACCTTGTCATTCAGGGGGAT	

	GAAAGAATGCATTTGCCAAGTCCTACAGACTCCAACTTCTACCGTGCCC TGATGGATGAAGAAGACATGGACGACGTGGTGGATGCCGACGAGTACC TCATCCCACAGCAGGGCTTCTTCAGCAGCCCCTCCACGTCACGGACTCC CCTCCTGAGCTCTCTGAGTGCAACCAGCAACAATTCCACCGTGGCTTGC ATTGATAGAAATGGGCTGCAAAGCTGTCCCATCAAGGAAGACAGCTTC TTGCAGCGATACAGCTCAGACCCCACAGGCGCCTTGACTGAGGACAGC ATAGACGACACCTTCCTCCCAGTGCCTGAATACATAAACCAGTCCGTTC CCAAAAGGCCCGCTGGCTCTGTGCAGAATCCTGTCTATCACAATCAGCC TCTGAACCCCGCGCCCAGCAGAGACCCACACTACCAGGACCCCCACAG CACTGCAGTGGGCAACCCCGAGTATCTCAACACTGTCCAGCCCACCTGT GTCAACAGCACATTCGACAGCCCTGCCCACTGGGCCCAGAAAGGCAGC CACCAAATTAGCCTGGACAACCCTGACTACCAGCAGGACTTCTTTCCCA AGGAAGCCAAGCCAAATGGCATCTTTAAGGGCTCCACAGCTGAAAATG CAGAATACCTAAGGGTCGCGCCACAAAGCAGTGAATTTATTGGAGCAT GACCACGGAGGATAGTATGAGCCCTAAAAATCCAGACTCTTTCGATACC CAGGACCAAGCCACAGCAGGTCCTCCATCCCAACAGCCATGCCCGCATT AGCTCTTAGACCCACAGACTGGTTTTGCAACGTTTACACCGACTAGCCA GGAAGTACTTCCACCTCGGGCACATTTTGGGAAGTTGCATTCCTTTGTCT TCAAACTGTGAAGCATTTACAGAAACGCATCCAGCAAGAATATTGTCCC TTTGAGCAGAAATTTATCTTTCAAAGAGGTATATTTGAAAAAAAAAAAA AGTATATGTGAGGATTTTTATTGATTGGGGATCTTGGAGTTTTTCATTGT CGCTATTGATTTTTACTTCAATGGGCTCTTCCAACAAGGAAGAAGCTTG CTGGTAGCACTTGCTACCCTGAGTTCATCCAGGCCCAACTGTGAGCAAG GAGCACAAGCCACAAGTCTTCCAGAGGATGCTTGATTCCAGTGGTTCTG CTTCAAGGCTTCCACTGCAAAACACTAAAGATCCAAGAAGGCCTTCATG GCCCCAGCAGGCCGGATCGGTACTGTATCAAGTCATGGCAGGTACAGT AGGATAAGCCACTCTGTCCCTTCCTGGGCAAAGAAGAAACGGAGGGGA TGGAATTCTTCCTTAGACTTACTTTTGTAAAAATGTCCCCACGGTACTTA CTCCCCACTGATGGACCAGTGGTTTCCAGTCATGAGCGTTAGACTGACT TGTTTGTCTTCCATTCCATTGTTTTGAAACTCAGTATGCTGCCCCTGTCTT GCTGTCATGAAATCAGCAAGAGAGGATGACACATCAAATAATAACTCG GATTCCAGCCCACATTGGATTCATCAGCATTTGGACCAATAGCCCACAG CTGAGAATGTGGAATACCTAAGGATAGCACCGCTTTTGTTCTCGCAAAA ACGTATCTCCTAATTTGAGGCTCAGATGAAATGCATCAGGTCCTTTGGG GCATAGATCAGAAGACTACAAAAATGAAGCTGCTCTGAAATCTCCTTTA GCCATCACCCCAACCCCCCAAAATTAGTTTGTGTTACTTATGGAAGATA GTTTTCTCCTTTTACTTCACTTCAAAAGCTTTTTACTCAAAGAGTATATG TTCCCTCCAGGTCAGCTGCCCCCAAACCCCCTCCTTACGCTTTGTCACAC AAAAAGTGTCTCTGCCTTGAGTCATCTATTCAAGCACTTACAGCTCTGG CCACAACAGGGCATTTTACAGGTGCGAATGACAGTAGCATTATGAGTA GTGTGGAATTCAGGTAGTAAATATGAAACTAGGGTTTGAAATTGATAAT GCTTTCACAACATTTGCAGATGTTTTAGAAGGAAAAAAGTTCCTTCCTA AAATAATTTCTCTACAATTGGAAGATTGGAAGATTCAGCTAGTTAGGAG CCCACCTTTTTTCCTAATCTGTGTGTGCCCTGTAACCTGACTGGTTAACA GCAGTCCTTTGTAAACAGTGTTTTAAACTCTCCTAGTCAATATCCACCCC ATCCAATTTATCAAGGAAGAAATGGTTCAGAAAATATTTTCAGCCTACA GTTATGTTCAGTCACACACACATACAAAATGTTCCTTTTGCTTTTAAAGT AATTTTTGACTCCCAGATCAGTCAGAGCCCCTACAGCATTGTTAAGAAA GTATTTGATTTTTGTCTCAATGAAAATAAAACTATATTCATTTCCACTCT AAAAAAAAAAAAAAAAA	
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CACTTAATGAATGGTGGCAAAGCAAAGCTATATTCAAGACCACATGCA
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	CAGCATGCGTTGCGAAGTGCTTGTGCCCTGCATGTGCGGTGTGTTCTCT GTACACAGGAGGCTGCCTCAGATGGGGCTGCGGGGTCTGCTGACCTCTG CCCTCTGCCCACAGAGCCCTGCCTGGCTCCCAGCCTGGAGCAGCAAGAG CAGGAGCTGACAGTAGCCCTTGGGCAGCCTGTGCGGCTGTGCTGTGGGC GGGCTGAGCGTGGTGGCCACTGGTACAAGGAGGGCAGTCGCCTGGCAC CTGCTGGCCGTGTACGGGGCTGGAGGGGCCGCCTAGAGATTGCCAGCTT CCTACCTGAGGATGCTGGCCGCTACCTCTGCCTGGCACGAGGCTCCATG ATCGTCCTGCAGAATCTCACCTTGATTACAGGTGACTCCTTGACCTCCA GCAACGATGATGAGGACCCCAAGTCCCATAGGGACCTCTCGAATAGGC ACAGTTACCCCCAGCAAGGTCAGTAGGTCTCCAAGGACTTGTGTCCCCG CTGCTGCTCATCTGATCACTGAGAAGAGGAGGCCTGTGTGGGAACACA CGGTCATTCTAGGGGCCTTCCCCTGCCCTCCAGCACCCTACTGGACACA CCCCCAGCGCATGGAGAAGAAACTGCATGCAGTACCTGCGGGGAACAC CGTCAAGTTCCGCTGTCCAGCTGCAGGCAACCCCACGCCCACCATCCGC TGGCTTAAGGATGGACAGGCCTTTCATGGGGAGAACCGCATTGGAGGC ATTCGGCTGCGCCATCAGCACTGGAGTCTCGTGATGGAGAGCGTGGTGC CCTCGGACCGCGGCACATACACCTGCCTGGTAGAGAACGCTGTGGGCA GCATCCGTTATAACTACCTGCTAGATGTGCTGGAGCGGTCCCCGCACCG GCCCATCCTGCAGGCCGGGCTCCCGGCCAACACCACAGCCGTGGTGGG CAGCGACGTGGAGCTGCTGTGCAAGGTGTACAGCGATGCCCAGCCCCA CATCCAGTGGCTGAAGCACATCGTCATCAACGGCAGCAGCTTCGGAGC CGACGGTTTCCCCTATGTGCAAGTCCTAAAGACTGCAGACATCAATAGC TCAGAGGTGGAGGTCCTGTACCTGCGGAACGTGTCAGCCGAGGACGCA GGCGAGTACACCTGCCTCGCAGGCAATTCCATCGGCCTCTCCTACCAGT CTGCCTGGCTCACGGTGCTGCCAGGTGAGCACCTGAAGGGCCAGGAGA TGCTGCGAGATGCCCCTCTGGGCCAGCAGTGGGGGCTGTGGCCTGTTGG GTGGTCAGTCTCTGTTGGCCTGTGGGGTCTGGCCTGGGGGGCAGTGTGT GGATTTGTGGGTTTGAGCTGTATGACAGCCCCTCTGTGCCTCTCCACAC GTGGCCGTCCATGTGACCGTCTGCTGAGGTGTGGGTGCCTGGGACTGGG CATAACTACAGCTTCCTCCGTGTGTGTCCCCACATATGTTGGGAGCTGG GAGGGACTGAGTTAGGGTGCACGGGGCGGCCAGTCTCACCACTGACCA GTTTGTCTGTCTGTGTGTGTCCATGTGCGAGGGCAGAGGAGGACCCCAC ATGGACCGCAGCAGCGCCCGAGGCCAGGTATACGGACATCATCCTGTA CGCGTCGGGCTCCCTGGCCTTGGCTGTGCTCCTGCTGCTGGCCAGGCTG TATCGAGGGCAGGCGCTCCACGGCCGGCACCCCCGCCCGCCCGCCACT GTGCAGAAGCTCTCCCGCTTCCCTCTGGCCCGACAGTTCTCCCTGGAGT CAGGCTCTTCCGGCAAGTCAAGCTCATCCCTGGTACGAGGCGTGCGTCT CTCCTCCAGCGGCCCCGCCTTGCTCGCCGGCCTCGTGAGTCTAGATCTA CCTCTCGACCCACTATGGGAGTTCCCCCGGGACAGGCTGGTGCTTGGGA AGCCCCTAGGCGAGGGCTGCTTTGGCCAGGTAGTACGTGCAGAGGCCTT TGGCATGGACCCTGCCCGGCCTGACCAAGCCAGCACTGTGGCCGTCAA GATGCTCAAAGACAACGCCTCTGACAAGGACCTGGCCGACCTGGTCTC GGAGATGGAGGTGATGAAGCTGATCGGCCGACACAAGAACATCATCAA CCTGCTTGGTGTCTGCACCCAGGAAGGGCCCCTGTACGTGATCGTGGAG TGCGCCGCCAAGGGAAACCTGCGGGAGTTCCTGCGGGCCCGGCGCCCC CCAGGCCCCGACCTCAGCCCCGACGGTCCTCGGAGCAGTGAGGGGCCG CTCTCCTTCCCAGTCCTGGTCTCCTGCGCCTACCAGGTGGCCCGAGGCA TGCAGTATCTGGAGTCCCGGAAGTGTATCCACCGGGACCTGGCTGCCCG CAATGTGCTGGTGACTGAGGACAATGTGATGAAGATTGCTGACTTTGGG CTGGCCCGCGGCGTCCACCACATTGACTACTATAAGAAAACCAGCAAC GGCCGCCTGCCTGTGAAGTGGATGGCGCCCGAGGCCTTGTTTGACCGGG TGTACACACACCAGAGTGACGTGTGGTCTTTTGGGATCCTGCTATGGGA GATCTTCACCCTCGGGGGCTCCCCGTATCCTGGCATCCCGGTGGAGGAG CTGTTCTCGCTGCTGCGGGAGGGACATCGGATGGACCGACCCCCACACT GCCCCCCAGAGCTGTACGGGCTGATGCGTGAGTGCTGGCACGCAGCGC CCTCCCAGAGGCCTACCTTCAAGCAGCTGGTGGAGGCGCTGGACAAGG	

	TCCTGCTGGCCGTCTCTGAGGAGTACCTCGACCTCCGCCTGACCTTCGG ACCCTATTCCCCCTCTGGTGGGGACGCCAGCAGCACCTGCTCCTCCAGC GATTCTGTCTTCAGCCACGACCCCCTGCCATTGGGATCCAGCTCCTTCCC CTTCGGGTCTGGGGTGCAGACATGAGCAAGGCTCAAGGCTGTGCAGGC ACATAGGCTGGTGGCCTTGGGCCTTGGGGCTCAGCCACAGCCTGACACA GTGCTCGACCTTGATAGCATGGGGCCCCTGGCCCAGAGTTGCTGTGCCG TGTCCAAGGGCCGTGCCCTTGCCCTTGGAGCTGCCGTGCCTGTGTCCTG ATGGCCCAAATGTCAGGGTTCTGCTCGGCTTCTTGGACCTTGGCGCTTA GTCCCCATCCCGGGTTTGGCTGAGCCTGGCTGGAGAGCTGCTATGCTAA ACCTCCTGCCTCCCAATACCAGCAGGAGGTTCTGGGCCTCTGAACCCCC TTTCCCCACACCTCCCCCTGCTGCTGCTGCCCCAGCGTCTTGACGGGAG CATTGGCCCCTGAGCCCAGAGAAGCTGGAAGCCTGCCGAAAACAGGAG CAAATGGCGTTTTATAAATTATTTTTTTGAAAT	
NM_004496	TAAGATCCACATCAGCTCAACTGCACTTGCCTCGCAGAGGCAGCCCGCT CACTTCCCGCGGAGGCGCTCCCCGGCGCCGCGCTCCGCGGCAGCCGCCT GCCCCCGGCGCTGCCCCCGCCCGCCGCGCCGCCGCCGCCGCGCACG CCGCGCCCCGCAGCTCTGGGCTTCCTCTTCGCCCGGGTGGCGTTGGGCC CGCGCGGGCGCTCGGGTGACTGCAGCTGCTCAGCTCCCCTCCCCCGCCC CGCGCCGCGCGGCCGCCCGTCGCTTCGCACAGGGCTGGATGGTTGTATT GGGCAGGGTGGCTCCAGGATGTTAGGAACTGTGAAGATGGAAGGGCAT GAAACCAGCGACTGGAACAGCTACTACGCAGACACGCAGGAGGCCTAC TCCTCCGTCCCGGTCAGCAACATGAACTCAGGCCTGGGCTCCATGAACT CCATGAACACCTACATGACCATGAACACCATGACTACGAGCGGCAACA TGACCCCGGCGTCCTTCAACATGTCCTATGCCAACCCGGGCCTAGGGGC CGGCCTGAGTCCCGGCGCAGTAGCCGGCATGCCGGGGGGCTCGGCGGG CGCCATGAACAGCATGACTGCGGCCGGCGTGACGGCCATGGGTACGGC GCTGAGCCCGAGCGGCATGGGCGCCATGGGTGCGCAGCAGGCGGCCTC CATGAATGGCCTGGGCCCCTACGCGGCCGCCATGAACCCGTGCATGAG CCCCATGGCGTACGCGCCGTCCAACCTGGGCCGCAGCCGCGCGGGCGG CGGCGGCGACGCCAAGACGTTCAAGCGCAGCTACCCGCACGCCAAGCC GCCCTACTCGTACATCTCGCTCATCACCATGGCCATCCAGCAGGCGCCC AGCAAGATGCTCACGCTGAGCGAGATCTACCAGTGGATCATGGACCTCT TCCCCTATTACCGGCAGAACCAGCAGCGCTGGCAGAACTCCATCCGCCA CTCGCTGTCCTTCAATGACTGCTTCGTCAAGGTGGCACGCTCCCCGGAC AAGCCGGGCAAGGGCTCCTACTGGACGCTGCACCCGGACTCCGGCAAC ATGTTCGAGAACGGCTGCTACTTGCGCCGCCAGAAGCGCTTCAAGTGCG AGAAGCAGCCGGGGGCCGGCGGCGGGGGCGGGAGCGGAAGCGGGGGC AGCGGCGCCAAGGGCGGCCCTGAGAGCCGCAAGGACCCCTCTGGCGCC TCTAACCCCAGCGCCGACTCGCCCCTCCATCGGGGTGTGCACGGGAAGA CCGGCCAGCTAGAGGGCGCGCCGGCCCCCGGGCCCGCCGCCAGCCCCC AGACTCTGGACCACAGTGGGGCGACGGCGACAGGGGGCGCCTCGGAGT TGAAGACTCCAGCCTCCTCAACTGCGCCCCCCATAAGCTCCGGGCCCGG GGCGCTGGCCTCTGTGCCCGCCTCTCACCCGGCACACGGCTTGGCACCC CACGAGTCCCAGCTGCACCTGAAAGGGGACCCCCACTACTCCTTCAACC ACCCGTTCTCCATCAACAACCTCATGTCCTCCTCGGAGCAGCAGCATAA GCTGGACTTCAAGGCATACGAACAGGCACTGCAATACTCGCCTTACGGC TCTACGTTGCCCGCCAGCCTGCCTCTAGGCAGCGCCTCGGTGACCACCA GGAGCCCCATCGAGCCCTCAGCCCTGGAGCCGGCGTACTACCAAGGTG TGTATTCCAGACCCGTCCTAAACACTTCCTAGCTCCCGGGACTGGGGGG TTTGTCTGGCATAGCCATGCTGGTAGCAAGAGAGAAAAAATCAACAGC AAACAAAACCACACAAACCAAACCGTCAACAGCATAATAAAATCCCAA CAACTATTTTTATTTCATTTTTCATGCACAACCTTTCCCCCAGTGCAAAA GACTGTTACTTTATTATTGTATTCAAAATTCATTGTGTATATTACTACAA AGACAACCCCAAACCAATTTTTTTCCTGCGAAGTTTAATGATCCACAAG TGTATATATGAAATTCTCCTCCTTCCTTGCCCCCCTCTCTTTCTTCCCTCT TTCCCCTCCAGACATTCTAGTTTGTGGAGGGTTATTTAAAAAAACAAAA	168

	AAGGAAGATGGTCAAGTTTGTAAAATATTTGTTTGTGCTTTTTCCCCCTC CTTACCTGACCCCCTACGAGTTTACAGGTCTGTGGCAATACTCTTAACC ATAAGAATTGAAATGGTGAAGAAACAAGTATACACTAGAGGCTCTTAA AAGTATTGAAAGACAATACTGCTGTTATATAGCAAGACATAAACAGAT TATAAACATCAGAGCCATTTGCTTCTCAGTTTACATTTCTGATACATGCA GATAGCAGATGTCTTTAAATGAAATACATGTATATTGTGTATGGACTTA ATTATGCACATGCTCAGATGTGTAGACATCCTCCGTATATTTACATAAC ATATAGAGGTAATAGATAGGTGATATACATGATACATTCTCAAGAGTTG CTTGACCGAAAGTTACAAGGACCCCAACCCCTTTGTCCTCTCTACCCAC AGATGGCCCTGGGAATCAATTCCTCAGGAATTGCCCTCAAGAACTCTGC TTCTTGCTTTGCAGAGTGCCATGGTCATGTCATTCTGAGGTCACATAAC ACATAAAATTAGTTTCTATGAGTGTATACCATTTAAAGAATTTTTTTTTC AGTAAAAGGGAATATTACAATGTTGGAGGAGAGATAAGTTATAGGGAG CTGGATTTCAAAACGTGGTCCAAGATTCAAAAATCCTATTGATAGTGGC CATTTTAATCATTGCCATCGTGTGCTTGTTTCATCCAGTGTTATGCACTT TCCACAGTTGGACATGGTGTTAGTATAGCCAGACGGGTTTCATTATTAT TTCTCTTTGCTTTCTCAATGTTAATTTATTGCATGGTTTATTCTTTTTCTTT ACAGCTGAAATTGCTTTAAATGATGGTTAAAATTACAAATTAAATTGTT AATTTTTATCAATGTGATTGTAATTAAAAATATTTTGATTTAAATAACAA AAATAATACCAGATTTTAAGCCGTGGAAAATGTTCTTGATCATTTGCAG TTAAGGACTTTAAATAAATCAAATGTTAACAAAAAAAAAAAAAAAAA	
NM_001453	ATGCAGGCGCGCTACTCCGTGTCCAGCCCCAACTCCCTGGGAGTGGTGC CCTACCTCGGCGGCGAGCAGAGCTACTACCGCGCGGCGGCCGCGGCGG CCGGGGGCGGCTACACCGCCATGCCGGCCCCCATGAGCGTGTACTCGC ACCCTGCGCACGCCGAGCAGTACCCGGGCGGCATGGCCCGCGCCTACG GGCCCTACACGCCGCAGCCGCAGCCCAAGGACATGGTGAAGCCGCCCT ATAGCTACATCGCGCTCATCACCATGGCCATCCAGAACGCCCCGGACAA GAAGATCACCCTGAACGGCATCTACCAGTTCATCATGGACCGCTTCCCC TTCTACCGGGACAACAAGCAGGGCTGGCAGAACAGCATCCGCCACAAC CTCTCGCTCAACGAGTGCTTCGTCAAGGTGCCGCGCGACGACAAGAAG CCGGGCAAGGGCAGCTACTGGACGCTGGACCCGGACTCCTACAACATG TTCGAGAACGGCAGCTTCCTGCGGCGGCGGCGGCGCTTCAAGAAGAAG GACGCGGTGAAGGACAAGGAGGAGAAGGACAGGCTGCACCTCAAGGA GCCGCCCCCGCCCGGCCGCCAGCCCCCGCCCGCGCCGCCGGAGCAGGC CGACGGCAACGCGCCCGGTCCGCAGCCGCCGCCCGTGCGCATCCAGGA CATCAAGACCGAGAACGGTACGTGCCCCTCGCCGCCCCAGCCCCTGTCC CCGGCCGCCGCCCTGGGCAGCGGCAGCGCCGCCGCGGTGCCCAAGATC GAGAGCCCCGACAGCAGCAGCAGCAGCCTGTCCAGCGGGAGCAGCCCC CCGGGCAGCCTGCCGTCGGCGCGGCCGCTCAGCCTGGACGGTGCGGAT TCCGCGCCGCCGCCGCCCGCGCCCTCCGCCCCGCCGCCGCACCATAGCC AGGGCTTCAGCGTGGACAACATCATGACGTCGCTGCGGGGGTCGCCGC AGAGCGCGGCCGCGGAGCTCAGCTCCGGCCTTCTGGCCTCGGCGGCCG CGTCCTCGCGCGCGGGGATCGCACCCCCGCTGGCGCTCGGCGCCTACTC GCCCGGCCAGAGCTCCCTCTACAGCTCCCCCTGCAGCCAGACCTCCAGC GCGGGCAGCTCGGGCGGCGGCGGCGGCGGCGCGGGGGCCGCGGGGGG CGCGGGCGGCGCCGGGACCTACCACTGCAACCTGCAAGCCATGAGCCT GTACGCGGCCGGCGAGCGCGGGGGCCACTTGCAGGGCGCGCCCGGGGG CGCGGGCGGCTCGGCCGTGGACGACCCCCTGCCCGACTACTCTCTGCCT CCGGTCACCAGCAGCAGCTCGTCGTCCCTGAGTCACGGCGGCGGCGGC GGCGGCGGCGGGGGAGGCCAGGAGGCCGGCCACCACCCTGCGGCCCAC CAAGGCCGCCTCACCTCGTGGTACCTGAACCAGGCGGGCGGAGACCTG GGCCACTTGGCGAGCGCGGCGGCGGCGGCGGCGGCCGCAGGCTACCCG GGCCAGCAGCAGAACTTCCACTCGGTGCGGGAGATGTTCGAGTCACAG AGGATCGGCTTGAACAACTCTCCAGTGAACGGGAATAGTAGCTGTCAA ATGGCCTTCCCTTCCAGCCAGTCTCTGTACCGCACGTCCGGAGCTTTCGT CTACGACTGTAGCAAGTTTTGACACACCCTCAAAGCCGAACTAAATCGA	169

	ACCCCAAAGCAGGAAAAGCTAAAGGAACCCATCAAGGCAAAATCGAA ACTAAAAAAAAAAAAATCCAATTAAAAAAAACCCCTGAGAATATTCACC ACACCAGCGAACAGAATATCCCTCCAAAAATTCAGCTCACCAGCACCA GCACGAAGAAAACTCTATTTTCTTAACCGATTAATTCAGAGCCACCTCC ACTTTGCCTTGTCTAAATAAACAAACCCGTAAACTGTTTTATACAGAGA CAGCAAAATCTTGGTTTATTAAAGGACAGTGTTACTCCAGATAACACGT AAGTTTCTTCTTGCTTTTCAGAGACCTGCTTTCCCCTCCTCCCGTCTCCCC TCTCTTGCCTTCTTCCTTGCCTCTCACCTGTAAGATATTATTTTATCCTAT GTTGAAGGGAGGGGGAAAGTCCCCGTTTATGAAAGTCGCTTTCTTTTTA TTCATGGACTTGTTTTAAAATGTAAATTGCAACATAGTAATTTATTTTTA ATTTGTAGTTGGATGTCGTGGACCAAACGCCAGAAAGTGTTCCCAAAAC CTGACGTTAAATTGCCTGAAACTTTAAATTGTGCTTTTTTTCTCATTATA AAAAGGGAAACTGTATTAATCTTATTCTATCCTCTTTTCTTTCTTTTTGTT GAACATATTCATTGTTTGTTTATTAATAAATTACCATTCAGTTTGAATGA GACCTATATGTCTGGATACTTTAATAGAGCTTTAATTATTACGAAAAAA GATTTCAGAGATAAAACACTAGAAGTTACCTATTCTCCACCTAAATCTC TGAAAAATGGAGAAACCCTCTGACTAGTCCATGTCAAATTTTACTAAAA GTCTTTTTGTTTAGATTTATTTTCCTGCAGCATCTTCTGCAAAATGTACT ATATAGTCAGCTTGCTTTGAGGCTAGTAAAAAGATATTTTTCTAAACAG ATTGGAGTTGGCATATAAACAAATACGTTTTCTCACTAATGACAGTCCA TGATTCGGAAATTTTAAGCCCATGAATCAGCCGCGGTCTTACCACGGTG ATGCCTGTGTGCCGAGAGATGGGACTGTGCGGCCAGATATGCACAGAT AAATATTTGGCTTGTGTATTCCATATAAAATTGCAGTGCATATTATACAT CCCTGTGAGCCAGATGCTGAATAGATATTTTCCTATTATTTCAGTCCTTT ATAAAAGGAAAAATAAACCAGTTTTTAAATGTATGTATATAATTCTCCC CCATTTACAATCCTTCATGTATTACATAGAAGGATTGCTTTTTTAAAAAT ATACTGCGGGTTGGAAAGGGATATTTAATCTTTGAGAAACTATTTTAGA AAATATGTTTGTAGAACAATTATTTTTGAAAAAGATTTAAAGCAATAAC AAGAAGGAAGGCGAGAGGAGCAGAACATTTTGGTCTAGGGTGGTTTCT TTTTAAACCATTTTTTCTTGTTAATTTACAGTTAAACCTAGGGGACAATC CGGATTGGCCCTCCCCCTTTTGTAAATAACCCAGGAAATGTAATAAATT CATTATCTTAGGGTGATCTGCCCTGCCAATCAGACTTTGGGGAGATGGC GATTTGATTACAGACGTTCGGGGGGGTGGGGGGCTTGCAGTTTGTTTTG GAGATAATACAGTTTCCTGCTATCTGCCGCTCCTATCTAGAGGCAACAC TTAAGCAGTAATTGCTGTTGCTTGTTGTCAAAATTTGATCATTGTTAAAG GATTGCTGCAAATAAATACACTTTAATTTCAGTCAAAAA	
AJ249248	GTGGCCTCGAGGTGGTGGCAGGGCCGCCCCCTGCAGTCCGGAGACGAA CGCACGGACCGGGCCTCCGGAGGCAGGTTCGGCTGGAAGGAACCGCTC TCGCTTCGTCCTACACTTGCGCAAATGTCTCCGAGCTTACTCACATAGC ATATTGGTATATCAAAATGAAATGCAAGGAACCAAAAATAACATAATT GAAGGCAGTAAAAGTGAAATTAAATAGGAAGATCATCAGTCAAGGAAG ACCCACTGGAGAGGACAGAAAATGAAGCAGTGTTTTATCATGTGTATTT CAGCAGGTCTTCTTGAAATTTAACTAAAAATATGACTGCTCTCTCTTCA GAGAACTGCTCTTTTCAGTACCAGTTACGTCAAACAAACCAGCCCCTAG ACGTTAACTATCTGCTATTCTTGATCATACTTGGGAAAATATTATTAAAT ATCCTTACACTAGGAATGAGAAGAAAAAACACCTGTCAAAATTTTATG GAATATTTTTGCATTTCACTAGCATTCGTTGATCTTTTACTTTTGGTAAA CATTTCCATTATATTGTATTTCAGGGATTTTGTACTTTTAAGCATTAGGT TCACTAAATACCACATCTGCCTATTTACTCAAATTATTTCCTTTACTTAT GGCTTTTTGCATTATCCAGTTTTCCTGACAGCTTGTATAGATTATTGCCT GAATTTCTCTAAAACAACCAAGCTTTCATTTAAGTGTCAAAAATTATTTT ATTTCTTTACAGTAATTTTAATTTGGATTTCAGTCCTTGCTTATGTTTTGG GAGACCCAGCCATCTACCAAAGCCTGAAGGCACAGAATGCTTATTCTCG TCACTGTCCTTTCTATGTCAGCATTCAGAGTTACTGGCTGTCATTTTTCA TGGTGATGATTTTATTTGTAGCTTTCATAACCTGTTGGGAAGAAGTTACT ACTTTGGTACAGGCTATCAGGATAACTTCCTATATGAATGAAACTATCT	170

	TATATTTTCCTTTTTCATCCCACTCCAGTTATACTGTGAGATCTAAAAAA ATATTCTTATCCAAGCTCATTGTCTGTTTTCTCAGTACCTGGTTACCATT TGTACTACTTCAGGTAATCATTGTTTTACTTAAAGTTCAGATTCCAGCAT ATATTGAGATGAATATTCCCTGGTTATACTTTGTCAATAGTTTTCTCATT GCTACAGTGTATTGGTTTAATTGTCACAAGCTTAATTTAAAAGACATTG GATTACCTTTGGATCCATTTGTCAACTGGAAGTGCTGCTTCATTCCACTT ACAATTCCTAATCTTGAGCAAATTGAAAAGCCTATATCAATAATGATTT GTTAATATTATTAATTAAAAGTTACAGCTGTCATAAGATCATAATTTTAT GAACAGAAAGAACTCAGGACATATTAAAAAATAAACTGAACTAAAACA ACTTTTGCCCCCTGACTGATAGCATTTCAGAATGTGTCTTTTGAAGGGCT ATACCAGTTATTAAATAGTGTTTTATTTTAAAAACAAAATAATTCCAAG AAGTTTTTATAGTTATTCAGGGACACTATATTACAAATATTACTTTGTTA TTAACACAAAAAGTGATAAGAGTTAACATTTGGCTATACTGATGTTTGT GTTACTCAAAAAAACTACTGGATGCAAACTGTTATGTAAATCTGAGATT TCACTGACAACTTTAAGATATCAACCTAAACATTTTTATTAAATGTTCA AATGTAAGCAAGAAAAAAAAAA	
NM_005310	ACCCGCCCCCATCTGCCCAAGATAATTTTAGTTTCCTTGGGCCTGGAAT CTGGACACACAGGGCTCCCCCCCGCCTCTGACTTCTCTGTCCGAAGTCG GGACACCCTCCTACCACCTGTAGAGAAGCGGGAGTGGATCTGAAATAA AATCCAGGAATCTGGGGGTTCCTAGACGGAGCCAGACTTCGGAACGGG TGTCCTGCTACTCCTGCTGGGGCTCCTCCAGGACAAGGGCACACAACTG GTTCCGTTAAGCCCCTCTCTCGCTCAGACGCCATGGAGCTGGATCTGTC TCCACCTCATCTTAGCAGCTCTCCGGAAGACCTTTGCCCAGCCCCTGGG ACCCCTCCTGGGACTCCCCGGCCCCCTGATACCCCTCTGCCTGAGGAGG TAAAGAGGTCCCAGCCTCTCCTCATCCCAACCACCGGCAGGAAACTTCG AGAGGAGGAGAGGCGTGCCACCTCCCTCCCCTCTATCCCCAACCCCTTC CCTGAGCTCTGCAGTCCTCCCTCACAGAGCCCAATTCTCGGGGGCCCCT CCAGTGCAAGGGGGCTGCTCCCCCGCGATGCCAGCCGCCCCCATGTAGT AAAGGTGTACAGTGAGGATGGGGCCTGCAGGTCTGTGGAGGTGGCAGC AGGTGCCACAGCTCGCCACGTGTGTGAAATGCTGGTGCAGCGAGCTCA CGCCTTGAGCGACGAGACCTGGGGGCTGGTGGAGTGCCACCCCCACCT AGCACTGGAGCGGGGTTTGGAGGACCACGAGTCCGTGGTGGAAGTGCA GGCTGCCTGGCCCGTGGGCGGAGATAGCCGCTTCGTCTTCCGGAAAAAC TTCGCCAAGTACGAACTGTTCAAGAGCTCCCCACACTCCCTGTTCCCAG AAAAAATGGTCTCCAGCTGTCTCGATGCACACACTGGTATATCCCATGA AGACCTCATCCAGAACTTCCTGAATGCTGGCAGCTTTCCTGAGATCCAG GGCTTTCTGCAGCTGCGGGGTTCAGGACGGAAGCTTTGGAAACGCTTTT TCTGCTTCTTGCGCCGATCTGGCCTCTATTACTCCACCAAGGGCACCTCT AAGGATCCGAGGCACCTGCAGTACGTGGCAGATGTGAACGAGTCCAAC GTGTACGTGGTGACGCAGGGCCGCAAGCTCTACGGGATGCCCACTGAC TTCGGTTTCTGTGTCAAGCCCAACAAGCTTCGAAATGGCCACAAGGGGC TTCGGATCTTCTGCAGTGAAGATGAGCAGAGCCGCACCTGCTGGCTGGC TGCCTTCCGCCTCTTCAAGTACGGGGTGCAGCTGTACAAGAATTACCAG CAGGCACAGTCTCGCCATCTGCATCCATCTTGTTTGGGCTCCCCACCCTT GAGAAGTGCCTCAGATAATACCCTGGTGGCCATGGACTTCTCTGGCCAT GCTGGGCGTGTCATTGAGAACCCCCGGGAGGCTCTGAGTGTGGCCCTGG AGGAGGCCCAGGCCTGGAGGAAGAAGACAAACCACCGCCTCAGCCTGC CCATGCCAGCCTCCGGCACGAGCCTCAGTGCAGCCATCCACCGCACCCA ACTCTGGTTCCACGGGCGCATTTCCCGTGAGGAGAGCCAGCGGCTTATT GGACAGCAGGGCTTGGTAGACGGCCTGTTCCTGGTCCGGGAGAGTCAG CGGAACCCCCAGGGCTTTGTCCTCTCTTTGTGCCACCTGCAGAAAGTGA AGCATTATCTCATCCTGCCGAGCGAGGAGGAGGGCCGCCTGTACTTCAG CATGGATGATGGCCAGACCCGCTTCACTGACCTGCTGCAGCTCGTGGAG TTCCACCAGCTGAACCGCGGCATCCTGCCGTGCTTGCTGCGCCATTGCT GCACGCGGGTGGCCCTCTGACCAGGCCGTGGACTGGCTCATGCCTCAGC CCGCCTTCAGGCTGCCCGCCGCCCCTCCACCCATCCAGTGGACTCTGGG	171

	GCGCGGCCACAGGGGACGGGATGAGGAGCGGGAGGGTTCCGCCACTCC AGTTTTCTCCTCTGCTTCTTTGCCTCCCTCAGATAGAAAACAGCCCCCAC TCCAGTCCACTCCTGACCCCTCTCCTCAAGGGAAGGCCTTGGGTGGCCC CCTCTCCTTCTCCTAGCTCTGGAGGTGCTGCTCTAGGGCAGGGAATTAT GGGAGAAGTGGGGGCAGCCCAGGCGGTTTCACGCCCCACACTTTGTAC AGACCGAGAGGCCAGTTGATCTGCTCTGTTTTATACTAGTGACAATAAA GATTATTTTTTGATACAAAAAAAAAAAAAAAAAAAAAAA	
NM_014176	AGTCAGAGGTCGCGCAGGCGCTGGTACCCCGTTGGTCCGCGCGTTGCTG CGTTGTGAGGGGTGTCAGCTCAGTGCATCCCAGGCAGCTCTTAGTGTGG AGCAGTGAACTGTGTGTGGTTCCTTCTACTTGGGGATCATGCAGAGAGC TTCACGTCTGAAGAGAGAGCTGCACATGTTAGCCACAGAGCCACCCCC AGGCATCACATGTTGGCAAGATAAAGACCAAATGGATGACCTGCGAGC TCAAATATTAGGTGGAGCCAACACACCTTATGAGAAAGGTGTTTTTAAG CTAGAAGTTATCATTCCTGAGAGGTACCCATTTGAACCTCCTCAGATCC GATTTCTCACTCCAATTTATCATCCAAACATTGATTCTGCTGGAAGGATT TGTCTGGATGTTCTCAAATTGCCACCAAAAGGTGCTTGGAGACCATCCC TCAACATCGCAACTGTGTTGACCTCTATTCAGCTGCTCATGTCAGAACC CAACCCTGATGACCCGCTCATGGCTGACATATCCTCAGAATTTAAATAT AATAAGCCAGCCTTCCTCAAGAATGCCAGACAGTGGACAGAGAAGCAT GCAAGACAGAAACAAAAGGCTGATGAGGAAGAGATGCTTGATAATCTA CCAGAGGCTGGTGACTCCAGAGTACACAACTCAACACAGAAAAGGAAG GCCAGTCAGCTAGTAGGCATAGAAAAGAAATTTCATCCTGATGTTTAGG GGACTTGTCCTGGTTCATCTTAGTTAATGTGTTCTTTGCCAAGGTGATCT AAGTTGCCTACCTTGAATTTTTTTTTAAATATATTTGATGACATAATTTT TGTGTAGTTTATTTATCTTGTACATATGTATTTTGAAATCTTTTAAACCT GAAAAATAAATAGTCATTTAATGTTGAAAAAAAAAAAAAAAAAAAAA AAAAAAA	172
NM_006845	ACGCTTGCGCGCGGGATTTAAACTGCGGCGGTTTACGCGGCGTTAAGAC TTCGTAGGGTTAGCGAAATTGAGGTTTCTTGGTATTGCGCGTTTCTCTTC CTTGCTGACTCTCCGAATGGCCATGGACTCGTCGCTTCAGGCCCGCCTG TTTCCCGGTCTCGCTATCAAGATCCAACGCAGTAATGGTTTAATTCACA GTGCCAATGTAAGGACTGTGAACTTGGAGAAATCCTGTGTTTCAGTGGA ATGGGCAGAAGGAGGTGCCACAAAGGGCAAAGAGATTGATTTTGATGA TGTGGCTGCAATAAACCCAGAACTCTTACAGCTTCTTCCCTTACATCCG AAGGACAATCTGCCCTTGCAGGAAAATGTAACAATCCAGAAACAAAAA CGGAGATCCGTCAACTCCAAAATTCCTGCTCCAAAAGAAAGTCTTCGAA GCCGCTCCACTCGCATGTCCACTGTCTCAGAGCTTCGCATCACGGCTCA GGAGAATGACATGGAGGTGGAGCTGCCTGCAGCTGCAAACTCCCGCAA GCAGTTTTCAGTTCCTCCTGCCCCCACTAGGCCTTCCTGCCCTGCAGTGG CTGAAATACCATTGAGGATGGTCAGCGAGGAGATGGAAGAGCAAGTCC ATTCCATCCGAGGCAGCTCTTCTGCAAACCCTGTGAACTCAGTTCGGAG GAAATCATGTCTTGTGAAGGAAGTGGAAAAAATGAAGAACAAGCGAGA AGAGAAGAAGGCCCAGAACTCTGAAATGAGAATGAAGAGAGCTCAGG AGTATGACAGTAGTTTTCCAAACTGGGAATTTGCCCGAATGATTAAAGA ATTTCGGGCTACTTTGGAATGTCATCCACTTACTATGACTGATCCTATCG AAGAGCACAGAATATGTGTCTGTGTTAGGAAACGCCCACTGAATAAGC AAGAATTGGCCAAGAAAGAAATTGATGTGATTTCCATTCCTAGCAAGTG TCTCCTCTTGGTACATGAACCCAAGTTGAAAGTGGACTTAACAAAGTAT CTGGAGAACCAAGCATTCTGCTTTGACTTTGCATTTGATGAAACAGCTT CGAATGAAGTTGTCTACAGGTTCACAGCAAGGCCACTGGTACAGACAA TCTTTGAAGGTGGAAAAGCAACTTGTTTTGCATATGGCCAGACAGGAAG TGGCAAGACACATACTATGGGCGGAGACCTCTCTGGGAAAGCCCAGAA TGCATCCAAAGGGATCTATGCCATGGCCTCCCGGGACGTCTTCCTCCTG AAGAATCAACCCTGCTACCGGAAGTTGGGCCTGGAAGTCTATGTGACAT TCTTCGAGATCTACAATGGGAAGCTGTTTGACCTGCTCAACAAGAAGGC CAAGCTGCGCGTGCTGGAGGACGGCAAGCAACAGGTGCAAGTGGTGGG	173

	GCTGCAGGAGCATCTGGTTAACTCTGCTGATGATGTCATCAAGATGATC GACATGGGCAGCGCCTGCAGAACCTCTGGGCAGACATTTGCCAACTCC AATTCCTCCCGCTCCCACGCGTGCTTCCAAATTATTCTTCGAGCTAAAG GGAGAATGCATGGCAAGTTCTCTTTGGTAGATCTGGCAGGGAATGAGC GAGGCGCGGACACTTCCAGTGCTGACCGGCAGACCCGCATGGAGGGCG CAGAAATCAACAAGAGTCTCTTAGCCCTGAAGGAGTGCATCAGGGCCC TGGGACAGAACAAGGCTCACACCCCGTTCCGTGAGAGCAAGCTGACAC AGGTGCTGAGGGACTCCTTCATTGGGGAGAACTCTAGGACTTGCATGAT TGCCACGATCTCACCAGGCATAAGCTCCTGTGAATATACTTTAAACACC CTGAGATATGCAGACAGGGTCAAGGAGCTGAGCCCCCACAGTGGGCCC AGTGGAGAGCAGTTGATTCAAATGGAAACAGAAGAGATGGAAGCCTGC TCTAACGGGGCGCTGATTCCAGGCAATTTATCCAAGGAAGAGGAGGAA CTGTCTTCCCAGATGTCCAGCTTTAACGAAGCCATGACTCAGATCAGGG AGCTGGAGGAGAAGGCTATGGAAGAGCTCAAGGAGATCATACAGCAA GGACCAGACTGGCTTGAGCTCTCTGAGATGACCGAGCAGCCAGACTAT GACCTGGAGACCTTTGTGAACAAAGCGGAATCTGCTCTGGCCCAGCAA GCCAAGCATTTCTCAGCCCTGCGAGATGTCATCAAGGCCTTGCGCCTGG CCATGCAGCTGGAAGAGCAGGCTAGCAGACAAATAAGCAGCAAGAAA CGGCCCCAGTGACGACTGCAAATAAAAATCTGTTTGGTTTGACACCCAG CCTCTTCCCTGGCCCTCCCCAGAGAACTTTGGGTACCTGGTGGGTCTAG GCAGGGTCTGAGCTGGGACAGGTTCTGGTAAATGCCAAGTATGGGGGC ATCTGGGCCCAGGGCAGCTGGGGAGGGGGTCAGAGTGACATGGGACAC TCCTTTTCTGTTCCTCAGTTGTCGCCCTCACGAGAGGAAGGAGCTCTTAG TTACCCTTTTGTGTTGCCCTTCTTTCCATCAAGGGGAATGTTCTCAGCAT AGAGCTTTCTCCGCAGCATCCTGCCTGCGTGGACTGGCTGCTAATGGAG AGCTCCCTGGGGTTGTCCTGGCTCTGGGGAGAGAGACGGAGCCTTTAGT ACAGCTATCTGCTGGCTCTAAACCTTCTACGCCTTTGGGCCGAGCACTG AATGTCTTGTACTTTAAAAAAATGTTTCTGAGACCTCTTTCTACTTTACT GTCTCCCTAGAGATCCTAGAGGATCCCTACTGTTTTCTGTTTTATGTGTT TATACATTGTATGTAACAATAAAGAGAAAAAATAAATCAGCTGTTTAA GTGTGTGGAAAAAAAAAAAAAAAAA	
NM_006101	ACTGCGCGCGTCGTGCGTAATGACGTCAGCGCCGGCGGAGAATTTCAA ATTCGAACGGCTTTGGCGGGCCGAGGAAGGACCTGGTGTTTTGATGACC GCTGTCCTGTCTAGCAGATACTTGCACGGTTTACAGAAATTCGGTCCCT GGGTCGTGTCAGGAAACTGGAAAAAAGGTCATAAGCATGAAGCGCAGT TCAGTTTCCAGCGGTGGTGCTGGCCGCCTCTCCATGCAGGAGTTAAGAT CCCAGGATGTAAATAAACAAGGCCTCTATACCCCTCAAACCAAAGAGA AACCAACCTTTGGAAAGTTGAGTATAAACAAACCGACATCTGAAAGAA AAGTCTCGCTATTTGGCAAAAGAACTAGTGGACATGGATCCCGGAATA GTCAACTTGGTATATTTTCCAGTTCTGAGAAAATCAAGGACCCGAGACC ACTTAATGACAAAGCATTCATTCAGCAGTGTATTCGACAACTCTGTGAG TTTCTTACAGAAAATGGTTATGCACATAATGTGTCCATGAAATCTCTAC AAGCTCCCTCTGTTAAAGACTTCCTGAAGATCTTCACATTTCTTTATGGC TTCCTGTGCCCCTCATACGAACTTCCTGACACAAAGTTTGAAGAAGAGG TTCCAAGAATCTTTAAAGACCTTGGGTATCCTTTTGCACTATCCAAAAG CTCCATGTACACAGTGGGGGCTCCTCATACATGGCCTCACATTGTGGCA GCCTTAGTTTGGCTAATAGACTGCATCAAGATACATACTGCCATGAAAG AAAGCTCACCTTTATTTGATGATGGGCAGCCTTGGGGAGAAGAAACTG AAGATGGAATTATGCATAATAAGTTGTTTTTGGACTACACCATAAAATG CTATGAGAGTTTTATGAGTGGTGCCGACAGCTTTGATGAGATGAATGCA GAGCTGCAGTCAAAACTGAAGGATTTATTTAATGTGGATGCTTTTAAGC TGGAATCATTAGAAGCAAAAAACAGAGCATTGAATGAACAGATTGCAA GATTGGAACAAGAAAGAGAAAAAGAACCGAATCGTCTAGAGTCGTTGA GAAAACTGAAGGCTTCCTTACAAGGAGATGTTCAAAAGTATCAGGCAT ACATGAGCAATTTGGAGTCTCATTCAGCCATTCTTGACCAGAAATTAAA TGGTCTCAATGAGGAAATTGCTAGAGTAGAACTAGAATGTGAAACAAT	174

	AAAACAGGAGAACACTCGACTACAGAATATCATTGACAACCAGAAGTA CTCAGTTGCAGACATTGAGCGAATAAATCATGAAAGAAATGAATTGCA GCAGACTATTAATAAATTAACCAAGGACCTGGAAGCTGAACAACAGAA GTTGTGGAATGAGGAGTTAAAATATGCCAGAGGCAAAGAAGCGATTGA AACACAATTAGCAGAGTATCACAAATTGGCTAGAAAATTAAAACTTATT CCTAAAGGTGCTGAGAATTCCAAAGGTTATGACTTTGAAATTAAGTTTA ATCCCGAGGCTGGTGCCAACTGCCTTGTCAAATACAGGGCTCAAGTTTA TGTACCTCTTAAGGAACTCCTGAATGAAACTGAAGAAGAAATTAATAA AGCCCTAAATAAAAAAATGGGTTTGGAGGATACTTTAGAACAATTGAA TGCAATGATAACAGAAAGCAAGAGAAGTGTGAGAACTCTGAAAGAAG AAGTTCAAAAGCTGGATGATCTTTACCAACAAAAAATTAAGGAAGCAG AGGAAGAGGATGAAAAATGTGCCAGTGAGCTTGAGTCCTTGGAGAAAC ACAAGCACCTGCTAGAAAGTACTGTTAACCAGGGGCTCAGTGAAGCTA TGAATGAATTAGATGCTGTTCAGCGGGAATACCAACTAGTTGTGCAAAC CACGACTGAAGAAAGACGAAAAGTGGGAAATAACTTGCAACGTCTGTT AGAGATGGTTGCTACACATGTTGGGTCTGTAGAGAAACATCTTGAGGA GCAGATTGCTAAAGTTGATAGAGAATATGAAGAATGCATGTCAGAAGA TCTCTCGGAAAATATTAAAGAGATTAGAGATAAGTATGAGAAGAAAGC TACTCTAATTAAGTCTTCTGAAGAATGAAGATAAAATGTTGATCATGTA TATATATCCATAGTGAATAAAATTGTCTCAGTAAAGTGTAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAA	
BC042437	CTCCCTCCTCTGCACCATGACTACCTGCAGCCGCCAGTTCACCTCCTCCA GCTCCATGAAGGGCTCCTGCGGCATCGGGGGCGGCATCGGGGGCGGCT CCAGCCGCATCTCCTCCGTCCTGGCCGGAGGGTCCTGCCGCGCCCCCAG CACCTACGGGGGCGGCCTGTCTGTCTCATCCTCCCGCTTCTCCTCTGGGG GAGCCTATGGGTTGGGGGGCGGCTATGGCGGTGGCTTCAGCAGCAGCA GCAGCAGCTTTGGTAGTGGCTTTGGGGGAGGATATGGTGGTGGCCTTGG TGCTGGCTTGGGTGGTGGCTTTGGTGGTGGCTTTGCTGGTGGTGATGGG CTTCTGGTGGGCAGTGAGAAGGTGACCATGCAGAACCTCAACGACCGC CTGGCCTCCTACCTGGACAAGGTGCGTGCTCTGGAGGAGGCCAACGCC GACCTGGAAGTGAAGATCCGTGACTGGTACCAGAGGCAGCGGCCTGCT GAGATCAAAGACTACAGTCCCTACTTCAAGACCATTGAGGACCTGAGG AACAAGATTCTCACAGCCACAGTGGACAATGCCAATGTCCTTCTGCAGA TTGACAATGCCCGTCTGGCCGCGGATGACTTCCGCACCAAGTATGAGAC AGAGTTGAACCTGCGCATGAGTGTGGAAGCCGACATCAATGGCCTGCG CAGGGTGCTGGACGAACTGACCCTGGCCAGAGCTGACCTGGAGATGCA GATTGAGAGCCTGAAGGAGGAGCTGGCCTACCTGAAGAAGAACCACGA GGAGGAGATGAATGCCCTGAGAGGCCAGGTGGGTGGAGATGTCAATGT GGAGATGGACGCTGCACCTGGCGTGGACCTGAGCCGCATTCTGAACGA GATGCGTGACCAGTATGAGAAGATGGCAGAGAAGAACCGCAAGGATGC CGAGGAATGGTTCTTCACCAAGACAGAGGAGCTGAACCGCGAGGTGGC CACCAACAGCGAGCTGGTGCAGAGCGGCAAGAGCGAGATCTCGGAGCT CCGGCGCACCATGCAGAACCTGGAGATTGAGCTGCAGTCCCAGCTCAG CATGAAAGCATCCCTGGAGAACAGCCTGGAGGAGACCAAAGGTCGCTA CTGCATGCAGCTGGCCCAGATCCAGGAGATGATTGGCAGCGTGGAGGA GCAGCTGGCCCAGCTCCGCTGCGAGATGGAGCAGCAGAACCAGGAGTA CAAGATCCTGCTGGACGTGAAGACGCGGCTGGAGCAGGAGATCGCCAC CTACCGCCGCCTGCTGGAGGGCGAGGACGCCCACCTCTCCTCCTCCCAG TTCTCCTCTGGATCGCAGTCATCCAGAGATGTGACCTCCTCCAGCCGCC AAATCCGCACCAAGGTCATGGATGTGCACGATGGCAAGGTGGTGTCCA CCCACGAGCAGGTCCTTCGCACCAAGAACTGAGGCTGCCCAGCCCCGCT CAGGCCTAGGAGGCCCCCCGTGTGGACACAGATCCCACTGGAAGATCC CCTCTCCTGCCCAAGCACTTCACAGCTGGACCCTGCTTCACCCTCACCCC CTCCTGGCAATCAATACAGCTTCATTATCTGAGTTGCATAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	175

	AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	
AK095281	CTCTTTTGCAGGGGCCGTTCCTCGGGGCATGACGCTGGCTCCTGCACAG ATCCTGCTCCTCTGTGGCCTTCCTGGGCTGCCCTCCCCTCCTCCGGGACT GCTCTGGACTGACACTGCTCAGGTTCGGATTCCCTCAAAGACTTTGGGA GACAAGACTTGGTCCCCCTTTTACAAACAAGGGAACGGAGGCTCTAGA ACTGACTTCCTGAAAGGCTTGGATCCAAAGCTCCCTCAGTTCAGCGGCC ACGTCTATTTCCCTCAGACACAGGGATCCTTGAACCTGTGGGCTGTATC TCCCCGCGGACTTGGAAGAATCCCAAGAGAGTGGGGCTCCCACAGGCT GGAGTGCAATGGTGTGATCTCGGCTCACTGCAACCTCCACCTCCCAGGT TCAAGCTATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGATC CTGGTGGCTGTGGTCGGTAATTCCAGCTTCGTGCTGGCTACAGGTGGAT GATGCCCACCTGGCTGCCGATGACCTCTGCACCAAGTGAGGCTGGGTCT CTGGAGCTGCCCCAGGGGCTGGACAAGCTGACCCTGGCCGGGGCCAAC CTGGAGATGCAGATTGAGAACCTCAAGGAGGACCTGGTCTACCTGAAG AAGAACCACAAGCAGGAAATGAACGTCCTTTGAGGTCAGGTGGATGAG GATGTCAGTGTGAAGATGGACACTGTGCCTGGAGTGAACCTGAGCTGC ATCCTGAATGAGATGCGTGACCAGGACAAGACATTGGTGGAGAAGAGC TGCAAGGATGCCGAGGGCTGGTTCTTCAGCATGGTGGGTGGCCGTGCGT AAGCAGGTGTGTACACGTGTGGGCACATGTGCTGCATGCTGGTGCAGCT GGAGCACTGGCAGATCCACAGGCTGTCCCAGTTGGAAGGACTTTTGGA AACCAGTTGGACCAGCCCCTCATGTTTTAGATGTAAAACGTGAGGCTCA GAGAGGACTCAAGCTCACACAGCCCTTCACTGTGGCCTGCAAAATAGA TCCAGGTCTCTACAAGTCTGGTCTTGGGTTTCCACCACAGCTGTTTACAG GATGTGCGTATTTGAATACATATGTATACCCTTGGCAAGCACAGGCTGA GTATCTCCGGTATCCTAGGGACAGCAACAGGCGCAAAAGAATAACACC CAGTGCCTGTCTTTGAGGTGCTGCAGTTCAGTAGGAAAAAGAAATGCA AATGACCGCAGAGCAGGCTGAATTCCTCCAAGTTCCAATGTGGGTGCA GAGGCTCTCTGTGTGCAGAAAGAGGGGCTGAACTGCGAGGTGGCCACC AACACAGAGGCCCTGCAGAGTGGCTGGATAGAGATATGGAGCTCTACG TCTCTGTGCAGAACCTGAGCCGTCCCAGCTCAGCAAGAAAGCATCGCTG GAGGGCAGCCTGGTGGAGATGGAGGTGTGTTACAGGACCCTGCCGGCC CAGCTGCAGGGGCTTAACAGAAGCATGGAGCAGCAGCTGTGCGAGCTC TGCTGCGACACGGAGCACCAGGACCACAAGCACAGGTCCTTCTGGACG TGAAGACGTGGCTGGAGCAGGAGATCGCCACCTACCGCCGCTTGCTGG AGGTTGAGGACGCCCAGAGGTGATACTGACGATGCAGGCTGGAGTCTG GCTGAGGAGCCTTGAATGCCAAGTTAAAGCGTCTGGACTAGATCACGT AGGCAATGGGGAGCCATGGAGGGATTTGGAGCAGGAGAGTGAAATGA ACATCAAGAGATTTTAGAACATTCACTCTGGCTGCAGAGGGAGAAATG GATCAGAGGGGTCAGGGCGGGGCCAGAGAGATGTGTCAGGGGGCTGG AGCAGGGAGTCTGGCCAGAGAAGTCCCGTGCGGTGGTGGGTAGTGGGG CAGGGGAAGGAAGGTGGTGCACGCAGAAGAGAGGTTATAGCTCAAAA CAGCGGGACTGGATGCCTGGATCTCGGGGTAAGCATGGCTCACAGTCA GGACTCAGTAAGTGTCGGGAGAACACATGAAGGAGCAGGCATTGATGG CCCTGGGTTTCTGGTTCTGATGACTGTGTGAGTGGTGAAGAGCAAGGTG GGTGGTGGTTGGGTTTGCAGTTGGGAAGGGTGATCAGGCCTTCAGCTGA GAGTGTCCCGGAGTCTCCATGCTTAGTCACACGTTGCAGCTTTTTGCTCC CCGGAAATGGTGAAGTCCATCTATAGTCTAACAACAGTCTCTCCTGCTT TAATTGGGTCTATTTGTTGGGCCCTCTGGGTTATGGAAAAACCACTTGC TCAGCTTCTCCTTGTAAATTCCTGGTGAGTAGCCACAGAGTGCCGCCAG ACCTACTGCTGTGCTGTTTCTTTTTCTTCTTCCTGCTGTGCTGAACCCCTG CCCTTTCATTCTTGGGCCTGCGCTAATTTCTGTGCATTCCCAACTGTGAT TTTTCACCAATTTAGGGGAACCTCCTCTGCCAGGGCCTACTTCTCCCCAG CAGTGCTTGCAGGTGCCTGGGCTGGCTGGCATCCCTGGGCTGATGGGTG CTTCTCTCCCTGCAGGCTGGCCACTCAGTACTCCTTGTCCCTGGCCTCGC AGCCCACCCGGGAAGCCACAGTGACCAGCCACCAGGTGTGCCATCGTG	176

	GAGGAAGTCCAGGTTGGAGAGGTGGTCTTCTTCTGTGAGCAGGTCCACT TCTCCACCCACTGAGACCCCTTTCTGTCTGCGACAGCCCCACCTCGAGG GCCACGGCACAGCCATCAGCTCCAGCTCCCAGCATGCTACTGCCACGCC CCGAGTGTCCGTCTGGGCCCCGGTGCATGGCCTGTTGTCTTTCTGTATCT ACTTTCTGCAGCCCCTCACTGAGGAGGCCTCCTGGGTTTGTCCAGTGCC TACTATTAAAGCTTTGCTCCAAGTTC	
M21389	GCATCCTTTTTGGGCTGCTCACAGCCCCCAGCCTCTATGGTGAAGACAT ACTTGCTAGCAGCGTCACCAACTTGCTGCCAAGAGATCAGTGCTGCAAG GCAAGGTTATTTCTAACTGAGCAGAGCCTGCCAGGAAGAAAGCGTTTG CACCCCACACCACTGTGCAGGTGTGACCGGTGAGCTCACAGCTGCCCCC CAGGCATGCCCAGCCCACTTAATCATTCACAGCTCGACAGCTCTCTCGC CCAGCCCAGTTCTGGAAGGGATAAAAAGGGGGCATCACCGTTCCTGGG TAACAGAGCCACCTTCTGCGTCCTGCTGAGCTCTGTTCTCTCCAGCACCT CCCAACCCACTAGTGCCTGGTTCTCTTGCTCCACCAGGAACAAGCCACC ATGTCTCGCCAGTCAAGTGTGTCCTTCCGGAGCGGGGGCAGTCGTAGCT TCAGCACCGCCTCTGCCATCACCCCGTCTGTCTCCCGCACCAGCTTCACC TCCGTGTCCCGGTCCGGGGGTGGCGGTGGTGGTGGCTTCGGCAGGGTCA GCCTTGCGGGTGCTTGTGGAGTGGGTGGCTATGGCAGCCGGAGCCTCTA CAACCTGGGGGGCTCCAAGAGGATATCCATCAGCACTAGAGGAGGCAG CTTCAGGAACCGGTTTGGTGCTGGTGCTGGAGGCGGCTATGGCTTTGGA GGTGGTGCCGGTAGTGGATTTGGTTTCGGCGGTGGAGCTGGTGGTGGCT TTGGGCTCGGTGGCGGAGCTGGCTTTGGAGGTGGCTTCGGTGGCCCTGG CTTTCCTGTCTGCCCTCCTGGAGGTATCCAAGAGGTCACTGTCAACCAG AGTCTCCTGACTCCCCTCAACCTGCAAATCGACCCCAGCATCCAGAGGG TGAGGACCGAGGAGCGCGAGCAGATCAAGACCCTCAACAATAAGTTTG CCTCCTTCATCGACAAGGTGCGGTTCCTGGAGCAGCAGAACAAGGTTCT GGACACCAAGTGGACCCTGCTGCAGGAGCAGGGCACCAAGACTGTGAG GCAGAACCTGGAGCCGTTGTTCGAGCAGTACATCAACAACCTCAGGAG GCAGCTGGACAGCATCGTGGGGGAACGGGGCCGCCTGGACTCAGAGCT GAGAAACATGCAGGACCTGGTGGAAGACTTCAAGAACAAGTATGAGGA TGAAATCAACAAGCGTACCACTGCTGAGAATGAGTTTGTGATGCTGAA GAAGGATGTAGATGCTGCCTACATGAACAAGGTGGAGCTGGAGGCCAA GGTTGATGCACTGATGGATGAGATTAACTTCATGAAGATGTTCTTTGAT GCGGAGCTGTCCCAGATGCAGACGCATGTCTCTGACACCTCAGTGGTCC TCTCCATGGACAACAACCGCAACCTGGACCTGGATAGCATCATCGCTGA GGTCAAGGCCCAGTATGAGGAGATTGCCAACCGCAGCCGGACAGAAGC CGAGTCCTGGTATCAGACCAAGTATGAGGAGCTGCAGCAGACAGCTGG CCGGCATGGCGATGACCTCCGCAACACCAAGCATGAGATCACAGAGAT GAACCGGATGATCCAGAGGCTGAGAGCCGAGATTGACAATGTCAAGAA ACAGTGCGCCAATCTGCAGAACGCCATTGCGGATGCCGAGCAGCGTGG GGAGCTGGCCCTCAAGGATGCCAGGAACAAGCTGGCCGAGCTGGAGGA GGCCCTGCAGAAGGCCAAGCAGGACATGGCCCGGCTGCTGCGTGAGTA CCAGGAGCTCATGAACACCAAGCTGGCCCTGGACGTGGAGATCGCCAC TTACCGCAAGCTGCTGGAGGGCGAGGAATGCAGACTCAGTGGAGAAGG AGTTGGACCAGTCAACATCTCTGTTGTCACAAGCAGTGTTTCCTCTGGA TATGGCAGTGGCAGTGGCTATGGCGGTGGCCTCGGTGGAGGTCTTGGCG GCGGCCTCGGTGGAGGTCTTGCCGGAGGTAGCAGTGGAAGCTACTACT CCAGCAGCAGTGGGGGTGTCGGCCTAGGTGGTGGGCTCAGTGTGGGGG GCTCTGGCTTCAGTGCAAGCAGTGGCCGAGGGCTGGGGGTGGGCTTTG GCAGTGGCGGGGGTAGCAGCTCCAGCGTCAAATTTGTCTCCACCACCTC CTCCTCCCGGAAGAGCTTCAAGAGCTAAGAACCTGCTGCAAGTCACTGC CTTCCAAGTGCAGCAACCCAGCCCATGGAGATTGCCTCTTCTAGGCAGT TGCTCAAGCCATGTTTTATCCTTTTCTGGAGAGTAGTCTAGACCAAGCC AATTGCAGAACCACATTCTTTGGTTCCCAGGAGAGCCCCATTCCCAGCC CCTGGTCTCCCGTGCCGCAGTTCTATATTCTGCTTCAAATCAGCCTTCAG GTTTCCCACAGCATGGCCCCTGCTGACACGAGAACCCAAAGTTTTCCCA	177

	AATCTAAATCATCAAAACAGAATCCCCACCCCAATCCCAAATTTTGTTT TGGTTCTAACTACCTCCAGAATGTGTTCAATAAAATGCTTTTATAATAT	
NM_001123066	GGACGGCCGAGCGGCAGGGCGCTCGCGCGCGCCCACTAGTGGCCGGAG GAGAAGGCTCCCGCGGAGGCCGCGCTGCCCGCCCCCTCCCCTGGGGAG GCTCGCGTTCCCGCTGCTCGCGCCTGCGCCGCCCGCCGGCCTCAGGAAC GCGCCCTCTTCGCCGGCGCGCGCCCTCGCAGTCACCGCCACCCACCAGC TCCGGCACCAACAGCAGCGCCGCTGCCACCGCCCACCTTCTGCCGCCGC CACCACAGCCACCTTCTCCTCCTCCGCTGTCCTCTCCCGTCCTCGCCTCT GTCGACTATCAGGTGAACTTTGAACCAGGATGGCTGAGCCCCGCCAGG AGTTCGAAGTGATGGAAGATCACGCTGGGACGTACGGGTTGGGGGACA GGAAAGATCAGGGGGGCTACACCATGCACCAAGACCAAGAGGGTGAC ACGGACGCTGGCCTGAAAGAATCTCCCCTGCAGACCCCCACTGAGGAC GGATCTGAGGAACCGGGCTCTGAAACCTCTGATGCTAAGAGCACTCCA ACAGCGGAAGATGTGACAGCACCCTTAGTGGATGAGGGAGCTCCCGGC AAGCAGGCTGCCGCGCAGCCCCACACGGAGATCCCAGAAGGAACCACA GCTGAAGAAGCAGGCATTGGAGACACCCCCAGCCTGGAAGACGAAGCT GCTGGTCACGTGACCCAAGAGCCTGAAAGTGGTAAGGTGGTCCAGGAA GGCTTCCTCCGAGAGCCAGGCCCCCCAGGTCTGAGCCACCAGCTCATGT CCGGCATGCCTGGGGCTCCCCTCCTGCCTGAGGGCCCCAGAGAGGCCAC ACGCCAACCTTCGGGGACAGGACCTGAGGACACAGAGGGCGGCCGCCA CGCCCCTGAGCTGCTCAAGCACCAGCTTCTAGGAGACCTGCACCAGGA GGGGCCGCCGCTGAAGGGGGCAGGGGGCAAAGAGAGGCCGGGGAGCA AGGAGGAGGTGGATGAAGACCGCGACGTCGATGAGTCCTCCCCCCAAG ACTCCCCTCCCTCCAAGGCCTCCCCAGCCCAAGATGGGCGGCCTCCCCA GACAGCCGCCAGAGAAGCCACCAGCATCCCAGGCTTCCCAGCGGAGGG TGCCATCCCCCTCCCTGTGGATTTCCTCTCCAAAGTTTCCACAGAGATCC CAGCCTCAGAGCCCGACGGGCCCAGTGTAGGGCGGGCCAAAGGGCAGG ATGCCCCCCTGGAGTTCACGTTTCACGTGGAAATCACACCCAACGTGCA GAAGGAGCAGGCGCACTCGGAGGAGCATTTGGGAAGGGCTGCATTTCC AGGGGCCCCTGGAGAGGGGCCAGAGGCCCGGGGCCCCTCTTTGGGAGA GGACACAAAAGAGGCTGACCTTCCAGAGCCCTCTGAAAAGCAGCCTGC TGCTGCTCCGCGGGGGAAGCCCGTCAGCCGGGTCCCTCAACTCAAAGCT CGCATGGTCAGTAAAAGCAAAGACGGGACTGGAAGCGATGACAAAAA AGCCAAGACATCCACACGTTCCTCTGCTAAAACCTTGAAAAATAGGCCT TGCCTTAGCCCCAAACACCCCACTCCTGGTAGCTCAGACCCTCTGATCC AACCCTCCAGCCCTGCTGTGTGCCCAGAGCCACCTTCCTCTCCTAAATA CGTCTCTTCTGTCACTTCCCGAACTGGCAGTTCTGGAGCAAAGGAGATG AAACTCAAGGGGGCTGATGGTAAAACGAAGATCGCCACACCGCGGGGA GCAGCCCCTCCAGGCCAGAAGGGCCAGGCCAACGCCACCAGGATTCCA GCAAAAACCCCGCCCGCTCCAAAGACACCACCCAGCTCTGCGACTAAG CAAGTCCAGAGAAGACCACCCCCTGCAGGGCCCAGATCTGAGAGAGGT GAACCTCCAAAATCAGGGGATCGCAGCGGCTACAGCAGCCCCGGCTCC CCAGGCACTCCCGGCAGCCGCTCCCGCACCCCGTCCCTTCCAACCCCAC CCACCCGGGAGCCCAAGAAGGTGGCAGTGGTCCGTACTCCACCCAAGT CGCCGTCTTCCGCCAAGAGCCGCCTGCAGACAGCCCCCGTGCCCATGCC AGACCTGAAGAATGTCAAGTCCAAGATCGGCTCCACTGAGAACCTGAA GCACCAGCCGGGAGGCGGGAAGGTGCAGATAATTAATAAGAAGCTGGA TCTTAGCAACGTCCAGTCCAAGTGTGGCTCAAAGGATAATATCAAACAC GTCCCGGGAGGCGGCAGTGTGCAAATAGTCTACAAACCAGTTGACCTG AGCAAGGTGACCTCCAAGTGTGGCTCATTAGGCAACATCCATCATAAAC CAGGAGGTGGCCAGGTGGAAGTAAAATCTGAGAAGCTTGACTTCAAGG ACAGAGTCCAGTCGAAGATTGGGTCCCTGGACAATATCACCCACGTCCC TGGCGGAGGAAATAAAAAGATTGAAACCCACAAGCTGACCTTCCGCGA GAACGCCAAAGCCAAGACAGACCACGGGGCGGAGATCGTGTACAAGTC GCCAGTGGTGTCTGGGGACACGTCTCCACGGCATCTCAGCAATGTCTCC TCCACCGGCAGCATCGACATGGTAGACTCGCCCCAGCTCGCCACGCTAG	178

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	ATTGCAACAGATGTTGGGCCCTTCGTGAGAATTGGCTTCCTGAAGATAA AGGGAAAGATAAAGGGGAAATCTCTGAGAAAGCCAAACTGGAAAACT CAACACAAGCTGAAGAGGGCTTTGATGTTCCTGATTGTAAAAAAACTAT AGTGAATGATTCCAGAGAGTCATGTGTTGAGGAAAATGATGATAAAAT TACACAAGCTTCACAATCACAAGAAAGTGAAGACTATTCTCAGCCATCA ACTTCTAGTAGCATTATTTATAGCAGCCAAGAAGATGTGAAAGAGTTTG AAAGGGAAGAAACCCAAGACAAAGAAGAGAGTGTGGAATCTAGTTTGC CCCTTAATGCCATTGAACCTTGTGTGATTTGTCAAGGTCGACCTAAAAA TGGTTGCATTGTCCATGGCAAAACAGGACATCTTATGGCCTGCTTTACA TGTGCAAAGAAGCTAAAGAAAAGGAATAAGCCCTGCCCAGTATGTAGA CAACCAATTCAAATGATTGTGCTAACTTATTTCCCCTAGTTGACCTGTCT ATAAGAGAATTATATATTTCTAACTATATAACCCTAGGAATTTAGACAA CCTGAAATTTATTCACATATATCAAAGTGAGAAAATGCCTCAATTCACA TAGATTTCTTCTCTTTAGTATAATTGACCTACTTTGGTAGTGGAATAGTG AATACTTACTATAATTTGACTTGAATATGTAGCTCATCCTTTACACCAAC TCCTAATTTTAAATAATTTCTACTCTGTCTTAAATGAGAAGTACTTGGTT TTTTTTTTCTTAAATATGTATATGACATTTAAATGTAACTTATTATTTTTT TTGAGACCGAGTCTTGCTCTGTTACCCAGGCTGGAGTGCAGTGGGTGAT CTTGGCTCACTGCAAGCTCTGCCCTCCCCGGGTTCGCACCATTCTCCTGC CTCAGCCTCCCAATTAGCTTGGCCTACAGTCATCTGCCACCACACCTGG CTAATTTTTTGTACTTTTAGTAGAGACAGGGTTTCACCGTGTTAGCCAGG ATGGTCTCGATCTCCTGACCTCGTGATCCGCCCACCTCGGCCTCCCAAA GTGCTGGGATTACAGGCATGAGCCACCG	
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NM_002417	TACCGGGCGGAGGTGAGCGCGGCGCCGGCTCCTCCTGCGGCGGACTTT GGGTGCGACTTGACGAGCGGTGGTTCGACAAGTGGCCTTGCGGGCCGG ATCGTCCCAGTGGAAGAGTTGTAAATTTGCTTCTGGCCTTCCCCTACGG ATTATACCTGGCCTTCCCCTACGGATTATACTCAACTTACTGTTTAGAAA ATGTGGCCCACGAGACGCCTGGTTACTATCAAAAGGAGCGGGGTCGAC GGTCCCCACTTTCCCCTGAGCCTCAGCACCTGCTTGTTTGGAAGGGGTA TTGAATGTGACATCCGTATCCAGCTTCCTGTTGTGTCAAAACAACATTG CAAAATTGAAATCCATGAGCAGGAGGCAATATTACATAATTTCAGTTCC ACAAATCCAACACAAGTAAATGGGTCTGTTATTGATGAGCCTGTACGGC TAAAACATGGAGATGTAATAACTATTATTGATCGTTCCTTCAGGTATGA AAATGAAAGTCTTCAGAATGGAAGGAAGTCAACTGAATTTCCAAGAAA AATACGTGAACAGGAGCCAGCACGTCGTGTCTCAAGATCTAGCTTCTCT TCTGACCCTGATGAGAAAGCTCAAGATTCCAAGGCCTATTCAAAAATCA CTGAAGGAAAAGTTTCAGGAAATCCTCAGGTACATATCAAGAATGTCA	182

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NM_024101	GCGCCGGGACGTGGCCAGTTGCCCGCCTGCCCCGGAGAGCCAGGCGCT AACCAGCCGCTCTGCGCCCCGCGCCCTGCTTGCCCCCATTATCCAGCCT TGCCCCGGCGCCCTGACCTGACGCCCTGGCCTGACGCCCTGCTTCGTCG CCTCCTTTCTCTCCCAGGTGCTGGACCAGGGACTGAGCGTCCCCCGGAG AGGGTCCGGTGTGACCCCGACAAGAAGCAGAAATGGGGAAGAAACTG GATCTTTCCAAGCTCACTGATGAAGAGGCCCAGCATGTCTTGGAAGTTG TTCAACGAGATTTTGACCTCCGAAGGAAAGAAGAGGAACGGCTAGAGG CGTTGAAGGGCAAGATTAAGAAGGAAAGCTCCAAGAGGGAGCTGCTTT CCGACACTGCCCATCTGAACGAGACCCACTGCGCCCGCTGCCTGCAGCC CTACCAGCTGCTTGTGAATAGCAAAAGGCAGTGCCTGGAATGTGGCCTC TTCACCTGCAAAAGCTGTGGCCGCGTCCACCCGGAGGAGCAGGGCTGG ATCTGTGACCCCTGCCATCTGGCCAGAGTCGTGAAGATCGGCTCACTGG AGTGGTACTATGAGCATGTGAAAGCCCGCTTCAAGAGGTTCGGAAGTG CCAAGGTCATCCGGTCCCTCCACGGGCGGCTGCAGGGTGGAGCTGGGC CTGAACTGATATCTGAAGAGAGAAGTGGAGACAGCGACCAGACAGATG AGGATGGAGAACCTGGCTCAGAGGCCCAGGCCCAGGCCCAGCCCTTTG GCAGCAAAAAAAAGCGCCTCCTCTCCGTCCACGACTTCGACTTCGAGGG AGACTCAGATGACTCCACTCAGCCTCAAGGTCACTCCCTGCACCTGTCC TCAGTCCCTGAGGCCAGGGACAGCCCACAGTCCCTCACAGATGAGTCCT GCTCAGAGAAGGCAGCCCCTCACAAGGCTGAGGGCCTGGAGGAGGCTG ATACTGGGGCCTCTGGGTGCCACTCCCATCCGGAAGAGCAGCCGACCA GCATCTCACCTTCCAGACACGGCGCCCTGGCTGAGCTCTGCCCGCCTGG AGGCTCCCACAGGATGGCCCTGGGGACTGCTGCTGCACTCGGGTCGAAT GTCATCAGGAATGAGCAGCTGCCCCTGCAGTACTTGGCCGATGTGGACA CCTCTGATGAGGAAAGCATCCGGGCTCACGTGATGGCCTCCCACCATTC CAAGCGGAGAGGCCGGGCGTCTTCTGAGAGTCAGATCTTTGAGCTGAA TAAGCATATTTCAGCTGTGGAATGCCTGCTGACCTACCTGGAGAACACA GTTGTGCCTCCCTTGGCCAAGGGTCTAGGTGCTGGAGTGCGCACGGAGG CCGATGTAGAGGAGGAGGCCCTGAGGAGGAAGCTGGAGGAGCTGACC AGCAACGTCAGTGACCAGGAGACCTCGTCCGAGGAGGAGGAAGCCAAG GACGAAAAGGCAGAGCCCAACAGGGACAAATCAGTTGGGCCTCTCCCC CAGGCGGACCCGGAGGTGGGCACGGCTGCCCATCAAACCAACAGACAG GAAAAAAGCCCCCAGGACCCTGGGGACCCCGTCCAGTACAACAGGACC ACAGATGAGGAGCTGTCAGAGCTGGAGGACAGAGTGGCAGTGACGGCC TCAGAAGTCCAGCAGGCAGAGAGCGAGGTTTCAGACATTGAATCCAGG	183

	ATTGCAGCCCTGAGGGCCGCAGGGCTCACGGTGAAGCCCTCGGGAAAG CCCCGGAGGAAGTCAAACCTCCCGATATTTCTCCCTCGAGTGGCTGGGA AACTTGGCAAGAGACCAGAGGACCCAAATGCAGACCCTTCAAGTGAGG CCAAGGCAATGGCTGTGCCCTATCTTCTGAGAAGAAAGTTCAGTAATTC CCTGAAAAGTCAAGGTAAAGATGATGATTCTTTTGATCGGAAATCAGTG TACCGAGGCTCGCTGACACAGAGAAACCCCAACGCGAGGAAAGGAATG GCCAGCCACACCTTCGCGAAACCTGTGGTGGCCCACCAGTCCTAACGGG ACAGGACAGAGAGACAGAGCAGCCCTGCACTGTTTTCCCTCCACCACA GCCATCCTGTCCCTCATTGGCTCTGTGCTTTCCACTATACACAGTCACCG TCCCAATGAGAAACAAGAAGGAGCACCCTCCACATGGACTCCCACCTG CAAGTGGACAGCGACATTCAGTCCTGCACTGCTCACCTGGGTTTACTGA TGACTCCTGGCTGCCCCACCATCCTCTCTGATCTGTGAGAAACAGCTAA GCTGCTGTGACTTCCCTTTAGGACAATGTTGTGTAAATCTTTGAAGGAC ACACCGAAGACCTTTATACTGTGATCTTTTACCCCTTTCACTCTTGGCTT TCTTATGTTGCTTTCATGAATGGAATGGAAAAAAGATGACTCAGTTAAG GCACCAGCCATATGTGTATTCTTGATGGTCTATATCGGGGTGTGAGCAG ATGTTTGCGTATTTCTTGTGGGTGTGACTGGATATTAGACATCCGGACA AGTGACTGAACTAATGATCTGCTGAATAATGAAGGAGGAATAGACACC CCAGTCCCCACCCTACGTGCACCCGCTCTGCAAGTTCCCATGTGATCTG TAGACCAGGGGAAATTACACTGCGGTCAAGGGCAGAGCCTGCACATGA CAGCAAGTGAGCATTTGATAGATGCTCAGATGCTAGTGCAGAGAGCCT GCTGGGAGACGAAGAGACAGCAGGCAGAGCTCCAGATGGGCAAGGAA GAGGCTTGGTTCTAGCCTGGCTCTGCCCCTCACTGCAGTGGATCCAGTG GGGCAGAGGACAGAGGGTCACAACCAATGAGGGATGTCTGCCAAGGAT GGGGGTGCAGAGGCCACAGGAGTCAGCTTGCCACTCGCCCATTGGTTA CATAGATGATCTCTCAGACAGGCTGGGACTCAGAGTTATTTCCTAGTAT CGGTGTGCCCCATCCAGTTTTAAGTGGAGCCCTCCAAGACTCTCCAGAG CTGCCTTTGAACATCCTAACAGTAATCACATCTCACCCTCCCTGAGGTTC ACTTTAGACAGGACCCAATGGCTGCACTGCCTTTGTCAGAGGGGGTGCT GAGAGGAGTGGCTTCTTTTAGAATCAAACAGTAGAGACAAGAGTCAAG CCTTGTGTCTTCAAGCATTGACCAAGTTAAGTGTTTCCTTCCCTCTCTCA ATAAGACACTTCCAGGAGCTTTCCAATCTCTCACTTAAAACTAAGGTTT GAATCTCAAAGTGTTGCTGGGAGGCTGATACTCCTGCAACTTCAGGAGA CCTGTGAGCACACATTAGCAGCTGTTTCTCTGACTCCTTGTGGCATCAG ATAAAAACGTGGGAGTTTTTCCATATAATTCCCAGCCTTACTTATAAAT TCTATTCTTTGAAAAAATTATTCAGGCTAGGTAAGGTGGCTCATACCTA TAATCCCAGCCCTTTGAGAGGCCAAGGTGGGAGAATTGCTTGAGGCCA GGAGTTTGAGACCTCCTGGGCAACATAGTGAGATCCCATCTCTACAAAA AACAAAACAAAAAAATTACCCAAGCATGATGGTATATGCCTGTAGTCG TACCTACTTACTTAGGAGGCTGAGGCAGGAGGATCACTTGAGCCCTGGA GGTTGGGGCTGCAGTGAGCCATGATCGCATCACTATACTCGAGCCTGGG CAACAGAGTGAGACCTTGTCTCTTAAAAAAATTAATAATAAATAAATG AAAATAATTCTTCAGAAAAAAAAAAAAAAAA	
NM_005940	AAGCCCAGCAGCCCCGGGGCGGATGGCTCCGGCCGCCTGGCTCCGCAG CGCGGCCGCGCGCGCCCTCCTGCCCCCGATGCTGCTGCTGCTGCTCCAG CCGCCGCCGCTGCTGGCCCGGGCTCTGCCGCCGGACGCCCACCACCTCC ATGCCGAGAGGAGGGGGCCACAGCCCTGGCATGCAGCCCTGCCCAGTA GCCCGGCACCTGCCCCTGCCACGCAGGAAGCCCCCCGGCCTGCCAGCA GCCTCAGGCCTCCCCGCTGTGGCGTGCCCGACCCATCTGATGGGCTGAG TGCCCGCAACCGACAGAAGAGGTTCGTGCTTTCTGGCGGGCGCTGGGA GAAGACGGACCTCACCTACAGGATCCTTCGGTTCCCATGGCAGTTGGTG CAGGAGCAGGTGCGGCAGACGATGGCAGAGGCCCTAAAGGTATGGAGC GATGTGACGCCACTCACCTTTACTGAGGTGCACGAGGGCCGTGCTGACA TCATGATCGACTTCGCCAGGTACTGGCATGGGGACGACCTGCCGTTTGA TGGGCCTGGGGGCATCCTGGCCCATGCCTTCTTCCCCAAGACTCACCGA GAAGGGGATGTCCACTTCGACTATGATGAGACCTGGACTATCGGGGAT	184

	GACCAGGGCACAGACCTGCTGCAGGTGGCAGCCCATGAATTTGGCCAC GTGCTGGGGCTGCAGCACACAACAGCAGCCAAGGCCCTGATGTCCGCC TTCTACACCTTTCGCTACCCACTGAGTCTCAGCCCAGATGACTGCAGGG GCGTTCAACACCTATATGGCCAGCCCTGGCCCACTGTCACCTCCAGGAC CCCAGCCCTGGGCCCCCAGGCTGGGATAGACACCAATGAGATTGCACC GCTGGAGCCAGACGCCCCGCCAGATGCCTGTGAGGCCTCCTTTGACGCG GTCTCCACCATCCGAGGCGAGCTCTTTTTCTTCAAAGCGGGCTTTGTGTG GCGCCTCCGTGGGGGCCAGCTGCAGCCCGGCTACCCAGCATTGGCCTCT CGCCACTGGCAGGGACTGCCCAGCCCTGTGGACGCTGCCTTCGAGGATG CCCAGGGCCACATTTGGTTCTTCCAAGGTGCTCAGTACTGGGTGTACGA CGGTGAAAAGCCAGTCCTGGGCCCCGCACCCCTCACCGAGCTGGGCCT GGTGAGGTTCCCGGTCCATGCTGCCTTGGTCTGGGGTCCCGAGAAGAAC AAGATCTACTTCTTCCGAGGCAGGGACTACTGGCGTTTCCACCCCAGCA CCCGGCGTGTAGACAGTCCCGTGCCCCGCAGGGCCACTGACTGGAGAG GGGTGCCCTCTGAGATCGACGCTGCCTTCCAGGATGCTGATGGCTATGC CTACTTCCTGCGCGGCCGCCTCTACTGGAAGTTTGACCCTGTGAAGGTG AAGGCTCTGGAAGGCTTCCCCCGTCTCGTGGGTCCTGACTTCTTTGGCT GTGCCGAGCCTGCCAACACTTTCCTCTGACCATGGCTTGGATGCCCTCA GGGGTGCTGACCCCTGCCAGGCCACGAATATCAGGCTAGAGACCCATG GCCATCTTTGTGGCTGTGGGCACCAGGCATGGGACTGAGCCCATGTCTC CTCAGGGGGATGGGGTGGGGTACAACCACCATGACAACTGCCGGGAGG GCCACGCAGGTCGTGGTCACCTGCCAGCGACTGTCTCAGACTGGGCAG GGAGGCTTTGGCATGACTTAAGAGGAAGGGCAGTCTTGGGCCCGCTAT GCAGGTCCTGGCAAACCTGGCTGCCCTGTCTCCATCCCTGTCCCTCAGG GTAGCACCATGGCAGGACTGGGGGAACTGGAGTGTCCTTGCTGTATCCC TGTTGTGAGGTTCCTTCCAGGGGCTGGCACTGAAGCAAGGGTGCTGGGG CCCCATGGCCTTCAGCCCTGGCTGAGCAACTGGGCTGTAGGGCAGGGCC ACTTCCTGAGGTCAGGTCTTGGTAGGTGCCTGCATCTGTCTGCCTTCTGG CTGACAATCCTGGAAATCTGTTCTCCAGAATCCAGGCCAAAAAGTTCAC AGTCAAATGGGGAGGGGTATTCTTCATGCAGGAGACCCCAGGCCCTGG AGGCTGCAACATACCTCAATCCTGTCCCAGGCCGGATCCTCCTGAAGCC CTTTTCGCAGCACTGCTATCCTCCAAAGCCATTGTAAATGTGTGTACAG TGTGTATAAACCTTCTTCTTCTTTTTTTTTTTTTAAACTGAGGATTGTC	
BX647151	TAGCAGCACACAAGGGTTCGTGTTTGTGGAACCAGGTAGCTTCCTTCAG AGCTGACATTTGCCCACAGCCAGCCTGGCCCAGCCCCATACCACCAGCC CTGGCGCTCTGGGGCGTGAGGTGCCTTTTCTGCCCCCCTGCTCTAGGGC AGGTGGAAATCACCCATGGTGGGTCTACATCTGATAGAAGCATCTTATA GTTCTGCTTCTGGACCAGACCATCCTGGGTTTTTCTCTGTTCTGCTGAAG GGTTCCCTCCACGTGTCCATCACCTCGGTGAACTCTTGGGAGACCTGGG AAGATGCTGGCCTCACCTCTCGCCTCTCCTTTCCCTCATTGTGCTGCCAC CATCCTTCTCACACAGGCTCTCCAGGGAGAGCTGGGCAGGATGGGATCT TCCTGGGTTCCCACCTTGCTCCGTGCCCCCTCTCACTGTTCCTGAAGTGT GGCCACGGACTGCCTTGTTTTCTGGAAAGTCCCAAGTCTGGACCATGAC TGAGCAGCATTCTCGGCTATCTGCCACCTGTCTGGGGCTCCTGGCCCCT CTTAGACTCCCCTCTCCCTTCTGTTTCCCCCGAGCCCCTGACTTGGACCT GCAGGGTGGGGAGAGGGATGGGACGAGAACCTGTGCTGGGGCCAAAG GTCGCACTGGGGGGAAGGTGGAGCCAGGGCAGCAGAGTGCCTGGCGTCG GCCCCTATCCTGTCACTAGTTCCCCCGTTCTGGCCCCTGGCAGGTTTGTA ACCCCAGATCAGAAGTACTCCATGGACAACACTCCCCACACGCCAACC CCGTTCAAGAACGCCCTGGAGAAGTACGGACCCCTGAAGCCCCTGGTA CGTGGTGTGGTCACTGCCGTGGATCTCTGCACAGTGGGATCCCTTCGGT TCATCCAACCATGTTCAGTCCACAGGACCCTTCCCTCTGAGGTCTCATTT GATTCTTTCTCCTGAGAAGATGCAGAGATCCTGATAATATAAATGGGGA AGCTGAGGCTGCTCTTTGTCACTTCCTCCGACTGCTCCTGAGCACCTGA GTTTGCAAGCACGCGCCGGCTGGTGCTAGAGACATGGTGGTATCCCGTG ACACTCAGCCTCAGGATGGGGGAGACTGATGTGAAATACAAATAACTT	185

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NM_000926	AGTCCACAGCTGTCACTAATCGGGGTAAGCCTTGTTGTATTTGTGCGTG TGGGTGGCATTCTCAATGAGAACTAGCTTCACTTGTCATTTGAGTGAAA TCTACAACCCGAGGCGGCTAGTGCTCCCGCACTACTGGGATCTGAGATC TTCGGAGATGACTGTCGCCCGCAGTACGGAGCCAGCAGAAGTCCGACC CTTCCTGGGAATGGGCTGTACCGAGAGGTCCGACTAGCCCCAGGGTTTT AGTGAGGGGGCAGTGGAACTCAGCGAGGGACTGAGAGCTTCACAGCAT	189

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AK093306	ATTCTATGCTGCAGCCTAAGCATCATTCCTCTTCTCTTCTTAGTGGAGAT AAAATTACCCACTGCTCTCCTTACATTTACTTTGTCCATATTTGCTCCTA TGCTCTAGGCTCGTGCACAACAAACACAGTGTGGGCCCTTACCCTAGAA GCCAACTTCTCATGACCTTTCTCTATCTCCAGAATCCATGCAGTGGGAA TGAAGGTAAAAGAAGGTTTTCATGGGATCCAGCTGAGAGCTCTACGGG GAAAATGGATCTGAGGAGCCATGTGCTCCATCTCTTTTATTTTACAGGT AGAGACTAGGGGTATAGAGTGAGGTGAATTACCGCAGTGACCCACACA TTGTTGGCAGACCTAGGATTAGAACTCTGTCTTCCTGGTTCCCAGCTTGG TGCTTTTGAAAGCATACTTGCTGCTTTCTTACCGGCCTGGTGTCTGCCAC TTTGGGACAGAGTGTGGACTTGCTCACCTGCCCCATTTCTTAGGGATTCT CATTCTGTGTTTGAGCAAGAATATTCTTATTCTGGAAAGAACCACATAC CACAGGATTCTGGGTGAGCATAAGGAAGATTGTCTTGGGGATCTGACTT AGCTCACGTATAGTGGCTATGATGAATTCAGTGTCTTATTTTTTGCATAT GTATATTTTTAGTCTAATATTGCCTGGGTGTCTGAGCAAGTCTAGATGA ATTTAATTGCTCTCATTTTTCCCCTGCCCCTCTTCCTTTGGTCTCTCTTTT AGGAAATGTTTTTCTTTCAACATTCGTTTCATTCATTATTTACTCATTCG GCCAACCAACATTTATTGAGTGCCTTCCCTGTATCAGGGACAGGGGCTT ACAAAGTAGAATTTGATCCCACCTCTGCCCTCAGTAGCTCAGTGTCTAA TGGAGGTAGTGATGTTCATTAAGCGTCGCCAGATACTGTGCTAGGTGCT GTGCCTGTTCTCTCTCGCTTGTTCCTCACACACTTGAGAAGGCCGAAGCT	190

	GATTCATAGCTTGGAAGGCAGGGGCCTTGGATTTGAACCCAGGCCTGAC CAATGGCAGAACCTATCAGATGTGTGGACAGATGACATTGCCTTTCTTT CTTTGGATATATCAAAATCAGCCAGCAGGCAGGAACTCCCATTTTGAGC AAGCAATGTGCAGGAATGATAGGGTATACAGAGAGGAACAGGAGATG GCCCCTGACTTCCAGCATGTGTCTGATGGACATCCAGGCTGCAGGCATC ATGGTGCTGTCTAGAGAGATGAGCCAGGTGCCCAGAGCCCATGGGCCA ATGCTGCCCTTTCTTGAGCATGCCAAACAAAGCGGTTGGTGTGTTAGAG GCACAGTCTCCTCCACTCTAAGTAAAAATCAGCATGAGTCCTAGCCCAC ATTTCCCTAGTGAGTACACCAAAGATATCTATGAACTGGCAGTCATCAG TGACTTCCTAAGGTTCCGGAAATGCATCTCTTACTCAGGAGTAAGCAAT GATGTGCCTGCGGCTTTACGAGTTCTCACAGAATGACTTTCTGGACCCA AATGTTTTTTCTGCTTCAGGACTGTGAAGGCCTTATTGTTCGCTCTGCCA CCAAGGTGACCGCTGATGTCATCAACGCAGCTGAGAAACTCCAGGTGG TGGGCAGGGCTGGCACAGGTGTGGACAATGTGGATCTGGAGGCCGCAA CAAGGAAGGGCATCTTGGTTATGAACACCCCCAATGGGAACAGCCTCA GTGCCGCAGAACTCACTTGTGGAATGATCATGTGCCTGGCCAGGCAGAT TCCCCAGGCGACGGCTTCGATGAAGGACGGCAAATGGGAGCGGAAGAA GTTCATGGGAACAGAGCTGAATGGAAAGACCCTGGGAATTCTTGGCCT GGGCAGGATTGGGAGAGAGGTAGCTACCCGGATGCAGTCCTTTGGGAT GAAGACTATAGGGTATGACCCCATCATTTCCCCAGAGGTCTCGGCCTCC TTTGGTGTTCAGCAGCTGCCCCTGGAGGAGATCTGGCCTCTCTGTGATTT CATCACTGTGCACACTCCTCTCCTGCCCTCCACGACAGGCTTGCTGAAT GACAACACCTTTGCCCAGTGCAAGAAGGGGGTGCGTGTGGTGAACTGT GCCCGTGGAGGGATCGTGGACGAAGGCGCCCTGCTCCGGGCCCTGCAG TCTGGCCAGTGTGCCGGGGCTGCACTGGACGTGTTTACGGAAGAGCCGC CACGGGACCGGGCCTTGGTGGACCATGAGAATGTCATCAGCTGTCCCCA CCTGGGTGCCAGCACCAAGGAGGCTCAGAGCCGCTGTGGGGAGGAAAT TGCTGTTCAGTTCGTGGACATGGTGAAGGGGAAATCTCTCACGGGGGTT GTGAATGCCCAGGCCCTTACCAGTGCCTTCTCTCCACACACCAAGCCTT GGATTGGTCTGGCAGAAGCTCTGGGGACACTGATGCGAGCCTGGGCTG GGTCCCCCAAAGGGACCATCCAGGTGATAACACAGGGAACATCCCTGA AGAATGCTGGGAACTGCCTAAGCCCCGCAGTCATTGTCGGCCTCCTGAA AGAGGCTTCCAAGCAGGCGGATGTGAACTTGGTGAACGCTAAGCTGCT GGTGAAAGAGGCTGGCCTCAATGTCACCACCTCCCACAGCCCTGCTGCA CCAGGGGGGCAAGGCTTCGGGGAATGCCTCCTGGCCGTGGCCCTGGCA GGCGCCCCTTACCAGGCTGTGGGCTTGGTCCAAGGCACTACACCTGTAC TGCAGGGGCTCAATGGAGCTGTCTTCAGGCCAGAAGTGCCTCTCCGCAG GGACCTGCCCCTGCTCCTATTCCGGACTCAGACCTCTGACCCTGCAATG CTGCCTACCATGATTGGCCTCCTGGCAGAGGCAGGCGTGCGGCTGCTGT CCTACCAGACTTCACTGGTGTCAGATGGGGAGACCTGGCACGTCATGGG CATCTCCTCCTTGCTGCCCAGCCTGGAAGCGTGGAAGCAGCATGTGACT GAAGCCTTCCAGTTCCACTTCTAACCTTGGAGCTCACTGGTCCCTGCCTC TGGGGCTTTTCTGAAGAAACCCACCCACTGTGATCAATAGGGAGAGAA AATCCACATTCTTGGGCTGAACGCGAGCCTCTGACACTGCTTACACTGC ACTCTGACCCTGTAGTACAGCAATAACCGTCTAATAAAGAGCCTACCCC C	
BE904476	CAAACAAAAACAGCCAAGCTTTTCTGCCAAAAAGATGACTGAGAAGAC TGTTAAAGCAAAAAGCTCTGTTCCTGCCTCAGATGATGCCTATCCAGAA ATAGAAAAATTCTTTCCCTTCAATCCTCTAGACTTTGAGAGTTTTGACCT GCCTGAAGAGCACCAGATTGCGCACCTCCCCTTGAGTGGAGTGCCTCTC ATGATCCTTGACGAGGAGAGAGAGCTTGAAAAGCTGTTTCAGCTGGGC CCCCCTTCACCTGTGAAGATGCCCTCTCCACCATGGGAATCCAATCTGT TGCAGTCTCCTTCAAGCATTCTGTCGACCCTGGATGTTGAATTGCCACCT GTTTGCTGTGACATAGATATTTAAATTTCTTAGTGCTTCAGAGTCTGTGT GTATTTGTATTAATAAAGCATTCTTTAACAGAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGGGGGGGAGACACAA	191

	AAAGAATTCCCCAAGAGGGGGCCACAAGATAATCAGAGGATATCACAC AAGATCTCTCGGCGCACCAACGACGGGGGCCCCAAATAAGGGAGAGAC CCAGAATCACAACAGCCAAGACACGGTGGACACGACGGAAACAAACA CACAGCCCAGACACGGGGGCAAACACGCGCGCACACCGCGGACACCAT GGGACAAAGCAGACACCACCCACAAAACAACACCGCGGAGGGGGAAG AACAACAAAACAAGTGCGCAAACAGAACACAACCACAGAAAGAGAAA AATTAAAACGGCCCCCAAGACGGCGACAACACAACAAAACAACCACTA CAGAGCGCTCAACAGCCGAGTAAAAACACAACAACGGACAACTAACAC ACAAAGGAATGAAACAAAGCGGGGCCACACACCGACACCGGAAATCC GGCGAACAACTCACACCGAGCGAGGGTCCCAGACAACAAATACACAGA CAACGAAACCGAGAAACAAGACCAGCAAGACGAGCAGGCAAAAGACA AACAAGACAGAGGAGACGACGACGAACGCAAAGGACAAGAGGACACA ACGACGCGAGGAGCGAGAGCGAGAGGAAGAGACAACAAAAAGACACA AAAGAACAACAAGCAAGCAGCGAAGAACGACACACAACCACACGAGA CAGCAGGAGCAGAGGCGGAGAAAACACAACGAGCAAGCCAAGACCAA GAGAGGAGAACAAAATAAAAAAATACGAGAGCAGGCGGACGAGAGCA CGAGACGAACAGACAAACGGGAATCAGAAGCATAACGATCCGCGACG CGAACAACN	
AK123010	GTGCACCCTGTCCCAGCCGTCCTGTCCTGGCTGCTCGCTCTGCTTCGCTG CGCCTCCACTATGCTCTCCCTCCGTGTCCCGCTCGCGCCCATCACGGACC CGCAGCAGCTGCAGCTCTCGCCGCTGAAGGGGCTCAGCTTGGTCGACA AGGAGAACACGCCGCCGGCCCTGAGCGGGACCCGCGTCCTGGCCAGCA AGACCGCGAGGAGGATCTTCCAGGAGAAAACCCCCGCCGCTTTGTCAT CTTCCCCATCGAGTACCATGATATCTGGCAGATGTATAAGAAGGCAGAG GCTTCCTTTTGGACCGCCGAGGAGGTGGACCTCTCCAAGGACATTCAGC ACTGGGAATCCCTGAAACCCGAGGAGAGATATTTTATATCCCATGTTCT GGCTTTCTTTGCAGCAAGCGATGGCATAGTAAATGAAAACTTGGTGGAG CGATTTAGCCAAGAAGTTCAGATTACAGAAGCCCGCTGTTTCTATGGCT TCCAAATTGCCATGGAAAACATACATTCTGAAATGTATAGTCTTCTTAT TGACACTTACATAAAAGATCCCAAAGAAAGGGAATTTCTCTTCAATGCC ATTGAAACGATGCCTTGTGTCAAGAAGAAGGCAGACTGGGCCTTGCGC TGGATTGGGGACAAAGAGGCTACCTATGGTGAACGTGTTGTAGCCTTTG CTGCAGTGGAAGGCATTTTCTTTTCCGGTTCTTTTGCGTCGATATTCTGG CTCAAGAAACGAGGACTGATGCCTGGCCTCACATTTTCTAATGAACTTA TTAGCAGAGATGAGGGTTTACACTGTGATTTTGCTTGCCTGATGTTCAA ACACCTGGTACACAAACCATCGGAGGAGAGAGTAAGAGAAATAATTAT CAATGCTGTTCGGATAGAACAGGAGTTCCTCACTGAGGCCTTGCCTGTG AAGCTCATTGGGATGAATTGCACTCTAATGAAGCAATACATTGAGTTTG TGGCAGACAGACTTATGCTGGAACTGGGTTTTAGCAAGGTTTTCAGAGT AGAGAACCCATTTGACTTTATGGAGAATATTTCACTGGAAGGAAAGACT AACTTCTTTGAGAAGAGAGTAGGCGAGTATCAGAGGATGGGAGTGATG TCAAGTCCAACAGAGAATTCTTTTACCTTGGATGCTGACTTCTAAATGA ACTGAAGATGTGCCCTTACTTGGCTGATTTTTTTTTTTCCATCTCATAAG AAAAATCAGCTGAAGTGTTACCAACTAGCCACACCATGAATTGTCCGTA ATGTTCATTAACAGCATCTTTAAAACTGTGTAGCTACCTCACAACCAGT CCTGTCTGTTTATAGTGCTGGTAGTATCACCTTTTGCCAGAAGGCCTGGC TGGCTGTGACTTACCATAGCAGTGACAATGGCAGTCTTGGCTTTAAAGT GAGGGGTGACCCTTTAGTGAGCTTAGCACAGCGGGATTAAACAGTCCTT TAACCAGCACAGCCAGTTAAAAGATGCAGCCTCACTGCTTCAACGCAG ATTTTAATGTTTACTTAAATATAAACCTGGCACTTTACAAACAAATAAA CATTGTTTGTACTCACAAGGCGATAATAGCTTGATTTATTTGGTTTCTAC ACCAAATACATTCTCCTGACCACTAATGGGAGCCAATTCACAATTCACT AAGTGACTAAAGTAAGTTAAACTTGTGTAGACTAAGCATGTAATTTTTA AGTTTTATTTTAATGAATTAAAATATTTGTTAACCAACTTTAAAGTCAGT CCTGTGTATACCTAGATATTAGTCAGTTGGTGCCAGATAGAAGACAGGT TGTGTTTTTATCCTGTGGCTTGTGTAGTGTCCTGGGATTCTCTGCCCCCT	192

	CTGAGTAGAGTGTTGTGGGATAAAGGAATCTCTCAGGGCAAGGAGCTT CTTAAGTTAAATCACTAGAAATTTAGGGGTGATCTGGGCCTTCATATGT GTGAGAAGCCGTTTCATTTTATTTCTCACTGTATTTTCCTCAACGTCTGG TTGATGAGAAAAAATTCTTGAAGAGTTTTCATATGTGGGAGCTAAGGTA GTATTGTAAAATTTCAAGTCATCCTTAAACAAAATGATCCACCTAAGAT CTTGCCCCTGTTAAGTGGTGAAATCAACTAGAGGTGGTTCCTACAAGTT GTTCATTCTAGTTTTGTTTGGTGTAAGTAGGTTGTGTGAGTTAATTCATT TATATTTACTATGTCTGTTAAATCAGAAATTTTTTATTATCTATGTTCTTC TAGATTTTACCTGTAGTTCATACTTCAGTCACCCAGTGTCTTATTCTGGC ATTGTCTAAATCTGAGCATTGTCTAGGGGGATCTTAAACTTTAGTAGGA AACCATGAGCTGTTAATACAGTTTCCATTCAAATATTAATTTCAGAATG AAACATAATTTTTTTTTTTTTTTTTTGAGATGGAGTCTCGCTCTGTTGCCC AGGCTGGAGTGCAGTGGCGCGATTTTGGCTCACTGTAACCTCCATCTCC TGGGTTCAAGCAATTCTCCTGTCTCAGCCTCCCTAGTAGCTGGGACTGC AGGTATGTGCTACCACACCTGGCTAATTTTTGTATTTTTAGTAGAGATG GAGTTTCACCATATTGGTCAGGCTGGTCTTGAACTCCTGACCTCAGGTG ATCCACCCACCTCGGCCTCCCAAAGTGCTGGGATTGCAGGCGTGATAAA CAAATATTCTTAATAGGGCTACTTTGAATTAATCTGCCTTTATGTTTGGG AGAAGAAAGCTGAGACATTGCATGAAAGATGATGAGAGATAAATGTTG ATCTTTTGGCCCCATTTGTTAATTGTATTCAGTATTTGAACGTCGTCCTG TTTATTGTTAGTTTTCTTCATCATTTATTGTATAGACAATTTTTAAATCTC TGTAATATGATACATTTTCCTATCTTTTAAGTTATTGTTACCTAAAGTTA ATCCAGATTATATGGTCCTTATATGTGTACAACATTAAAATGAAAGGCT TTGTCTTGCATTGTGAGGTACAGGCGGAAGTTGGAATCAGGTTTTAGGA TTCTGTCTCTCATTAGCTGAATAATGTGAGGATTAACTTCTGCCAGCTCA GACCATTTCCTAATCAGTTGAAAGGGAAACAAGTATTTCAGTCTCAAAA TTGAATAATGCACAAGTCTTAAGTGATTAAAATAAAACTGTTCTTATGT CAGTTT	
BC036503	AGCGGGGGCACTCCAGCCCTGCAGCCTCCGGAGTCAGTGCCGCGCGCC CGCCGCCCCGCGCCTTCCTGCTCGCCGCACCTCCGGGAGCCGGGGCGCA CCCAGCCCGCAGCGCCGCCTCCCCGCCCGCGCCGCCTCCGACCGCAGGC CGAGGGCCGCCACTGGCCGGGGGGACCGGGCAGCAGCTTGCGGCCGCG GAGCCGGGCAACGCTGGGGACTGCGCCTTTTGTCCCCGGAGGTCCCTGG AAGTTTGCGGCAGGACGCGCGCGGGGAGGCGGCGGAGGCAGCCCCGAC GTCGCGGAGAACAGGGCGCAGAGCCGGCATGGGCATCGGGCGCAGCG AGGGGGGCCGCCGCGGGGCAGCCCTGGGCGTGCTGCTGGCGCTGGGCG CGGCGCTTCTGGCCGTGGGCTCGGCCAGCGAGTACGACTACGTGAGCTT CCAGTCGGACATCGGCCCGTACCAGAGCGGGCGCTTCTACACCAAGCC ACCTCAGTGCGTGGACATCCCCGCGGACCTGCGGCTGTGCCACAACGTG GGCTACAAGAAGATGGTGCTGCCCAACCTGCTGGAGCACGAGACCATG GCGGAGGTGAAGCAGCAGGCCAGCAGCTGGGTGCCCCTGCTCAACAAG AACTGCCACGCCGGCACCCAGGTCTTCCTCTGCTCGCTCTTCGCGCCCG TCTGCCTGGACCGGCCCATCTACCCGTGTCGCTGGCTCTGCGAGGCCGT GCGCGACTCGTGCGAGCCGGTCATGCAGTTCTTCGGCTTCTACTGGCCC GAGATGCTTAAGTGTGACAAGTTCCCCGAGGGGGACGTCTGCATCGCC ATGACGCCGCCCAATGCCACCGAAGCCTCCAAGCCCCAAGGCACAACG GTGTGTCCTCCCTGTGACAACGAGTTGAAATCTGAGGCCATCATTGAAC ATCTCTGTGCCAGCGAGTTTGCACTGAGGATGAAAATAAAAGAAGTGA AAAAAGAAAATGGCGACAAGAAGATTGTCCCCAAGAAGAAGAAGCCC CTGAAGTTGGGGCCCATCAAGAAGAAGGACCTGAAGAAGCTTGTGCTG TACCTGAAGAATGGGGCTGACTGTCCCTGCCACCAGCTGGACAACCTCA GCCACCACTTCCTCATCATGGGCCGCAAGGTGAAGAGCCAGTACTTGCT GACGGCCATCCACAAGTGGGACAAGAAAAACAAGGAGTTCAAAAACTT CATGAAGAAAATGAAAAACCATGAGTGCCCCACCTTTCAGTCCGTGTTT AAGTGATTCTCCCGGGGGCAGGGTGGGGAGGGAGCCTCGGGTGGGGTG GGAGCGGGGGGGACAGTGCCCCGGGAACCCGGTGGGTCACACACACGC	193

	ACTGCGCCTGTCAGTAGTGGACATTTAATCCAGTCGGCTTGTTCTTGCA GCATTCCCGCTCCCTTCCCTCCATAGCCACGCTCCAAACCCCAGGGTAG CCATGGCCGGGTAAAGCAAGGGCCATTTAGATTAGGAAGGTTTTTAAG ATCCGCAATGTGGAGCAGCAGCCACTGCACAGGAGGAGGTGACAAACC ATTTCCAACAGCAACACAGCCACTAAAACACAAAAAGGGGGATTGGGC GGAAAGTGAGAGCCAGCAGCAAAAACTACATTTTGCAACTTGTTGGTG TGGATCTATTGGCTGATCTATGCCTTTCAACTAGAAAATTCTAATGATTG GCAAGTCACGTTGTTTTCAGGTCCAGAGTAGTTTCTTTCTGTCTGCTTTA AATGGAAACAGACTCATACCACACTTACAATTAAGGTCAAGCCCAGAA AGTGATAAGTGCAGGGAGGAAAAGTGCAAGTCCATTATGTAATAGTGA CAGCAAAGGGACCAGGGGAGAGGCATTGCCTTCTCTGCCCACAGTCTTT CCGTGTGATTGTCTTTGAATCTGAATCAGCCAGTCTCAGATGCCCCAAA GTTTCGGTTCCTATGAGCCCGGGGCATGATCTGATCCCCAAGACATGTG GAGGGGCAGCCTGTGCCTGCCTTTGTGTCAGAAAAAGGAAACCACAGT GAGCCTGAGAGAGACGGCGATTTTCGGGCTGAGAAGGCAGTAGTTTTC AAAACACATAGTTAAAAAAGAAACAAATGAAAAAAATTTTAGAACAGT CCAGCAAATTGCTAGTCAGGGTGAATTGTGAAATTGGGTGAAGAGCTT ACGATTCTAATCTCATGTTTTTTCCTTTTCACATTTTTAAAAGAACAATG ACAAACACCCACTTATTTTTCAAGGTTTTAAAACAGTCTACATTGAGCA TTTGAAAGGTGTGCTAGAACAAGGTCTCCTGATCCGTCCGAGGCTGCTT CCCAGAGGAGCAGCTCTCCCCAGGCATTTGCCAAGGGAGGCGGATTTC CCTGGTAGTGTAGCTGTGTGGCTTTCCTTCCTGAAGAGTCCGTGGTTGCC CTAGAACCTAACACCCCCTAGCAAAACTCACAGAGCTTTCCGTTTTTTT CTTTCCTGTAAAGAAACATTTCCTTTGAACTTGATTGCCTATGGATCAAA GAAATTCAGAACAGCCTGCCTGTCCCCCCGCACTTTTTACATATATTTGT TTCATTTCTGCAGATGGAAAGTTGACATGGGTGGGGTGTCCCCATCCAG CGAGAGAGTTTAAAAAGCAAAACATCTCTGCAGTTTTTCCCAAGTGCCC TGAGATACTTCCCAAAGCCCTTATGTTTAATCAGCGATGTATATAAGCC AGTTCACTTAGACAACTTTACCCTTCTTGTCCAATGTACAGGAAGTAGT TCTAAAAAAAAATGCATATTAATTTCTTCCCCCAAAGCCGGATTCTTAAT TCTCTGCAACACTTTGAGGACATTTATGATTGTCCCTCTGGGCCAATGCT TATACCCAGTGAGGATGCTGCAGTGAGGCTGTAAAGTGGCCCCCTGCG GCCCTAGCCTGACCCGGAGGAAAGGATGGTAGATTCTGTTAACTCTTGA AGACTCCAGTATGAAAATCAGCATGCCCGCCTAGTTACCTACCGGAGA GTTATCCTGATAAATTAACCTCTCACAGTTAGTGATCCTGTCCTTTTAAC ACCTTTTTTGTGGGGTTCTCTCTGACCTTTCATCGTAAAGTGCTGGGGAC CTTAAGTGATTTGCCTGTAATTTTGGATGATTAAAAAATGTGTATATAT ATTAGCTAATTAGAAATATTCTACTTCTCTGTTGTCAAACTGAAATTCAG AGCAAGTTCCTGAGTGCGTGGATCTGGGTCTTAGTTCTGGTTGATTCAC TCAAGAGTTCAGTGCTCATACGTATCTGCTCATTTTGACAAAGTGCCTC ATGCAACCGGGCCCTCTCTCTGCGGCAGAGTCCTTAGTGGAGGGGTTTA CCTGGAACATTAGTAGTTACCACAGAATACGGAAGAGCAGGTGACTGT GCTGTGCAGCTCTCTAAATGGGAATTCTCAGGTAGGAAGCAACAGCTTC AGAAAGAGCTCAAAATAAATTGGAAATGTGAATCGCAGCTGTGGGTTT TACCACCGTCTGTCTCAGAGTCCCAGGACCTTGAGTGTCATTAGTTACTT TATTGAAGGTTTTAGACCCATAGCAGCTTTGTCTCTGTCACATCAGCAA TTTCAGAACCAAAAGGGAGGCTCTCTGTAGGCACAGAGCTGCACTATC ACGAGCCTTTGTTTTTCTCCACAAAGTATCTAACAAAACCAATGTGCAG ACTGATTGGCCTGGTCATTGGTCTCCGAGAGAGGAGGTTTGCCTGTGAT TTCCTAATTATCGCTAGGGCCAAGGTGGGATTTGTAAAGCTTTACAATA ATCATTCTGGATAGAGTCCTGGGAGGTCCTTGGCAGAACTCAGTTAAAT CTTTGAAGAATATTTGTAGTTATCTTAGAAGATAGCATGGGAGGTGAGG ATTCCAAAAACATTTTATTTTTAAAATATCCTGTGTAACACTTGGCTCTT GGTACCTGTGGGTTAGCATCAAGTTCTCCCCAGGGTAGAATTCAATCAG AGCTCCAGTTTGCATTTGGATGTGTAAATTACAGTAATCCCATTTCCCA AACCTAAAATCTGTTTTTCTCATCAGACTCTGAGTAACTGGTTGCTGTGT	

	CATAACTTCATAGATGCAGGAGGCTCAGGTGATCTGTTTGAGCAGAGCA CCCTAGGCAGCCTGCAGGGAATAACATACTGGCCGTTCTGACCTGTTGC CAGCAGATACACAGGACATGGATGAAATTCCCGTTTCCTCTAGTTTCTT CCTGTAGTACTCCTCTTTTAGATCCTAAGTCTCTTACAAAAGCTTTGAAT ACTGTGAAAATGTTTTACATTCCATTTCATTTGTGTTGTTTTTTTAACTGC ATTTTACCAGATGTTTTGATGTTATCGCTTATGTTAATAGTAATTCCCGT ACGTGTTCATTTTATTTTCATGCTTTTTCAGCCATGTATCAATATTCACTT GACTAAAATCACTCAATTAATCAAAAAAAAAAAAAAAA	
NM_012319	AGTCCTGGGCGAAGGGGGCGGTGGTTCCCCGCGGCGCTGCGCGCGGCG GTAATTAGTGATTGTCTTCCAGCTTCGCGAAGGCTAGGGGCGCGGCTGC CGGGTGGCTGCGCGGCGCTGCCCCCGGACCGAGGGGCAGCCAACCCAA TGAAACCACCGCGTGTTCGCGCCTGGTAGAGATTTCTCGAAGACACCAG TGGGCCCGTTCCGAGCCCTCTGGACCGCCCGTGTGGAACCAAACCTGCG CGCGTGGCCGGGCCGTGGGACAACGAGGCCGCGGAGACGAAGGCGCA ATGGCGAGGAAGTTATCTGTAATCTTGATCCTGACCTTTGCCCTCTCTGT CACAAATCCCCTTCATGAACTAAAAGCAGCTGCTTTCCCCCAGACCACT GAGAAAATTAGTCCGAATTGGGAATCTGGCATTAATGTTGACTTGGCAA TTTCCACACGGCAATATCATCTACAACAGCTTTTCTACCGCTATGGAGA AAATAATTCTTTGTCAGTTGAAGGGTTCAGAAAATTACTTCAAAATATA GGCATAGATAAGATTAAAAGAATCCATATACACCATGACCACGACCAT CACTCAGACCACGAGCATCACTCAGACCATGAGCGTCACTCAGACCAT GAGCATCACTCAGACCACGAGCATCACTCTGACCATGATCATCACTCTC ACCATAATCATGCTGCTTCTGGTAAAAATAAGCGAAAAGCTCTTTGCCC AGACCATGACTCAGATAGTTCAGGTAAAGATCCTAGAAACAGCCAGGG GAAAGGAGCTCACCGACCAGAACATGCCAGTGGTAGAAGGAATGTCAA GGACAGTGTTAGTGCTAGTGAAGTGACCTCAACTGTGTACAACACTGTC TCTGAAGGAACTCACTTTCTAGAGACAATAGAGACTCCAAGACCTGGA AAACTCTTCCCCAAAGATGTAAGCAGCTCCACTCCACCCAGTGTCACAT CAAAGAGCCGGGTGAGCCGGCTGGCTGGTAGGAAAACAAATGAATCTG TGAGTGAGCCCCGAAAAGGCTTTATGTATTCCAGAAACACAAATGAAA ATCCTCAGGAGTGTTTCAATGCATCAAAGCTACTGACATCTCATGGCAT GGGCATCCAGGTTCCGCTGAATGCAACAGAGTTCAACTATCTCTGTCCA GCCATCATCAACCAAATTGATGCTAGATCTTGTCTGATTCATACAAGTG AAAAGAAGGCTGAAATCCCTCCAAAGACCTATTCATTACAAATAGCCT GGGTTGGTGGTTTTATAGCCATTTCCATCATCAGTTTCCTGTCTCTGCTG GGGGTTATCTTAGTGCCTCTCATGAATCGGGTGTTTTTCAAATTTCTCCT GAGTTTCCTTGTGGCACTGGCCGTTGGGACTTTGAGTGGTGATGCTTTTT TACACCTTCTTCCACATTCTCATGCAAGTCACCACCATAGTCATAGCCAT GAAGAACCAGCAATGGAAATGAAAAGAGGACCACTTTTCAGTCATCTG TCTTCTCAAAACATAGAAGAAAGTGCCTATTTTGATTCCACGTGGAAGG GTCTAACAGCTCTAGGAGGCCTGTATTTCATGTTTCTTGTTGAACATGTC CTCACATTGATCAAACAATTTAAAGATAAGAAGAAAAAGAATCAGAAG AAACCTGAAAATGATGATGATGTGGAGATTAAGAAGCAGTTGTCCAAG TATGAATCTCAACTTTCAACAAATGAGGAGAAAGTAGATACAGATGAT CGAACTGAAGGCTATTTACGAGCAGACTCACAAGAGCCCTCCCACTTTG ATTCTCAGCAGCCTGCAGTCTTGGAAGAAGAAGAGGTCATGATAGCTC ATGCTCATCCACAGGAAGTCTACAATGAATATGTACCCAGAGGGTGCA AGAATAAATGCCATTCACATTTCCACGATACACTCGGCCAGTCAGACGA TCTCATTCACCACCATCATGACTACCATCATATTCTCCATCATCACCACC ACCAAAACCACCATCCTCACAGTCACAGCCAGCGCTACTCTCGGGAGG AGCTGAAAGATGCCGGCGTCGCCACTCTGGCCTGGATGGTGATAATGG GTGATGGCCTGCACAATTTCAGCGATGGCCTAGCAATTGGTGCTGCTTT TACTGAAGGCTTATCAAGTGGTTTAAGTACTTCTGTTGCTGTGTTCTGTC ATGAGTTGCCTCATGAATTAGGTGACTTTGCTGTTCTACTAAAGGCTGG CATGACCGTTAAGCAGGCTGTCCTTTATAATGCATTGTCAGCCATGCTG GCGTATCTTGGAATGGCAACAGGAATTTTCATTGGTCATTATGCTGAAA	194

	ATGTTTCTATGTGGATATTTGCACTTACTGCTGGCTTATTCATGTATGTT GCTCTGGTTGATATGGTACCTGAAATGCTGCACAATGATGCTAGTGACC ATGGATGTAGCCGCTGGGGGTATTTCTTTTTACAGAATGCTGGGATGCT TTTGGGTTTTGGAATTATGTTACTTATTTCCATATTTGAACATAAAATCG TGTTTCGTATAAATTTCTAGTTAAGGTTTAAATGCTAGAGTAGCTTAAA AAGTTGTCATAGTTTCAGTAGGTCATAGGGAGATGAGTTTGTATGCTGT ACTATGCAGCGTTTAAAGTTAGTGGGTTTTGTGATTTTTGTATTGAATAT TGCTGTCTGTTACAAAGTCAGTTAAAGGTACGTTTTAATATTTAAGTTAT TCTATCTTGGAGATAAAATCTGTATGTGCAATTCACCGGTATTACCAGT TTATTATGTAAACAAGAGATTTGGCATGACATGTTCTGTATGTTTCAGG GAAAAATGTCTTTAATGCTTTTTCAAGAACTAACACAGTTATTCCTATA CTGGATTTTAGGTCTCTGAAGAACTGCTGGTGTTTAGGAATAAGAATGT GCATGAAGCCTAAAATACCAAGAAAGCTTATACTGAATTTAAGCAAAG AAATAAAGGAGAAAAGAGAAGAATCTGAGAATTGGGGAGGCATAGAT TCTTATAAAAATCACAAAATTTGTTGTAAATTAGAGGGGAGAAATTTAG AATTAAGTATAAAAAGGCAGAATTAGTATAGAGTACATTCATTAAACA TTTTTGTCAGGATTATTTCCCGTAAAAACGTAGTGAGCACTTTTCATATA CTAATTTAGTTGTACATTTAACTTTGTATAATACAGAAATCTAAATATAT TTAATGAATTCAAGCAATATATCACTTGACCAAGAAATTGGAATTTCAA AATGTTCGTGCGGGTATATACCAGATGAGTACAGTGAGTAGTTTTATGT ATCACCAGACTGGGTTATTGCCAAGTTATATATCACCAAAAGCTGTATG ACTGGATGTTCTGGTTACCTGGTTTACAAAATTATCAGAGTAGTAAAAC TTTGATATATATGAGGATATTAAAACTACACTAAGTATCATTTGATTCG ATTCAGAAAGTACTTTGATATCTCTCAGTGCTTCAGTGCTATCATTGTGA GCAATTGTCTTTTATATACGGTACTGTAGCCATACTAGGCCTGTCTGTGG CATTCTCTAGATGTTTCTTTTTTACACAATAAATTCCTTATATCAGCTTG AAAAAAAAAAAAAAAAAA	
AK098106	AACGCACTTGGCGCGCGGCGCGGGCTGCAGACGGCTGCGAGGCGCTGG GCACAGGTGTCCTGATGGCAAATTTCAAGGGCCACGCGCTTCCAGGGA GTTTCTTCCTGATCATTGGGCTGTGTTGGTCAGTGAAGTACCCGCTGAA GTACTTTAGCCACACGCGGAAGAACAGCCCACTACATTACTATCAGCGT CTCGAGATCGTCGAAGCCGCAATTAGGACTTTGTTTTCCGTCACTGGGA TCCTGGCAGAGCAGTTTGTTCCGGATGGGCCCCACCTGCACCTCTACCA TGAGAACCACTGGATAAAGTTAATGAATTGGCAGCACAGCACCATGTA CCTATTCTTTGCAGTCTCAGGAATTGTTGACATGCTCACCTATCTGGTCA GCCACGTTCCCTTGGGGGTGGACAGACTGGTTATGGCTGTGGCAGTATT CATGGAAGGTTTCCTCTTCTACTACCACGTCCACAACCGGCCTCCGCTG GACCAGCACATCCACTCACTCCTGCTGTATGCTCTGTTCGGAGGGTGTG TTAGTATCTCCCTAGAGGTGATCTTCCGGGACCACATTGTGCTGGAACT TTTCCGAACCAGTCTCATCATTCTTCAGGGAACCTGGTTCTGGCAGATT GGGTTTGTGCTGTTCCCACCTTTTGGAACACCCGAATGGGACCAGAAGG ATGATGCCAACCTCATGTTCATCACCATGTGCTTCTGCTGGCACTACCTG GCTGCCCTCAGCATTGTGGCCGTCAACTATTCTCTTGTTTACTGCCTTTT GACTCGGATGAAGAGACACGGAAGGGGAGAAATCATTGGAATTCAGAA GCTGAATTCAGATGACACTTACCAGACCGCCCTCTTGAGTGGCTCAGAT GAGGAATGAGCCGAGATGCGGAGGGCGCAGATGTCCCACTGCACAGCT GGAATGAATGGAGTTCATCCCCTCCACCTGAATGCCTGCTGTGGTCTGA TCTTAAGGGTCTATATATTTGCACCTCCTCATTCAACACAGGGCTGGAG GTTCTACAACAGGAAATCAGGCCTACAGCATCCTGTGTATCTTGCAGTT GGGATTTTTAAACATACTATAAAGTCTGTGTTGGTATAGTACCCTTCAT AAGGAAAAATGAAGTAATGCCTATAAGTAGCAGGCCTTTGTGCCTCAG TGTCAAGAGAAATCAAGAGATGCTAAAAGCTTTACAATGGAAGTGGCC TCATGGATGAATCCGGGGTATGAGCCCAGGAGAACGTGCTGCTTTTGGT AACTTATCCCTTTTTCTCTTAAGAAAGCAGGTACTTTCTTATTAGAAATA TGTTAGAATGTGTAAGCAAACGACAGTGCCTTTAGAATTACAATTCTAA CTTACATATTTTTTGAAAGTAAAATAATTCACAAGCTTTGGTATTTTAAA	195

	ATTATTGTTAAACATATCATAACTAATCATACCAGGGTACTGCAATACC ACTGTTTATAAGTGACAAAATTAGGCCAAAGGTGATTTTTTTTTAAATC AGGAAGCTGGTTACTGGCTCTACTGAGAGTTGGAGCCCTGATGTTCTGA TTCTTCAAAGTCACCCTAAAAGAAGATCTGACAGGAAAGCTGTATAATG AGATAGAAAAACGTCAGGTATGGAAGGCTTTCAGTTTTAATATGGCTGA AAGCAAAGGATAACGAATTCAGAATTAGTAATGTAAAATCTTGATACC CTAATCTTGCTTCTGGATCTGTTCTTTTTTTAAAAAAACTTCCTTCACCG CGCCTATAATCCTAGCACTTTGGGAGGCCGAGGCAGGCAGATCACGGG GTCAGGAGATCAAGACCATCCTGGCTAACATGGTGAAACCCCGTCTCTA CTGAAAATACAAAAAATTAGCCGGGTGTGGTGGCGGGCGCCTGTAGTT CCAGCTACTCGGGAGGCTGAGGCAAGAGAATGGCATGAACCCGGTAGG GGAGCTTGCAGTGAGCCCAGATCATGCCACTGTACTCCAGCCTAGGTGA CAGAGCAAGACTCTGTCTCAAAAACAAGCAAACAGACTTCCTTCAACA AATATTTATTAAATATCCACTTTGCAACAGCACTGAAATGGCTGTAAGG ACTCCTGAGATATGTGTCCAGCAAGGAGTTTACAGTCAAACAGGAGAG ACATGCCTGTAGTTACATCCAGTGTGATGGGTGCTGAGAGGCAAGTACA AACCACGATG	
BQ056428	TCCCGCCGCGCCACTTCGCCTGCCTCCGTCCCCCGCCCGCCGCGCCATG CCTGTGGCCGGCTCGGAGCTGCCGCGCCGGCCCTTGCCCCCCGCCGCAC AGGAGCGGGACGCCGAGCCGCGTCCGCCGCACGGGGAGCTGCAGTACC TGGGGCAGATCCAACACATCCTCCGCTGCGGCGTCAGGAAGGACGCCC GCCCGGGCACCGGTACCCTGCCGGTATTCGGCATGCAGGCGCGCTACA GCCTGAGAGATGAATTCCCTCTGCTGACAACCAAACGTGTGTTCTGGAA CGGTGCTTCGGAGGAGCTGCTGTGGCTTATCAAGGGATCCACAAACGCT ATAGACCTGTCTTCCCCGGCAGCGAAAATCTCGGGATGCCACTGGATCC CGACACTCTCTGGACACCCTGGGATTCTCCACCAGAGAAGAACGCGACT TGGGCCCAGTTTGTGGCTCTCAGCGGAGGCCTCCTGTGGCAGAATACAT ACATTTCCAATCAGATCACTTCCCGGACACGGACCNTGACCAGCCTGCC AAAAAGTGGATTTCCCCCCACCCCAGAACCCANCCCCTGACGCACAGA AACCAACCCATTCGTTGTTGCCGCCTTGCGAACCCCAACCAGAATCTCT CCCCCCTGGCCGGCGCGCCTGCCGCTGCCAATGCCCCTATGGCGGCCTC TTGGCCCGCACCTTCCAATTGGTCGCCCTGCGCAACCAGCGAGAAAACA CTGGCCCGCCCGTCTCCCCCCCCGCTCCGCCTACCCCACTTAATGCGCCTC CGTGGCATGACGCACGCGTTTGGTGTCCGCCGCCGTCTCATGTCCGCGC GGTGTGGACCCCCTTTTCTCTCGCGGCACATCCCCCCTATTCCCTTGCCC TTTGGGGGGCACCCCCTCTAGACCCGCGCTTCTCTTCTCGTCCGGTGGG GGACATTGGTTTGCCTGCCGCGGCGGGGGCGNTAAAAATAAAAACAGC CTGTTAGCCCGGCCCAGTACCCCCCCCCCGGCCGGGGCCGCCTTNCGTTT GCATTTATACCCCAACCCATAAAGCCGCGCCCCTTTAGCNCCNTAACTT TTGTGGTGTGGCCTCCCCCCTTTTTCCCGGGGAGCAGCAACGGACATCT GTACACTAATGCTGGCCCCGACCTTTCCCAAAAACCCCCCGCCCGTGTC CCGTATAAATTTGGTGCCAANCCTGACGNGTTCTCCCCCGCCCTCGCCC CGTTGGCCGCCCGTTTAAAGCCCCCCCGGTGGTTGCGCCGCCCAACGAG TCCACCTATAGTTAANTCCACCAACACCCCCACCTTTTCCTCCCCGCCGC ATCTTCCCCACGTACCCCCTTTTGTCGCGAGATGGCCACTCCCCCCCCCC TGTTTGTTTAAAACAACGAGAATGGTGCTGCCAACGCTGGTCTTTTCCC CCCCCGGACCGCGACCGCCAGGGGGAATACGTACCATAAGCCCCCGCG CCCNCCTTTTTTCCCCCCTCCCCGCCAATCAAGATCCGCCGTCCATTAGA CGTATTATTTTTCCCGCGATACACGAAAAAACAGGGCCGCCCATTTATA ACTAAATTCCCGTCGCCGCCGCGCGGATATGTTTCCCAAAATACCACCC CCCCCCCCCCCATTTTCTTTGCCCCCAACTCCTGCGCACCGGTGTTCACCA GCCTCGCGCCGC	196
BC032677	GGACGCGTGGGTCGACCCACGCGTCCGGACCCACGCGTCCGGTCGTGTT CTCCGAGTTCCTGTCTCTCTGCCAACGCCGCCCGGATGGCTTCCCAAAA CCGCGACCCAGCCGCCACTAGCGTCGCCGCCGCCCGTAAAGGAGCTGA GCCGAGCGGGGGCGCCGCCCGGGGTCCGGTGGGCAAAAGGCTACAGCA	197

	GGAGCTGATGACCCTCATGGTGAGTGATTAAGTGCCCAGAACCCCAGC CTTCCATCCAATTTTCAGTAGCCTCCTTTTTTCCGTCAGCTTTTTTGCTAG ACATAGGGGTAATGTAATTTGCTCCCTCCTGGGAAAGAAGTTCATACAC CCCACCTACACCATTTCTTCCAGCAGTCCCTCCTCCCAATTCCATCCCCC CACACGAAGTTATCTCGAACACTTCCCTGAAGTCATACAAGACCCTCCC TATCCAGTGTGTCCCTACTTCCTAGCCCCAACCAAGCTTTACCCACACCC AACTCCCCGCCCTTCTTGGTATTTCTAGCCTATGAATTTGGTTGCTTTAT TTTGGATCAGAGTGATGAGATTAAGGGGAGGCTGGGCGCGGTAGCTCA CACCTTATAATCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGCGCC CGGCCAGCAACTAATATTCTAATTGAACTAAAGCACAGGATGCCAATTT ACAATCCTTAGACCAAAGAGTCACTGATGTCTCCACCAGATAAGAGGA AAGCATCAGGCTAGGCATAGTGGCTCACACCTGTAATCTCAGCACTTTG GGAGGCTGAGGCAGGCAGATCACATGAGCCCAGGAGTTTGAGACTGGC CTGGGCAACATGGTGAAACCCTGTCTCTAAAATAAAAACTAAACTAAA AAAACTTTTTAAAAAGGCAGTGGGGAGCATCAGAACCAGCTCAACAGT TTGTCTACTGTCCGGTCCCAGAGAAACTCAAGATTCTAGCAAGCCCCTT GTGTGGGGCTTGGGTTGGGACATGAGGCTGCTGCTGGAGCTTACTCTGC AACTGTTTCTCCAAATGCCAGGTATATGAAGACCTGAGGTATAAGCTCT CGCTAGAGTTCCCCAGTGGCTACCCTTACAATGCGCCCACAGTGAAGTT CCTCACGCCCTGCTATCACCCCAACGTGGACACCCAGGGTAACATATGC CTGGACATCCTGAAGGAAAAGTGGTCTGCCCTGTATGATGTCAGGACCA TTCTGCTCTCCATCCAGAGCCTTCTAGGAGAACCCAACATTGATAGTCC CTTGAACACACATGCTGCCGAGCTCTGGAAAAACCCCACAGCTTTTAAG AAGTACCTGCAAGAAACCTACTCAAAGCAGGTCACCAGCCAGGAGCCC TGACCCAGGCTGCCCAGCCTGTCCTTGTGTCGTCTTTTTAATTTTTCCTT AGATGGTCTGTCCTTTTTGTGATTTCTGTATAGGACTCTTTATCTTGAGC TGTGGTATTTTTGTTTTGTTTTTGTCTTTTAAATTAAGCCTCGGTTGAGCC CTTGTATATTAAATAAATGCATTTTTGTCCTTTTTTAAAAAAAAAATAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	

[51] The NANO46 gene expression assay, as described herein, is able to identify intrinsic subtype from standard formalin fixed paraffin embedded tumor tissue (also *see*, Parker *et al. J. Clin Oncol.*, 27(8):1160-7 (2009) and U.S. Patent Application Publication No. 2013/0337444 The methods utilize a supervised algorithm to classify subject samples according to breast cancer intrinsic subtype. This algorithm, referred to herein as the "NANO46 classification model", is based on the gene expression profile of a defined subset of intrinsic genes that has been identified herein as superior for classifying breast cancer intrinsic subtypes; *see*, U.S. Patent Application Publication No. 2013/0337444. In particular, expression of 46 of the genes listed in Table 1 is determined (which is by determining the expression of all 50 genes in Table 1 with the exception of determining the expression of *MYBL2*, *BIRC5*, *GRB7* and *CCNB1*), *i.e.*, the "NANO46" set of genes. The skilled artisan can utilize any primer and/or target sequence-specific probe for detecting any of (or each of) the genes in Table 1.

[52] At least 10, at least 15, at least 20, at least 25, at least 40, at least 41, at least 42, at least 43, at least 44, at least 46, at least 47, at least 48, at least 49 or all 50 of the genes in Table 1 can

be utilized in the methods and kits of the present invention. Preferably, the expression of each of the 50 genes is determined in a biological sample. More preferably, the expression of each of the genes in the NANO46 set of genes is determined in a biological sample. The prototypical gene expression profiles (*i.e.*, centroid) of the four intrinsic subtypes were pre-defined from a training set of formalin fixed paraffin embedded tissues (FFPE) breast tumor samples using hierarchical clustering analysis of gene expression data. **Table 4** shows the actual values of the prototypical gene expression profiles (*i.e.*, centroids) of these four subtypes and for a normal sample.

[53] Table 4. Subtype Centroids for Comparison to a Sample

[54] **Table 4.**

Subtype Centroids for Comparison to a Sample					
Target Gene	Basal-like	Her2-enriched	Luminal A	Luminal B	Normal
ACTR3B	-0.2052	-0.7965	-0.2790	-0.4380	0.6676
ANLN	1.0227	0.5006	-0.7289	0.1149	-1.7879
BAG1	-0.4676	-0.3132	0.4716	0.5879	-0.3280
BCL2	-0.7365	-0.7237	0.7234	0.6363	0.5144
BIRC5	0.9542	0.4541	-0.6921	0.3421	-1.6821
BLVRA	-0.8761	0.2270	0.1628	0.7138	-0.2665
CCNB1	0.7337	0.3114	-0.8626	0.2165	-1.5967
CCNE1	1.3100	0.2201	-0.6231	-0.2729	-1.0925
CDC20	1.0995	0.1445	-1.0518	-0.1173	-1.2069
CDC6	0.5817	0.6601	-0.7032	0.3134	-1.2255
CDCA1	0.9367	0.1623	-0.4509	0.2692	-1.9055
CDH3	0.7639	0.0144	-0.0502	-1.0229	0.5007
CENPF	1.0222	0.2944	-0.5657	0.2437	-1.8612
CEP55	1.0442	0.4881	-0.6365	0.2921	-1.9241
CXXC5	-0.9732	0.1866	0.5687	0.9463	-0.3030
EGFR	0.3352	-0.1326	-0.0011	-0.9755	1.4238
ERBB2	-0.7045	1.4182	0.2420	0.1978	-0.5530
ESR1	-1.1847	-0.4926	0.7177	1.0101	0.0087
EXO1	1.0546	0.4317	-0.7259	0.2559	-1.6488
FGFR4	-0.2073	1.4562	0.1707	-0.2223	-0.5802
FOXA1	-1.3590	0.5726	0.7131	0.7963	-0.2353
FOXC1	1.0666	-0.7362	-0.4078	-0.9877	0.6650
GPR160	-1.0540	0.5524	0.6032	0.7305	-0.3224
GRB7	-0.4848	1.3418	0.0124	0.0690	-0.2520
KIF2C	0.9242	0.1104	-1.1001	-0.2771	-1.3455

KNTC2	1.1373	0.2266	-0.7593	0.1656	-1.1881
KRT14	0.4759	-0.5269	0.8187	-0.8879	1.1352
KRT17	0.6863	-0.3777	0.6149	-1.1415	0.9238
KRT5	0.7136	-0.4146	0.5832	-0.9462	1.0985
MAPT	-1.1343	-0.2711	1.0957	0.8372	0.4007
MDM2	-0.7498	-0.4855	-0.1788	0.2397	0.1097
MELK	1.0209	0.2678	-0.8016	0.1012	-1.6272
MIA	1.2408	-0.5475	0.3289	-0.6320	0.6975
MKI67	1.0446	0.4630	-0.6717	0.3161	-1.7680
MLPH	-1.4150	0.4842	0.8829	0.8194	-0.2419
MMP11	-0.1295	0.5220	0.3402	0.5653	-1.7370
MYBL2	0.9571	0.5492	-0.7814	0.1548	-1.4404
MYC	0.5639	-0.9904	-0.3015	-0.2791	0.9833
NAT1	-0.9711	-0.2708	1.2256	0.9576	-0.5287
ORC6L	1.0086	0.5152	-1.0385	-0.0336	-1.4084
PGR	-0.9216	-0.5755	1.2061	0.9278	0.6220
PHGDH	0.9192	0.0322	-0.5194	-0.5371	0.5184
PTTG1	0.9541	0.2079	-1.1207	0.1052	-1.4067
RRM2	0.7895	0.6336	-0.8099	0.3228	-1.7630
SFRP1	0.7694	-0.8271	0.2617	-1.0846	1.3790
SLC39A6	-0.9992	-0.4573	0.6607	0.9222	-0.2463
TMEM45B	-1.0721	0.7926	0.3190	0.2016	-0.2250
TYMS	0.9823	-0.0960	-0.8593	0.1827	-1.3192
UBE2C	0.8294	0.3358	-1.0141	0.0608	-1.7637
UBE2T	0.6258	0.0617	-0.8652	-0.0487	-1.8602

[55] Figure 9 outlines the assay processes associated with the Breast Cancer Intrinsic Subtyping test. Following RNA isolation, the test will simultaneously measure the expression levels of at least 40 target genes (*e.g.*, 46 or 50) plus eight housekeeping genes. For example, the housekeeping genes described in U.S. Patent Publication 2008/0032293 can be used for normalization. Exemplary housekeeping genes include *MRPL19, PSMC4, SF3A1, PUM1, ACTB, GAPD, GUSB, RPLP0,* and *TFRC.* The housekeeping genes are used to normalize the expression of the tumor sample. Each assay run may also include a reference sample consisting of *in vitro* transcribed RNA's of the target genes and the housekeeping genes for normalization purposes.

[56] After performing the Breast Cancer Intrinsic Subtyping test with a test breast cancer tumor sample and the reference sample provided as part of a test kit or as used in a method, a

computational algorithm based on a Pearson's correlation compares the normalized and scaled gene expression profile of the at least 40 genes or the PAM50 or NANO46 intrinsic gene sets of the test sample to the prototypical expression signatures of the four breast cancer intrinsic subtypes. *See*, U.S. Patent Application Publication Nos. 2011/0145176 and 2013/0337444. In embodiments, the intrinsic subtype analysis is determined by determining the expression of a PAM50 or NANO46 sets of genes and the risk of recurrence ("ROR") is determined using the NANO46 set of genes (which is determining the expression of all 50 genes in Table 1 with the exception of determining the expression of *MYBL2*, *BIRC5*, *GRB7* and *CCNB1*). Specifically, the intrinsic subtype is identified by comparing the expression of the at least 40 genes or the PAM50 or NANO46 set of genes in the biological sample with the expected expression profiles for the four intrinsic subtypes. The subtype with the most similar expression profile is assigned to the biological sample. The ROR score is an integer value on a 0-100 scale that is related to an individual patient's probability of distant recurrence within 10 years for the defined intended use population. The ROR score is calculated by comparing the expression profiles of the at least 40 genes, *e.g.*, the NANO46 genes, in the biological sample with the expected profiles for the four intrinsic subtypes, as described above, to calculate four different correlation values. These correlation values may then be combined with a proliferation score (and optionally one or more clinicopathological variables, such as tumor size) to calculate the ROR score. Preferably, the ROR score is calculated by comparing only the expression profiles of the NANO46 genes.

[57] A ROR score can be calculated using any method or formula known in the art. Exemplary formulae include Equations 1 to 6, *as described herein*.

[58] Figure 10 provides a schematic of specific algorithm transformations. The tumor sample is assigned the subtype with the largest positive correlation to the sample. Kaplan Meier survival curves are generated from a training set of untreated breast cancer patients demonstrate that the intrinsic subtypes are a prognostic indicator of recurrence free survival (RFS).

[59] The training set of formalin fixed paraffin embedded tissues (FFPE) breast tumor samples, which had well defined clinical characteristics and clinical outcome data, were used to establish a continuous Risk of Recurrence (ROR) score. The score is calculated using coefficients from a Cox model that includes correlation to each intrinsic subtype, a proliferation score (mean gene expression of a subset of 18 of the 46 genes), and tumor size. *See*, **Table 5**.

Table 5. Coefficients to calculate ROR-PT (Equation 1)	
Test Variables	**Coefficient**
Basal-like Pearson's correlation (A)	- 0.0067
HER2-enriched Pearson's correlation (B)	0.4317
Luminal A Pearson's correlation (C)	- 0.3172
Luminal B Pearson's correlation (D)	0.4894
Proliferation Score (E)	0.1981
Tumor Size (F)	0.1133

[60] The test variables in **Table 5** are multiplied by the corresponding coefficients and summed to produce a risk score ("ROR-PT") as shown in the following equation (Equation 1):

[61] ROR-PT equation = -0.0067*A + 0.4317*B + -0.3172*C + 0.4894*D + 0.1981*E + 0.1133*F.

[62] In previous studies, the ROR score provided a continuous estimate of the risk of recurrence for ER-positive, node-negative patients who were treated with tamoxifen for 5 years (Nielsen *et al. Clin. Cancer Res.*, 16(21):5222-5232 (2009)). The ROR score also exhibited a statistically significant improvement over a clinical model based in determining relapse-free survival (RFS) within this test population providing further evidence of the improved accuracy of this decision making tool when compared to traditional clinicopathological measures (Nielsen *et al. Clin. Cancer Res.*, 16(21):5222-5232 (2009)).

[63] The ROR score is an integer value on a 0-100 scale that is related to an individual patient's probability of distant recurrence within 10 years for the defined intended use population. The ROR score is calculated by comparing the expression profiles of 46 genes in an unknown sample with the expected profiles for the four intrinsic subtypes, as described above, to calculate four different correlation values. These correlation values are then combined with a proliferation score and the tumor size to calculate the ROR score. Risk classification is also provided to allow interpretation of the ROR score by using cutoffs related to clinical outcome in tested patient populations. *See*, Table 6.

[64] **Table 6.** Risk classification by ROR range and nodal status

Nodal Status	ROR Range	Risk Classification
Node-Negative	0-40	Low
	41-60	Intermediate
	61-100	High
Node-Positive (1-3 nodes)	0-15	Low
	16-40	Intermediate
	41-100	High

[65] The methods and kits of the present invention can further include steps and/or reagents for providing a VEGF-signature score. The VEGF-signature score can be determined from the expression of at least one of, a combination of, or each of, a 13-gene set of genes associated with *VEGF* signaling or regulation. The 13-gene set includes *RRAGD*, *FABP5*, *UCHL1*, *GAL*, *PLOD*, *DDIT4*, *VEGF*, *ADM*, *ANGPTL4*, *NDRG1*, *NP*, *SLC16A3*, and *C14ORF58*. Table 7 provides the Genbank Accession Numbers and select nucleic acid sequences of the 13-gene set for determining the VEGF-signature score.

[66] **Table 7. VEGF Signature Score Gene Set**

GENE NAME GENBANK ACCESSION NUMBER	SEQUENCE	SEQ ID NO:
RRAGD NM_021244.4	CGCAGTCTCTCTCTCTCCCTCCTCCGGGAGGAACTGCCGCGCTCCGGCT GACTCCTCCGCCGGCGGGCGGGGCGGGGGAGGGGGCTTCGGGCGCGCTG GGAACCGCGGGACCCGGACCTGGGCGCCGCCCGCCGGGGGACGCGCGGC CCCCGCTTCCGCCGGGCCCCGCTGAGCTCTAGACAAACCTCCGCTTCAGA AATAGGCTGCGGGCGGCCGGCTAGGAGGCTTGGCCCCCACCCCGGGACC CCCGCCGTCCCCGGGCCGGCCGGCCGGTGGGCACGATGAGCCAGGTGCTG GGGAAGCCGCAGCCGCAGGACGAGGACGACGCGGAGGAGGAGGAGGAG GAGGATGAGCTGGTGGGGCTAGCGGACTACGGAGACGGGCCCGACTCCT CCGACGCCGATCCGGACAGCGGCACAGAGGAGGGAGTTCTGGACTTCAG TGACCCCTTCAGCACTGAAGTGAAGCCGAGAATCCTGCTCATGGGCCTGA GGAGAAGCGGCAAGTCGTCTATTCAGAAAGTTGTCTTTCACAAAATGTCT CCCAACGAAACTCTGTTCTTGGAGAGCACTAATAAGATATGCCGGGAAGA TGTTTCCAACAGCTCCTTTGTCAATTTTCAGATTTGGGACTTCCCAGGACA GATTGACTTTTTTGACCCTACATTTGACTATGAGATGATCTTCCGGGGAAC AGGAGCACTGATATTTGTCATTGACTCACAGGATGATTACATGGAAGCCC TGGCCAGGCTCCACCTCACGGTGACCAGGGCCTACAAAGTGAATACTGAC	198

ATCAACTTCGAGGTGTTTATTCATAAAGTGGATGGTCTGTCAGATGACCA
CAAAATTGAAACCCAAAGAGATATTCACCAGAGGGCAAACGATGACCTT
GCAGATGCTGGATTAGAAAAAATTCACCTCAGCTTTTATCTGACAAGCAT
ATATGATCATTCAATATTTGAAGCTTTTAGCAAAGTTGTTCAGAAACTGAT
TCCACAACTCCCAACTCTGGAGAATTTGCTGAACATCTTTATCTCAAATTC
TGGAATTGAAAAGGCATTTCTATTTGATGTGGTCAGTAAAATTTATATTGC
AACTGATAGTACTCCGGTGGATATGCAAACCTATGAGCTCTGCTGTGATA
TGATAGATGTGGTTATTGACATCTCTTGTATTTATGGTCTCAAAGAAGATG
GAGCAGGAACCCCCTATGACAAGGAATCCACAGCCATCATAAAGCTTAAT
AATACAACCGTGCTTTATTTAAAAGAGGTGACAAAGTTCCTGGCTCTCGT
TTGCTTTGTCAGAGAGGAAAGCTTTGAAAGAAAAGGGCTAATTGACTATA
ATTTTCATTGCTTCCGGAAGGCCATTCATGAAGTTTTTGAGGTGAGAATGA
AAGTAGTAAAATCTCGAAAGGTTCAGAATCGGCTGCAGAAGAAAAAGAG
AGCCACCCCTAATGGGACCCCTAGAGTGCTGCTGTAGGTGAGGTTTCAGG
AATGTCTTTTGAAATCAGACCTTATCCATGAGGCTGCTGCGCCATGTTGCA
CTAAAGGAAGAGGAAGAAGGAGATTGGGACACATACCATTGATTTGTTG
TTAAAAAAAAAAAAATTCCTGCAACCCTCTTGATCTTCTCTTTTATAAATAA
AGTAAGCACTTTGAAGCAAAAACTTGTATATTAACAGTGATGTGAAATCC
ATTGTCATTTCATTACACAAATGTAAACTTTTATGGTCTGTAGTCAAAAAA
ATCCCGTGTGAGAACTGCCAGGAATTGTACATATTTTGCACTTTTTCATGT
TTCTCATTGAACTGAACTTTGATAAAACGACTTTTCTAAGCTTTTTTTCTGT
ACTTGGTGTCAAGGACATGCATACTGTAGTCCATATCTATATGGCAATCA
GAAATTAATCAAAAAGTGATGCATTGGTAATGACTTTTTGTAAATTTGGA
AATCTTTGCTACCAATTGTTGAGAAAAATCATTTTTCAGTGGAGCTGGAA
CAGATTGGAGCTACAAGCTCCAGGAGCAATAAGAACTGTCCCCTATTTAT
AATGGGTGTAAACAGTTTTGTAGAATAATGCTAGCACCAGACTTACCTAA
AAATTTCTATAGCAGTGGCTGTGCTTCCCTGCTCAACGGTTTTTATGAAGC
TGTTTACCTCAACACACATCTCTATAATCACTTTATACAGAGAGGTTATTT
CTTTTTGTTGCATTAGTATTCTTTTGAAACTTTGGGACCAGATTTCCAAAA
TGGTGCCGAACACTGGAGAGAAGTAAGAATGTCACTGAATTGTAGGGTTT
CTGGAGGCTTTTCTGTACCTACCACCCAGGGCTAAAGTAACATCAGAGGC
CTAAAGTTGTTCCAAAAGTATGTGATTGGCAACTGCAGACTAAAAAACAT
AGATACAATTCTGGACTTTTGGCCCTGTGCGATGGTCTGGTGTGCTGCATT
TAAAATGCTTATTCAGGACCAGTTCTTTATTGCTCCATGACCATAGTGAAT
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TGTCACCTCCACATCTCCTTCTCACTGGTGATAACATGCCTCATGTACTCC
ACTTGTTCCCACCTTATGATTAAGCCAAGCTCAGCCTGCCACCAGCATGCT
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AGGATGGCTGGAGAGACATTACAATTAGCTGTGTAATTGTTTCTGTGAAA
TTATTTCACTTATGTTTACTTTAGACTAACAGGAAATTAAGAGTCCTAAAT
CTACCCCTATGCCAAATCATTCCAAGTAGATAATTTTACGTGCATCTCAAG
GGTTAGCACCCTAAGGCATGCTTGTGGGGCATTAGAAAATGAGATTTTTT
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ATAGCTCACTGTTACCTCTTGGGCTCAAGGGATCCTTCCACCTCAGCCTCC
CTAGTAGCTAGAACTACAGGTGTGCACAACCACGCCCGGCTAATTCTTAA
ATTTTGTTTTTGTAGAGACAGGATCTCACTGTGTTGCCCAAGATGGTCTCA
AACTCCTGGCCCCAAGCAATCCTCCTGCCTTGGCCTCCTCAAATGCTGAG
ATTACAGGCCTGAGCTACTGTGCCCAGCCTAAACTTTCCCACTTCTCTCTG
TGGCTTCTTTCCAACCTCTCTCCTTCCTCTCCCCAAGTCCTGTTTCTTTGAA
GCTGGTAACTGAATTTAAGATGATATCTGGTTGGTGTTTAAGGTTTGAGCC
TCCCAAGGTTCTGTGCATTTTGAAAGGAGATTTCTAAAAATAATTAAGGT
GCCCTAACTCCTTTCCTCATGATTCCTACTCCGAAACCTGGATGGTTAGGA
GCCCAGGGCTCCCTGATTTCCAGAGCTATATCCTGTTGGACCTTTGCCAAC
AGACCTGACACTTAGGGGTTATTGTTATAAATCTAATTCTCTAATATTTTT

	TACATGTTGTTTCACTTTGAATAAGCAAATGAAGAATCAGTTTTCTAATAT GACTTTATCCTCAAGCTAGAGACACTAGCCTATTTGGTAAATCACACATT ACTTAGGTATATTTATTACTATAACCAGGTTGGAGCTTCCATGTTTAAGCT GGGTATATGATGGGTTTTTGTTAAAATGTGCCTTAAAAAGCCTATTACTTC AAGAGCAAATGATTCTTTGGGGGAAAGGCAAAAATAATTCTATGACATA GGGCCCAAGTTCATGGTAGTAAGTGTACTCTTTGATTAATCACACGCTAA TATAGATTACTGCCTCTAACTTTGTAAGTGTGGCAATGACTTCTTAATTAA AGAAAGATGCAGGAGTTATGTCTAAGCGTTCAGTTTTTCAAATCTGTGTT ATTGGAAATGTCTTCAAGTCATTTTGCATTGTATTTTTGATATGAGAGGCA GCTTATTGCGATGTGTATGGCCATGTTTCATTCTCAAATTTAATTCTATAA ATACAAATCCTAAATACATGGCTACAGCAACTGCACTGGAACATTTTTGC TTGGTTTTAGGGATTGAGAACTTGCCTTGCAGGTTTCCTTCCTCAAAAGGA GCAGGGCAGTCCTTTCCCTGTTGAGTCAATTAGAATTTTTACATAGAGGTG AGACTGTGAATTATTTTGGTTATTTTCAGTGATGTAGATTAGTGTGAATGA CCAGGGTGGAATGTTTTTGAAGGAATATAAAGCAAAAACTGGTTGACATT CACAAACTGTTCTTTTGTGAACATATTTTGGACCCTTAAATATGACTAAAA TCACAGCAATATTGTTACATACGGGTTATATGCCAACTCTGTTTGAAATAT ACTCTGGAAAAACAGCTGAATTGTCTTGGTTATTAAAGTATGGTATGTATT CAACTTGTACAGACTGGATGTAATTTGTAATCAGGTATAGTCCATGTTTTA CTTTAAGCAGTACATCACTTAATAACCATTGTTAAGCCATTGCTTTCAAGA ATGTTAACTGCCAATTTAAAAGCATGTGTCCTAGGTTCATGCTTTGGTAAA GCTCTCATTTCAAGTGTATTCATAGCTAAGCTTTCTGGGAGCAGAATTGTC TCTTTGGTGAAAAGGAAGTACAGCCTTTCCTGTTTCTGAGGTTGCTTACCA TACATGTATGTCACTGTTTCATTGGCCCTGTTACATCCATTTGGTAAAATT TATTTGTCCTGATTAACCAGCTCTCATTTTATGGAAATGATGATAAATCTC ACTACTTAAATTTAATTTATGCTTTTATTTTTAA	
FABP5 NM_001444.2	CGCCGCCCAGCGCGGGCCGCCGTTATAAAGCAGCCGCCGGCGCCGGGTG CCTCACAGCACGCTGCCACGCCGACGCAGACCCCTCTCTGCACGCCAGCC CGCCCGCACCCACCATGGCCACAGTTCAGCAGCTGGAAGGAAGATGGCG CCTGGTGGACAGCAAAGGCTTTGATGAATACATGAAGGAGCTAGGAGTG GGAATAGCTTTGCGAAAAATGGGCGCAATGGCCAAGCCAGATTGTATCAT CACTTGTGATGGTAAAAACCTCACCATAAAAACTGAGAGCACTTTGAAAA CAACACAGTTTTCTTGTACCCTGGGAGAGAAGTTTGAAGAAACCACAGCT GATGGCAGAAAAACTCAGACTGTCTGCAACTTTACAGATGGTGCATTGGT TCAGCATCAGGAGTGGGATGGGAAGGAAAGCACAATAACAAGAAAATTG AAAGATGGGAAATTAGTGGTGGAGTGTGTCATGAACAATGTCACCTGTAC TCGGATCTATGAAAAAGTAGAATAAAAATTCCATCATCACTTTGGACAGG AGTTAATTAAGAGAATGACCAAGCTCAGTTCAATGAGCAAATCTCCATAC TGTTTCTTTCTTTTTTTTTTCATTACTGTGTTCAATTATCTTTATCATAAACA TTTTACATGCAGCTATTTCAAAGTGTGTTGGATTAATTAGGATCATCCCTT TGGTTAATAAATAAATGTGTTTGTGCTAATAAAAAAAAAAAAAAAAAAA AA	199
UCHL1 NM_004181.4	AGTGCGTCTGGCCGGCGCTTTATAGCTGCAGCCTGGGCGGCTCCGCTAGC TGTTTTTCGTCTTCCCTAGGCTATTTCTGCCGGGCGCTCCGCGAAGATGCA GCTCAAGCCGATGGAGATCAACCCCGAGATGCTGAACAAAGTGCTGTCCC GGCTGGGGGTCGCCGGCCAGTGGCGCTTCGTGGACGTGCTGGGGCTGGAA GAGGAGTCTCTGGGCTCGGTGCCAGCGCCTGCCTGCGCGCTGCTGCTGCT GTTTCCCCTCACGGCCCAGCATGAGAACTTCAGGAAAAAGCAGATTGAAG AGCTGAAGGGACAAGAAGTTAGTCCTAAAGTGTACTTCATGAAGCAGAC CATTGGGAATTCCTGTGGCACAATCGGACTTATTCACGCAGTGGCCAATA ATCAAGACAAACTGGGATTTGAGGATGGATCAGTTCTGAAACAGTTTCTT TCTGAAACAGAGAAAATGTCCCCTGAAGACAGAGCAAAATGCTTTGAAA AGAATGAGGCCATACAGGCAGCCCATGATGCCGTGGCACAGGAAGGCCA ATGTCGGGTAGATGACAAGGTGAATTTCCATTTTATTCTGTTTAACAACGT GGATGGCCACCTCTATGAACTTGATGGACGAATGCCTTTTCCGGTGAACC ATGGCGCCAGTTCAGAGGACACCCTGCTGAAGGACGCTGCCAAGGTCTGC	200

	AGAGAATTCACCGAGCGTGAGCAAGGAGAAGTCCGCTTCTCTGCCGTGGC TCTCTGCAAGGCAGCCTAATGCTCTGTGGGAGGGACTTTGCTGATTTCCCC TCTTCCCTTCAACATGAAAATATATACCCCCCCATGCAGTCTAAAATGCTT CAGTACTTGTGAAACACAGCTGTTCTTCTGTTCTGCAGACACGCCTTCCCC TCAGCCACACCCAGGCACTTAAGCACAAGCAGAGTGCACAGCTGTCCACT GGGCCATTGTGGTGTGAGCTTCAGATGGTGAAGCATTCTCCCCAGTGTAT GTCTTGTATCCGATATCTAACGCTTTAAATGGCTACTTTGGTTTCTGTCTGT AAGTTAAGACCTTGGATGTGGTTTAATTGTTTGTCCTCAAAAGGAATAAA ACTTTTCTGCTGATAAGATAAAAAAAAAAAAAAAAAA	
GAL NM_015973.3	ATATAGCAGCGGCGGCGGTGGCGGCGGCCACACCGGGCGGCGGACACGT GGAGGGACCCGGCCCGCGCCTTCTGCCCCTGCTGCCGGCCGCGCCATGCG GTGAGCGCCCCAGGCCGCCAGAGCCCACCCGACCCGGCCCGACGCCCGG ACCTGCCGCCCAGACCCGCCACCGCACCCGGACCCCGACGCTCCGAACCC GGGCGCAGCCGCAGCTCAAGATGGCCCGAGGCAGCGCCCTCCTGCTCGCC TCCCTCCTCCTCGCCGCGGCCCTTTCTGCCTCTGCGGGGCTCTGGTCGCCG GCCAAGGAAAAACGAGGCTGGACCCTGAACAGCGCGGGCTACCTGCTGG GCCCACATGCCGTTGGCAACCACAGGTCATTCAGCGACAAGAATGGCCTC ACCAGCAAGCGGGAGCTGCGGCCCGAAGATGACATGAAACCAGGAAGCT TTGACAGGTCCATACCTGAAAACAATATCATGCGCACAATCATTGAGTTT CTGTCTTTCTTGCATCTCAAAGAGGCCGGTGCCCTCGACCGCCTCCTGGAT CTCCCCGCCGCAGCCTCCTCAGAAGACATCGAGCGGTCCTGAGAGCCTCC TGGGCATGTTTGTCTGTGTGCTGTAACCTGAAGTCAAACCTTAAGATAAT GGATAATCTTCGGCCAATTTATGCAGAGTCAGCCATTCCTGTTCTCTTTGC CTTGATGTTGTGTTGTTATCATTTAAGATTTTTTTTTTTTGGTAATTATTTT GAGTGGCAAAATAAAGAATAGCAATTA	201
PLOD L06419.1	CCACCATATCGGTCCCGTATTTCACATTGATAAGGTCCTGTTTCATTTCTC GTGACATTGGGTAGAATGAGGATCCTGTTTTCAATGGGTCGCTTTACCCTG GGACTGACAGGGAGGCTCTGACCATTTAGCCACCAAATGTAGGTGTAGTT CTCACTCTTAGGTTCACCCCGCGGCCGATCGTCCCCCATACCTCGGCCATG CGGCCCCTGCTGCTACTGGCCCTGCTGGGCTGGCTGCTGCTGGCCGAAGC GAAGGGCGACGCCAAGCCGGAGGACAACCTTTTAGTCCTCACGGTGGCC ACTAAGGAGACCGAGGGATTCCGTCGCTTCAAGCGCTCAGCTCAGTTCTT CAACTACAAGATCCAGGCGCTTGGCCTAGGGGAGGACTGGAATGTGGAG AAGGGGACGTCGGCAGGTGGAGGGCAGAAGGTCCGGCTGCTGAAGAAAG CTCTGGAGAAGCACGCAGACAAGGAGGATCTGGTCATTCTCTTCACAGAC AGCTATGACGTGCTGTTTGCATCGGGGCCCCGGGAGCTCCTGAAGAAGTT CCGGCAGGCCAGGAGCCAGGTGGTCTTCTCTGCTGAGGAGCTCATCTACC CAGACCGCAGGCTGGAGACCAAGTATCCGGTGGTGTCCGATGGCAAGAG GTTCCTGGGCTCTGGAGGCTTCATCGGTTATGCCCCCAACCTCAGCAAACT GGTGGCCGAGTGGGAGGGCCAGGACAGCGACAGCGATCAGCTGTTTTAC ACCAAGATCTTCTTGGACCCGGAGAAGAGGGAGCAGATCAATATCACCCT GGACCACCGCTGCCGTATCTTCCAGAACCTGGATGGAGCCTTGGATGAGG TCGTGCTCAAGTTTGAAATGGGCCATGTGAGAGCGAGGAACCTGGCCTAT GACACCCTCCCGGTCCTGATCCATGGCAACGGGCCAACCAAGCTGCAGTT GAACTACCTGGGCAACTACATCCCGCGCTTCTGGACCTTCGAAACAGGCT GCACCGTGTGTGACGAAGGCTTGCGCAGCCTCAAGGGCATTGGGGATGA AGCTCTGCCCACGGTCCTGGTCGGCGTGTTCATCGAACAGCCCACGCCGT TTGTGTCCCTGTTCTTCCAGCGGCTCCTGCGGCTCCACTACCCCCAGAAAC ACATGCGACTTTTCATCCACAACCACGAGCAGCACCACAAGGCTCAGGTG GAAGAGTTCCTGGCACAGCATGGCAGCGAGTACCAGTCTGTGAAGCTGGT GGGCCCTGAGGTGCGGATGGCGAATGCAGATGCCAGGAACATGGGCGCA GACCTGTGCCGGCAGGACCGCAGCTGCACCTACTACTTCAGCGTGGATGC TGACGTGGCCCTGACCGAGCCCAACAGCCTGCGGCTGCTGATCCAACAGA ACAAGAATGTCATTGCCCCGCTGATGACCCGGCATGGGAGGCTGTGGTCG AACTTCTGGGGGGCTCTCAGTGCAGATGGCTACTATGCCCGTTCCGAGGA CTACGTGGACATTGTGCAGGGGCGGCGTGTTGGTGTCTGGAATGTGCCCT	202

	ATATTTCAAACATCTACTTGATCAAGGGCAGTGCCCTGCGGGGTGAGCTG CAGTCCTCAGATCTCTTCCACCACAGCAAGCTGGACCCCGACATGGCCTT CTGTGCCAACATCCGGCAGCAGGATGTGTTCATGTTCCTGACCAACCGGC ACACCCTTGGCCATCTGCTCTCCCTAGACAGCTACCGCACCACCCACCTGC ACAACGACCTCTGGGAGGTGTTCAGCAACCCCGAGGACTGGAAGGAGAA GTACATCCACCAGAACTACACCAAAGCCCTGGCAGGGAAGCTGGTGGAG ACGCCCTGCCCGGATGTCTATTGGTTCCCCATCTTCACGGAGGTGGCCTGT GATGAGCTGGTGGAGGAGATGGAGCACTTTGGCCAGTGGTCTCTGGGCAA CAACAAGGACAACCGCATCCAGGGTGGCTACGAGAACGTGCCGACTATT GACATCCACATGAACCAGATCGGCTTTGAGCGGGAGTGGCACAAATTCCT GCTGGAGTACATTGCGCCCATGACGGAGAAGCTCTACCCCGGCTACTACA CCAGGGCCCAGTTTGACCTGGCCTTTGTCGTCCGCTACAAGCCTGATGAG CAGCCCTCACTGATGCCACACCATGATGCCTCCACCTTCACCATCAACATC GCCCTGAACCGAGTCGGGGTGGATTACGAGGGCGGGGGCTGTCGGTTCCT GCGCTACAACTGTTCCATCCGAGCCCCAAGGAAGGGCTGGACCCTCATGC ACCCTGGACGACTCACGCATTACCATGAGGGGCTCCCCACCACCAGGGGC ACCCGCTACATCGCAGTCTCCTTCGTCGATCCCTAATTGGCCAGGCCTGAC CCTCTTGGACCTTTCTTCTTTGCCGACAACCACTGCCCAGCAGCCTCTGGG ACCTCGGGGTCCCAGGGAACCCAGTCCAGCCTCCTGGCTGTTGACTTCCC ATTGCTCTTGGAGCCACCAATCAAAGAGATTCAAAGAGATTCCTGCAGGC CAGAGGCCGGAACACACCTTTATGGCTGGGGCTCTCCGTGGTGTTCTGGA CCCAGCCCCTGGAGACACCATTCACTTTTACTGCTTTGTAGTGACTCGTGC TCTCCAACCTGTCTTCCTGAAAAACCAAGGCCCCCTTCCCCCACCTCTTCC ATGGGGTGAGACTTGAGCAGAACAGGGGCTTCCCCAAGTTGCCCAGAAA GACTGTCTGGGTGAGAAGCCATGGCCAGAGCTTCTCCCAGGCACAGGTGT TGCACCAGGGACTTCTGCTTCAAGTTTTGGGGTAAAGACACCTGGATCAG ACTCCAAGGGCTGCCCTGAGTCTGGGACTTCTGCCTCCATGGCTGGTCAT GAGAGCAAACCGTAGTCCCCTGGAGACAGCCACTCCAGAGAACCTCTTGG GAGACAGAAGAGGCATCTGTGCACAGCTCGATCTTCTACTTGCCTGTGGG GAGGGGAGTGACAGGTCCACACACCACACTGGGTCACCCTGTCCTGGATG CCTCTGAAGAGAGGGACAGACCGTCAGAAACTGGAGAGTTTCTATTAAA GGTCATTTAAACCAC	
DDIT4 NM_019058.2	AGGGCGCAGCAGGCCAAGGGGGAGGTGCGAGCGTGGACCTGGGACGGGT CTGGGCGGCTCTCGGTGGTTGGCACGGGTTCGCACACCCATTCAAGCGGC AGGACGCACTTGTCTTAGCAGTTCTCGCTGACCGCGCTAGCTGCGGCTTCT ACGCTCCGGCACTCTGAGTTCATCAGCAAACGCCCTGGCGTCTGTCCTCA CCATGCCTAGCCTTTGGGACCGCTTCTCGTCGTCGTCCACCTCCTCTTCGC CCTCGTCCTTGCCCCGAACTCCCACCCCAGATCGGCCGCCGCGCTCAGCCT GGGGGTCGGCGACCCGGGAGGAGGGGTTTGACCGCTCCACGAGCCTGGA GAGCTCGGACTGCGAGTCCCTGGACAGCAGCAACAGTGGCTTCGGGCCG GAGGAAGACACGGCTTACCTGGATGGGGTGTCGTTGCCCGACTTCGAGCT GCTCAGTGACCCTGAGGATGAACACTTGTGTGCCAACCTGATGCAGCTGC TGCAGGAGAGCCTGGCCCAGGCGCGGCTGGGCTCTCGACGCCCTGCGCGC CTGCTGATGCCTAGCCAGTTGGTAAGCCAGGTGGGCAAAGAACTACTGCG CCTGGCCTACAGCGAGCCGTGCGGCCTGCGGGGGGCGCTGCTGGACGTCT GCGTGGAGCAGGGCAAGAGCTGCCACAGCGTGGGCCAGCTGGCACTCGA CCCCAGCCTGGTGCCCACCTTCCAGCTGACCCTCGTGCTGCGCCTGGACTC ACGACTCTGGCCCAAGATCCAGGGGCTGTTTAGCTCCGCCAACTCTCCCTT CCTCCCTGGCTTCAGCCAGTCCCTGACGCTGAGCACTGGCTTCCGAGTCAT CAAGAAGAAGCTGTACAGCTCGGAACAGCTGCTCATTGAGGAGTGTTGA ACTTCAACCTGAGGGGCCGACAGTGCCCTCCAAGACAGAGACGACTGA ACTTTTGGGGTGGAGACTAGAGGCAGGAGCTGAGGGACTGATTCCTGTGG TTGGAAAACTGAGGCAGCCACCTAAGGTGGAGGTGGGGGAATAGTGTTT CCCAGGAAGCTCATTGAGTTGTGTGCGGGTGGCTGTGCATTGGGGACACA TACCCCTCAGTACTGTAGCATGAAACAAAGGCTTAGGGGCCAACAAGGCT TCCAGCTGGATGTGTGTGTAGCATGTACCTTATTATTTTTGTTACTGACAG	203

	TTAACAGTGGTGTGACATCCAGAGAGCAGCTGGGCTGCTCCCGCCCCAGC CCGGCCCAGGGTGAAGGAAGAGGCACGTGCTCCTCAGAGCAGCCGGAGG GAGGGGGGAGGTCGGAGGTCGTGGAGGTGGTTTGTGTATCTTACTGGTCT GAAGGGACCAAGTGTGTTTGTTGTTTGTTTTGTATCTTGTTTTTCTGATCG GAGCATCACTACTGACCTGTTGTAGGCAGCTATCTTACAGACGCATGAAT GTAAGAGTAGGAAGGGGTGGGTGTCAGGGATCACTTGGGATCTTTGACAC TTGAAAAATTACACCTGGCAGCTGCGTTTAAGCCTTCCCCCATCGTGTACT GCAGAGTTGAGCTGGCAGGGGAGGGGCTGAGAGGGTGGGGGCTGGAACC CCTCCCCGGGAGGAGTGCCATCTGGGTCTTCCATCTAGAACTGTTTACATG AAGATAAGATACTCACTGTTCATGAATACACTTGATGTTCAAGTATTAAG ACCTATGCAATATTTTTTACTTTTCTAATAAACATGTTTGTTAAAACAGTT	
VEGF AY047581.1	TCGGGCCTCCGAAACCATGAACTTTCTGCTGTCTTGGGTGCATTGGAGCCT TGCCTTGCTGCTCTACCTCCACCATGCCAAGTGGTCCCAGGCTGCACCCAT GGCAGAAGGAGGGGGGCAGAATCATCACGAAGTGGTGAAGTTCATGGAT GTCTATCAGCGCAGCTACTGCCATCCAATCGAGACCCTGGTGGACATCTT CCAGGAGTACCCTGATGAGATCGAGTACATCTTCAAGCCATCCTGTGTGC CCCTGATGCGATGCGGGGGCTGCTGCAATGACGAGGGCCTGGAGTGTGTG CCCACTGAGGAGTCCAACATCACCATGCAGATTATGCGGATCAAACCTCA CCAAGGCCAGCACATAGGAGAGATGAGCTTCCTACAGCACAACAAATGT GAATGCAGACCAAAGAAAGATAGAGCAAGACAAGAAAATCCCTGTGGGC CTTGCTCAGAGCGGAGAAAGCATTTGTTTGTACAAGATCCGCAGACGTGT AAATGTTCCTGCAAAAACACAGACTCGCGTTGCAAGGCGAGGCAGCTTGA GTTAAACGAACGTACTTGCAGATGTGACAAGCCGAGGCGGTGAGCCGGG CAGGAGGAAGGAGCCTCCCTCAGGGTTTCGGGAACCAGATCT	204
ADM NM_001124.1	CTGGATAGAACAGCTCAAGCCTTGCCACTTCGGGCTTCTCACTGCAGCTG GGCTTGGACTTCGGAGTTTTGCCATTGCCAGTGGGACGTCTGAGACTTTCT CCTTCAAGTACTTGGCAGATCACTCTCTTAGCAGGGTCTGCGCTTCGCAGC CGGGATGAAGCTGGTTTCCGTCGCCCTGATGTACCTGGGTTCGCTCGCCTT CCTAGGCGCTGACACCGCTCGGTTGGATGTCGCGTCGGAGTTTCGAAAGA AGTGGAATAAGTGGGCTCTGAGTCGTGGGAAGAGGGAACTGCGGATGTC CAGCAGCTACCCCACCGGGCTCGCTGACGTGAAGGCCGGGCCTGCCCAGA CCCTTATTCGGCCCCAGGACATGAAGGGTGCCTCTCGAAGCCCCGAAGAC AGCAGTCCGGATGCCGCCCGCATCCGAGTCAAGCGCTACCGCCAGAGCAT GAACAACTTCCAGGGCCTCCGGAGCTTTGGCTGCCGCTTCGGGACGTGCA CGGTGCAGAAGCTGGCACACCAGATCTACCAGTTCACAGATAAGGACAA GGACAACGTCGCCCCCAGGAGCAAGATCAGCCCCCAGGGCTACGGCCGC CGGCGCCGGCGCTCCCTGCCCGAGGCCGGCCCGGGTCGGACTCTGGTGTC TTCTAAGCCACAAGCACACGGGGCTCCAGCCCCCCCGAGTGGAAGTGCTC CCCACTTTCTTTAGGATTTAGGCGCCCATGGTACAAGGAATAGTCGCGCA AGCATCCCGCTGGTGCCTCCCGGGACGAAGGACTTCCCGAGCGGTGTGGG GACCGGGCTCTGACAGCCCTGCGGAGACCCTGAGTCCGGGAGGCACCGTC CGGCGGCGAGCTCTGGCTTTGCAAGGGCCCCTCCTTCTGGGGGCTTCGCTT CCTTAGCCTTGCTCAGGTGCAAGTGCCCCAGGGGGCGGGGTGCAGAAGA ATCCGAGTGTTTGCCAGGCTTAAGGAGAGGAGAAACTGAGAAATGAATG CTGAGACCCCCCGGAGCAGGGGTCTGAGCCACAGCCGTGCTCGCCCACAA ACTGATTTCTCACGGCGTGTCACCCCACCAGGGCGCAAGCCTCACTATTA CTTGAACTTTCCAAAACCTAAAGAGGAAAAGTGCAATGCGTGTTGTACAT ACAGAGGTAACTATCAATATTTAAGTTTGTTGCTGTCAAGATTTTTTTTGT AACTTCAAATATAGAGATATTTTTGTACGTTATATATTGTATTAAGGGCAT TTTAAAAGCAATTATATTGTCCTCCCCTATTTTAAGACGTGAATGTCTCAG CGAGGTGTAAAGTTGTTCGCCGCGTGGAATGTGAGTGTGTTTGTGTGCAT GAAAGAGAAAGACTGATTACCTCCTGTGTGGAAGAAGGAAACACCGAGT CTCTGTATAATCTATTTACATAAAATGGGTGATATGCGAACAGCAAACC	205
ANGPTL4 BC023647.2	GACTGTGATCCGATTCTTTCCAGCGGCTTCTGCAACCAAGCGGGTCTTACC CCCGGTCCTCCGCGTCTCCAGTCCTCGCACCTGGAACCCCAACGTCCCCG AGAGTCCCCGAATCCCCGCTCCCAGGCTACCTAAGAGGATGAGCGGTGCT	206

	CCGACGGCCGGGGCAGCCCTGATGCTCTGCGCCGCCACCGCCGTGCTACT GAGCGCTCAGGGCGGACCCGTGCAGTCCAAGTCGCCGCGCTTTGCGTCCT GGGACGAGATGAATGTCCTGGCGCACGGACTCCTGCAGCTCGGCCAGGG GCTGCGCGAACACGCGGAGCGCACCCGCAGTCAGCTGAGCGCGCTGGAG CGGCGCCTGAGCGCGTGCGGGTCCGCCTGTCAGGGAACCGAGGGGTCCA CCGACCTCCCGTTAGCCCCTGAGAGCCGGGTGGACCCTGAGGTCCTTCAC AGCCTGCAGACACAACTCAAGGCTCAGAACAGCAGGATCCAGCAACTCTT CCACAAGGTGGCCCAGCAGCAGCGGCACCTGGAGAAGCAGCACCTGCGA ATTCAGCATCTGCAAAGCCAGTTTGGCCTCCTGGACCACAAGCACCTAGA CCATGAGGTGGCCAAGCCTGCCCGAAGAAAGAGGCTGCCCGAGATGGCC CAGCCAGTTGACCCGGCTCACAATGTCAGCCGCCTGCACCGGCTGCCCAG GGATTGCCAGGAGCTGTTCCAGGTTGGGGAGAGGCAGAGTGGACTATTTG AAATCCAGCCTCAGGGGTCTCCGCCATTTTTGGTGAACTGCAAGATGACC TCAGATGGAGGCTGGACAGTAATTCAGAGGCGCCACGATGGCTCAGTGG ACTTCAACCGGCCCTGGGAAGCCTACAAGGCGGGGTTTGGGGATCCCCAC GGCGAGTTCTGGCTGGGTCTGGAGAAGGTGCATAGCATCACGGGGGACC GCAACAGCCGCCTGGCCGTGCAGCTGCGGGACTGGGATGGCAACGCCGA GTTGCTGCAGTTCTCCGTGCACCTGGGTGGCGAGGACACGGCCTATAGCC TGCAGCTCACTGCACCCGTGGCCGGCCAGCTGGGCGCCACCACCGTCCCA CCCAGCGGCCTCTCCGTACCCTTCTCCACTTGGGACCAGGATCACGACCTC CGCAGGGACAAGAACTGCGCCAAGAGCCTCTCTGGAGGCTGGTGGTTTGG CACCTGCAGCCATTCCAACCTCAACGGCCAGTACTTCCGCTCCATCCCAC AGCAGCGGCAGAAGCTTAAGAAGGGAATCTTCTGGAAGACCTGGCGGGG CCGCTACTACCCACTGCAGGCCACCACCATGTTGATCCAGCCCATGGCAG CAGAGGCAGCCTCCTAGCGTCCTGGCTGGGCCTGGTCCCAGGCCCACGAA AGACGGTGACTCTTGGCTCTGCCCGAGGATGTGGCCGTTCCCTGCCTGGG CAGGGGCTCCAAGGAGGGGCCATCTGGAAACTTGTGGACAGAGAAGAAG ACCACGACTGGAGAAGCCCCCTTTCTGAGTGCAGGGGGGCTGCATGCGTT GCCTCCTGAGATCGAGGCTGCAGGATATGCTCAGACTCTAGAGGCGTGGA CCAAGGGGCATGGAGCTTCACTCCTTGCTGGCCAGGGAGTTGGGGACTCA GAGGGACCACTTGGGGCCAGCCAGACTGGCCTCAATGGCGGACTCAGTC ACATTGACTGACGGGGACCAGGGCTTGTGTGGGTCGAGAGCGCCCTCATG GTGCTGGTGCTGTTGTGTGTAGGTCCCCTGGGGACACAAGCAGGCGCCAA TGGTATCTGGGCGGAGCTCACAGAGTTCTTGGAATAAAAGCAACCTCAGA AAAAAAAAAAAAAAAAAA	
NDRG1 CR456842.1	ATGTCTCGGGAGATGCAGGATGTAGACCTCGCTGAGGTGAAGCCTTTGGT GGAGAAAGGGGAGACCATCACCGGCCTCCTGCAAGAGTTTGATGTCCAG GAGCAGGACATCGAGACTTTACATGGCTCTGTTCACGTCACGCTGTGTGG GACTCCCAAGGGAAACCGGCCTGTCATCCTCACCTACCATGACATCGGCA TGAACCACAAAACCTGCTACAACCCCCTCTTCAACTACGAGGACATGCAG GAGATCACCCAGCACTTTGCCGTCTGCCACGTGGACGCCCCTGGCCAGCA GGACGGCGCAGCCTCCTTCCCCGCAGGGTACATGTACCCCTCCATGGATC AGCTGGCTGAAATGCTTCCTGGAGTCCTTCAACAGTTTGGGCTGAAAAGC ATTATTGGCATGGGAACAGGAGCAGGCGCCTACATCCTAACTCGATTTGC TCTAAACAACCCTGAGATGGTGGAGGGCCTTGTCCTTATCAACGTGAACC CTTGTGCGGAAGGCTGGATGGACTGGGCCGCCTCCAAGATCTCAGGATGG ACCCAAGCTCTGCCGGACATGGTGGTGTCCCACCTTTTTGGGAAGGAAGA AATGCAGAGTAACGTGGAAGTGGTCCACACCTACCGCCAGCACATTGTGA ATGACATGAACCCCGGCAACCTGCACCTGTTCATCAATGCCTACAACAGC CGGCGCGACCTGGAGATTGAGCGACCAATGCCGGGAACCCACACAGTCA CCCTGCAGTGCCCTGCTCTGTTGGTGGTTGGGGACAGCTCGCCTGCAGTG GATGCCGTGGTGGAGTGCAACTCAAAATTGGACCCAACAAAGACCACTCT CCTCAAGATGGCGGACTGTGGCGGCCTCCCGCAGATCTCCCAGCCGGCCA AGCTCGCTGAGGCCTTCAAGTACTTCGTGCAGGGCATGGGATACATGCCC TCGGCTAGCATGACCCGCCTGATGCGGTCCCGCACAGCCTCTGGTTCCAG CGTCACTTCTCTGGATGGCACCCGCAGCCGCTCCCACACCAGCGAGGGCA	207

	CCCGAAGCCGCTCCCACACCAGCGAGGGCACCCGCAGCCGCTCGCACACC AGCGAGGGGGCCCACCTGGACATCACCCCCAACTCGGGTGCTGCTGGGA ACAGCGCCGGGCCCAAGTCCATGGAGGTCTCCTGTTAA	
NP NM_000270.3	ATAAGCCAGAGCCTAGACCAGTGAGCCAACTGTGCGAACCAGACCCGGC AGCCTTGCTCAGTTCAGCATAGCGGAGCGGATCCGATCGGATCGGAGCGG ATCGGAGCACACCGGAGCAGGCTCATCGAGAAGGCGTCTGCGAGACCAT GGAGAACGGATACACCTATGAAGATTATAAGAACACTGCAGAATGGCTT CTGTCTCACACTAAGCACCGACCTCAAGTTGCAATAATCTGTGGTTCTGG ATTAGGAGGTCTGACTGATAAATTAACTCAGGCCCAGATCTTTGACTACG GTGAAATCCCCAACTTTCCCCGAAGTACAGTGCCAGGTCATGCTGGCCGA CTGGTGTTTGGGTTCCTGAATGGCAGGGCCTGTGTGATGATGCAGGGCAG GTTCCACATGTATGAAGGGTACCCACTCTGGAAGGTGACATTCCCAGTGA GGGTTTTCCACCTTCTGGGTGTGGACACCCTGGTAGTCACCAATGCAGCA GGAGGGCTGAACCCCAAGTTTGAGGTTGGAGATATCATGCTGATCCGTGA CCATATCAACCTACCTGGTTTCAGTGGTCAGAACCCTCTCAGAGGGCCCA ATGATGAAAGGTTTGGAGATCGTTTCCCTGCCATGTCTGATGCCTACGAC CGGACTATGAGGCAGAGGGCTCTCAGTACCTGGAAACAAATGGGGGAGC AACGTGAGCTACAGGAAGGCACCTATGTGATGGTGGCAGGCCCCAGCTTT GAGACTGTGGCAGAATGTCGTGTGCTGCAGAAGCTGGGAGCAGACGCTG TTGGCATGAGTACAGTACCAGAAGTTATCGTTGCACGGCACTGTGGACTT CGAGTCTTTGGCTTCTCACTCATCACTAACAAGGTCATCATGGATTATGAA AGCCTGGAGAAGGCCAACCATGAAGAAGTCTTAGCAGCTGGCAAACAAG CTGCACAGAAATTGGAACAGTTTGTCTCCATTCTTATGGCCAGCATTCCAC TCCCTGACAAAGCCAGTTGACCTGCCTTGGAGTCGTCTGGCATCTCCCAC ACAAGACCCAAGTAGCTGCTACCTTCTTTGGCCCCTTGCTGGAGTCATGTG CCTCTGTCCTTAGGTTGTAGCAGAAAGGAAAAGATTCCTGTCCTTCACCTT TCCCACTTTCTTCTACCAGACCCTTCTGGTGCCAGATCCTCTTCTCAAAGC TGGGATTACAGGTGTGAGCATAGTGAGACCTTGGCGCTACAAAATAAAGC TGTTCTCATTCCTGTTCTTTCTTACACAAGAGCTGGAGCCCGTGCCCTACC ACACATCTGTGGAGATGCCCAGGATTTGACTCGGGCCTTAGAACTTTGCA TAGCAGCTGCTACTAGCTCTTTGAGATAATACATTCCGAGGGGCTCAGTT CTGCCTTATCTAAATCACCAGAGACCAAACAAGGACTAATCCAATACCTC TTGGATTTTATTTAATGTCATAATGTTGTCAGAATAAAGAGAAAGATGAA ATAATTTCATTTTTTTGTGTAACTTGGTATGGGGCTGGGGCACAGACCAAG ATTGACATGAAAGGATGTGAGATCGCATGTCTTGTGTGACTATCTGCTTCT CAGACAAGCAGTTAGGAACTGAGATGAGATAGTATGTGAGGGCAGCAAA GGATGAAGAAGGGCAAAATGATGAAAGGTGAGGTGGAAAGAGGTTATGA GATGGTAAAGAAAAGTTAACTTCTGGCACTTGATTGCCACTTCTGTCAGG CTGGTCCTGCCTCTCTCCCTTGCCTTCTGATTGTTTCATTTCCTGTTTATTT GATCATATCTGAATTAGTTCACTGGTTAGCCTCTTCCTTAGTTCCCACTTC CTTACCAAAGCCCTAATTATATTTCCTCTTGTTTGCCTTTTCTCTCCTACTC TTCTCTAACATCTGCAGCCACACTCTCCATTCACTCCATGCTGACAAGGCA GTGGCAAACACTTTTCTCTGCTGCCAGCCACTCCACTGTTGACTGGATTGC TGCCAGCCCCAGGCAAACCTGTGAAGTTGTTTCATACTCTGCTTCTCTTTG AGTGCCTCCTTCTCTCCTTCCTCTTCCTTTCTGGGCTCCAGTCTTTCTCTTC ACTTGTGCTTGTCAGAACCTCCCTGTGATACTGCCTCCAGGCATTTCCCCC ATGTTGGCTCACCGCACTATTATCTTTGCTTATCAACTTGCATTCAGCTGG CTGGCATGTTTCAAAACCACACTGCCCTCCCAGGCCTGTGTGCCTTTTGAG AAAGACCAGTGCTGGATGAGCCTCTAGTAATGACAACATTTTAGTTGTTA GTGGTATAATACGGAAGAGATATTTTGCACAGGCTGCTTTGGAGAACTTT CAAATTATCCTTTGTTTGGTAACTGACCTACTTAACTGCCCAATACAAAGA AAAAGCAAAAAAAAAAAAAAAAAA	208
SLC16A3 BC112269.1	GAATTCGCCCTTCAGGTGAGGCGGAACCAACCCTCCTGGCCATGGGAGGG GCCGTGGTGGACGAGGGCCCCACAGGCGTCAAGGCCCCTGACGGCGGCT GGGGCTGGGCCGTGCTCTTCGGCTGTTTCGTCATCACTGGCTTCTCCTACG CCTTCCCCAAGGCCGTCAGTGTCTTCTTCAAGGAGCTCATACAGGAGTTTG	209

	GGATCGGCTACAGCGACACAGCCTGGATCTCCTCCATCCTGCTGGCCATG CTCTACGGGACAGGTCCGCTCTGCAGTGTGTGCGTGAACCGCTTTGGCTG CCGGCCCGTCATGCTTGTGGGGGGTCTCTTTGCGTCGCTGGGCATGGTGG CTGCGTCCTTTTGCCGGAGCATCATCCAGGTCTACCTCACCACTGGGGTCA TCACGGGGTTGGGTTTGGCACTCAACTTCCAGCCCTCGCTCATCATGCTGA ACCGCTACTTCAGCAAGCGGCGCCCCATGGCCAACGGGCTGGCGGCAGC AGGTAGCCCTGTCTTCCTGTGTGCCCTGAGCCCGCTGGGGCAGCTGCTGC AGGACCGCTACGGCTGGCGGGGCGGCTTCCTCATCCTGGGCGGCCTGCTG CTCAACTGCTGCGTGTGTGCCGCACTCATGAGGCCCCTGGTGGTCACGGC CCAGCCGGGCTCGGGGCCGCCGCGACCCTCCCGGCGCCTGCTAGACCTGA GCGTCTTCCGGGACCGCGGCTTTGTGCTTTACGCCGTGGCCGCCTCGGTCA TGGTGCTGGGGCTCTTCGTCCCGCCCGTGTTCGTGGTGAGCTACGCCAAG GACCTGGGCGTGCCCGACACCAAGGCCGCCTTCCTGCTCACCATCCTGGG CTTCATTGACATCTTCGCGCGGCCGGCCGCGGGCTTCGTGGCGGGGCTTG GGAAGGTGCGGCCCTACTCCGTCTACCTCTTCAGCTTCTCCATGTTCTTCA ACGGCCTCGCGGACCTGGCGGGCTCTACGGCGGGCGACTACGGCGGCCTC GTGGTCTTCTGCATCTTCTTTGGCATCTCCTACGGCATGGTGGGGGCCCTG CAGTTCGAGGTGCTCATGGCCATCGTGGGCACCCACAAGTTCTCCAGTGC CATTGGCCTGGTGCTGCTGATGGAGGCGGTGGCCGTGCTCGTCGGGCCCC CTTCGGGAGGCAAACTCCTGGATGCGACCCACGTCTACATGTACGTGTTC ATCCTGGCGGGGGCCGAGGTGCTCACCTCCTCCCTGATTTTGCTGCTGGGC AACTTCTTCTGCATTAGGAAGAAGCCCAAAGAGCCACAGCCTGAGGTGGC GGCCGCGGAGGAGGAGAAGCTCCACAAGCCTCCTGCAGACTCGGGGGTG GACTTGCGGGAGGTGGAGCATTTCCTGAAGGCTGAGCCTGAGAAAAACG GGGAGGTGGTTCACACCCCGGAAACAAGTGTCTGAGTGGCTGGGCGGGG CCGGCAGGCACAGGGAGGAGGTACAGAAGCCGGCAACGCTTGCTATTTA TTTTACAAACTGGACTGGCTCAGGCAGGGCCACGGCTGGGCTCCAGCTGC CGGCCCAGCGGATCGTCGCCCGATCAGTGTTTTGAG	
C14ORF58 NM_017791.2	GCGAGGCCCCAAGCTGGCCCGGGAGAGGACTCTGCGGGCGAAGTGGCTG CGCAAGGAGAGAACTTTTCCTGCACAAGGAACGCCTCGTGGGGAGACCC AAGGCAGGAGCGGTCCGGAGCCGGCTGCGGCGTGTGCGGCCGGCCTTGG GACAGCGATCGCCGCGGGTGGCAACAGAGAGCCCCAAGCAAAAGTGGGA GCAGGAGCTTGGAGGTGAGCACAGGAAGCCCCACTTGAGGCTTTTACGCA GCCTCTAGTCTCTGTTTCTTCTGGAATAGGCAAGTGTCCTTTCAACTCTAA GAGACCAGCAGAGGCCACTGTCCCTTAAGACTGCCGGAGTCCTCACCACT TCTCCAGGATTCCAGAGGAGACTGTGGCGATGGTGAATGAAGGTCCCAAC CAGGAAGAGAGCGATGACACCCCTGTGCCGGAGTCCGCACTCCAAGCGG ACCCCAGCGTCTCGGTCCATCCCAGCGTCTCGGTCCATCCCAGCGTCTCCA TCAACCCCAGCGTCTCTGTCCACCCCAGCAGTTCGGCCCACCCCAGTGCCT TAGCCCAACCCAGTGGCTTGGCTCACCCCAGTAGCTCGGGCCCTGAGGAC CTCAGCGTGATCAAGGTGAGCAGGCGCCGTTGGGCCGTGGTCCTGGTGTT TAGCTGCTACTCCATGTGCAACTCCTTTCAGTGGATCCAGTACGGCTCCAT CAATAACATCTTCATGCACTTCTACGGTGTCAGTGCCTTTGCCATTGACTG GCTGTCCATGTGCTACATGCTGACTTACATCCCTCTGCTCCTGCCAGTGGC TTGGCTGCTGGAGAAGTTCGGCCTGCGCACCATTGCTCTCACTGGCTCGG CTCTCAACTGCCTGGGGGCCTGGGTGAAGCTGGGCAGCCTGAAGCCGCAT CTCTTTCCGGTCACCGTGGTGGGCCAGCTCATCTGCTCTGTGGCCCAGGTT TTCATCCTGGGCATGCCCTCCCGCATCGCTTCCGTCTGGTTCGGGGCTAAT GAGGTTTCAACAGCCTGCTCCGTGGCTGTCTTTGGCAATCAGCTTGGAATT GCGATTGGGTTCTTGGTCCCTCCTGTTTTGGTACCCAACATTGAAGACCGG GACGAGCTTGCCTACCACATCAGCATCATGTTCTATATAATAGGAGGTGT GGCCACTCTCCTCCTCATCCTTGTCATCATTGTGTTCAAGGAGAAACCTAA ATATCCCCCCAGCAGGGCCCAATCCCTGAGCTATGCCTTGACCTCTCCTGA TGCCTCATACTTAGGTTCCATCGCCCGGCTCTTCAAAAATCTCAACTTTGT GCTGCTTGTCATCACCTATGGTCTGAATGCTGGTGCTTTTTATGCCTTGTC CACTCTTCTGAATCGCATGGTGATCTGGCACTACCCGGGGGAAGAAGTGA	210

	ATGCTGGAAGAATTGGCCTGACGATCGTCATTGCAGGAATGCTTGGGGCT GTGATCTCAGGAATCTGGCTGGATAGGTCCAAAACCTACAAAGAGACAA CCCTGGTAGTCTATATCATGACACTGGTGGGCATGGTGGTGTACACGTTT ACCTTGAACCTGGGACACCTGTGGGTAGTGTTCATCACTGCTGGCACAAT GGGCTTCTTTATGACTGGCTATCTCCCACTGGGATTTGAGTTTGCTGTGGA GCTCACGTACCCAGAATCAGAAGGCATCTCCTCCGGCCTCCTCAACATAT CTGCACAGGTATTTGGGATCATCTTTACCATCTCCCAGGGCCAGATTATTG ACAACTATGGAACCAAGCCTGGGAACATCTTCCTGTGTGTGTTCCTTACTC TTGGAGCAGCCCTCACTGCATTCATTAAGGCAGATCTCCGGAGACAGAAA GCAAACAAAGAAACTCTTGAGAACAAACTCCAAGAGGAGGAGGAGGAG AGCAACACCAGCAAAGTGCCCACTGCTGTGTCAGAGGATCATCTCTGAGA GGAAGGTGGTGACAACTCAGGGAACACGAACACCCCACCTTTTCCTTCAG CACAGCTCTCACCGCCAGCACAAAGGGCTTCGCTAGAGATGTTTTTGGAG GGAATCAGTGGGACTATTTGTGGCATGGATGGCCTATTCCTCCTAGAACC CACGTAAGAGCTTGGATGATTTAGTTGGAGAAAATTGCACCTATCACCAA ATGCAAATTTGATTCCCACCTCCACCCCCTTTTAGGTTATGGGAGTTGGTG TTGGGACAGGGTGGCAGAGAATATTGGAGTCAATCCTAGCTTGGTCTCTT GCCTTCCCTCTTTTCCTCCATCCATCGTGGACAATGCCTGCAAAATTTTCA CAGGAAGAAAGCCTATTCAGGATATTAACTTGAAATTTCCAGTGTCCTAA GAGCCTCTCATGAAGCCCAGTTCTAATAAGTGGCAAGCTGCTCTGCCGGG GTCATCTCCTGGGTCATCGGACTGATTGCTCAAGTTCTGCAGGAGAGGAA GCACCATTAGAACAACTCCATCAGAACAGCTCCACCGGGACTTGTGGGCC TAAATTTTCCTGGCCTAACGGGTCTGTCTCCAAACCCTCTTTCCTAAGAGC TGAGCAAACCAACCATAATAAACTTGACAAAAGACTTTGTTGTGGCCATG ACAGAGATACCGACTCAGGAGGGCTACCTACCTAGGTGTGATCATGCTGG GGGCTACCTTCTGAGTATATTTGTGAAAGCACATATTTGGGAACTCTGGT AGCTTGAGTTGGGAATGGGAAGGTTCTTTTTTACAGAAGTACTTCCCCAG GGACTTCTGTGTGTCACAGTCACCTCTGATGCCTTTATCTTGATGTTGCAT TGGGAATCTCAGCCATCAGCCCAAGTGCTTGTTTTATTCCAAGGCAGGGT AATCCCCGTCAACTTACTCTAACCTTTGCTGAAAACTAATCTTGATTCATT CTACTCTGAAAATCCAAAGGTGCTTCTGAGAGATAAGAGGGAAGGGGTA GAAGGAAAGGTGCCCCTTGAAATGGGAATTGAGCCTGTTAGAATTAAAA GCTTATCTCACCTCTGCTGGGGACAGTATTTGCACCACCAACCCCTCTCCT CACCTGCTTTGAGCGATAATCTTTATCAGATATTCTAAACTTAAAGGGATT CCCTTTAAACCAACTCAAGCTGATCTTTCCTATCTAGCCTGCTGTTTGGCT GTACTCATGGGCTTTGGTAATATCTCCTAAAAATGAGGTTTTGGTAATTTT TCCTATGCATTGGGCAACTGTGATCGTGACCACTGTGCTGTCTTGCTCCAG CCACTGCCCTGGCCTCAGCATATCAGGGCAGCCTGTGCTGGCTGCAATAC TGTGGTGCTTGGGCCACTGCCTGAGAGGAGCCAGGTTTGTGTGTGTCTGC ATGTGTGTGTGTGTGTGTTTGTACAGATTCAAGCAATGGATGCAAGGAAC ATGCTGTATGTAATAGAAGAAAGAAGTCCACGTTTTCGGCAGAAGTAGTG AGTCAGTGTGGAAGAGAGGTGAGGGTGTGCTTTACTTTTTGATAAAGAGA AAGATGTTTACTCATAAACCCTTCAAAAGGTATTAACAAAATGTTTACCA AACCTATTGCTTTATTTTAAAAACATAATTTGTGTTTTCTATTTGTAAGATC TGACATTTCGAGGCAATAAAAACTTCTCAGAAAGTAAAAAAAAAAAAAA A	

[67] Preferably, the expression of each of the 13-gene set is determined to provide the VEGF-signature score. An average expression value across the genes can be determined, *i.e.,* by determining a $\log_2$ expression ratio. The sample may be assigned or classified into a high expression group, an intermediate expression group, and a low expression group based on the 13-gene average $\log_2$ expression ratio using cutoff values (*i.e.*, -0.63/0.08) identified using X-tile

and relapse-free survival, as described in Camp *et al.*, *Clin. Cancer Res.* 10(21):7252-7259. The methods for determining the VEGF-signature score from a biological sample are as described in Hu *et al.*, *BMC Medicine* 7:9 (2009) and supplemental online material.

[68] The methods of the present invention may further include measuring the expression of DNA repair genes, such as *RAD17*, *RAD50*, and tumor suppressor *RB1*. Select nucleic acid sequences for these additional genes are shown in Table 8 below.

[69] Table 8.

GENE NAME GENBANK ACCESSIONNUMBER	SEQUENCE	SEQ ID NO:
RAD17 AF076838.1	ACCTGTATACCTTTTGAAACGTCACAGTCTCTAATCGTGAACGATTT GGGGCGGAGGGCTGAACAATGTGTTTTCTAGTGTGTCGAGGTGTTTA TAGGCTATGTGTGCCTCCAAACTGTAAAGTAGTCCAGTATACTTTCC AATGTATAAGTTTGTAGACCTTAAACTTTTCTTCTGGCTAACTTAAAA TCGTTGAATTCACTAGTTTGCATAAACATTTAAGAATTTGAAAACAC GGTTGAAAAACAGTGTTACCAAGAAATTTTGTAATAACATGTTCAAA TGAAGACAAAAATTTTACAGTTTAAGACTTAAATTCTTCGTCCACAG CAAGTGAATTCATGGTATTTTACTTTTTTGGGAAATACTGGAAATGA AGACCTGCAACTGTAATTTGAAATAAGGAAAACTTTAATTTTCAGTA TAAAAATTGCTCAAATAGAATTGCCTGATTTTAATGACAAAAGTATA TGGGAGTCCACATTTATGTAAGAAATGAAACTATAAAATGTATAAAT AATTTGCAAATCAGAATTGCTGTCGAAAGTTTTACTATAATGAAAGA TATTTTCATACTCTCAAAAATATAGAGGAAAGGGGCCAAGATTATAG TACCAGTCACAATCTTTTGATGAGGACGAAATGAATCAGGTAACAG ACTGGGTTGACCCATCATTTGATGATTTTCTAGAGTGTAGTGGCGTCT CTACTATTACTGCCACATCATTAGGTGTGAATAACTCAAGTCATAGA AGAAAAAATGGGCCTTCTACATTAGAAAGCAGCAGATTTCCAGCGA GAAAAAGAGGAAATCTATCTTCCTTAGAACAGATTTATGGTTTAGAA AATTCAAAAGAATATCTGTCTGAAAATGAACCATGGGTGGATAAAT ATAAACCAGAAACTCAGCATGAACTTGCTGTGCATAAAAAGAAAAT TGAAGAAGTCGAAACCTGGTTAAAAGCTCAAGTTTTAGAAAGGCAA CCAAAACAGGGTGGATCTATTTTATTAATAACAGGTCCTCCTGGATG TGGAAAGACAACGACCTTAAAAATACTATCAAAGGAGCATGGTATT CAAGTACAAGAGTGGATTAATCCAGTTTTACCAGACTTCCAAAAAG ATGATTTCAAGGGGATGTTTAATACTGAATCAAGCTTCCATATGTTT CCCTATCAGTCTCAGATAGCAGTTTTCAAAGAGTTTCTACTAAGAGC GACAAAGTATAACAAGTTACAAATGCTTGGAGATGATCTGAGAACT GATAAGAAGATAATTCTGGTTGAAGATTTACCTAACCAGTTTTATCG GGATTCTCATACTTTACATGAAGTTCTAAGGAAGTATGTGAGGATTG GTCGATGTCCTCTTATATTTATAATCTCGGACAGTCTCAGTGGAGAT AATAATCAAAGGTTATTGTTTCCCAAAGAAATTCAGGAAGAGTGTTC TATCTCAAATATTAGTTTCAACCCTGTGGCACCAACAATTATGATGA AATTTCTTAATCGAATAGTGACTATAGAAGCTAACAAGAATGGAGG AAAAATTACTGTCCCTGACAAAACTTCTCTAGAGTTGCTCTGTCAGG GATGTTCTGGTGATATCAGAAGTGCAATAAACAGCCTCCAGTTTTCT TCTTCAAAAGGAGAAAACAACTTACGGCCAAGGAAAAAAGGAATGT CTTTAAAATCAGATGCTGTGCTGTCAAAATCAAAACGAAGAAAAAA	211

	ACCTGATAGGGTTTTTGAAAATCAAGAGGTCCAAGCTATTGGTGGCA AAGATGTTTCTCTGTTTCTCTTCAGAGCTTTGGGGAAAATTCTATATT GTAAAAGAGCATCTTTAACAGAATTAGACTCACCTCGGTTGCCCTCT CATTTATCAGAATATGAACGGGATACATTACTTGTTGAACCTGAGGA GGTAGTAGAAATGTCACACATGCCTGGAGACTTATTTAATTTATATC TTCACCAAAACTACATAGATTTCTTCATGGAAATTGATGATATTGTG AGAGCCAGTGAATTTCTGAGTTTTGCAGATATCCTCAGTGGTGACTG GAATACACGCTCTTTACTCAGGGAATATAGCACATCTATAGCTACGA GAGGTGTGATGCATTCCAACAAAGCCCGAGGATATGCTCATTGCCA AGGAGGAGGATCAAGTTTTCGACCCTTGCACAAACCTCAGTGGTTTC TAATAAATAAAAAGTATCGGGAAAATTGCCTGGCAGCAAAAGCACT TTTTCCTGACTTCTGCCTACCAGCTTTATGCCTCCAAACTCAGCTATT GCCATACCTTGCTCTACTAACCATTCCAATGAGAAATCAAGCTCAGA TTTCTTTTATCCAAGATATTGGAAGGCTCCCTCTGAAGCGACACTTTG GAAGATTGAAAATGGAAGCCCTGACTGACAGGGAACATGGAATGAT AGACCCTGACAGCGGAGATGAAGCCCAGCTTAATGGAGGACATTCT GCAGAGGAATCTCTGGGTGAACCCACTCAAGCCACTGTGCCGGAAA CCTGGTCTCTTCCTTTGAGTCAGAATAGTGCCAGTGAACTGCCTGCT AGCCAGCCCCAGCCCTTTTCAGCCCAAGGAGACATGGAAGAAAACA TAATAATAGAAGACTACGAGAGTGATGGGACATAGAAGCCAGCCTG CTAATCAGATTGCTACTTCACAGCTTCATTTTTGTTTCATTCAGTGGT ACTTCAGCAGAGTTAATATGCTTTTCTGATGAATTACACAACAGTTT GTTAATTCTTCATTCTTGTAGTATTTCATCACAAGAAACCTACTCTTC TGTCATCTTGAAGTAAATAGAAGATCAAGCCTTCAAATCTCTTAATT TTTTCGGTATTTATTAAATCTGTGAGTGGTTTAAGGAGCGGTCAGTGT GTATAAAGTGTGTTTGAACATTATGCCAAATATCAAGATGTGAAGGA CTAATTCAGGATGCAAAAACGTTATTGGGGGGTTGTAAATATCAACT ATTCAACAGTTTAGGATGCAATTACGAGTGTAAACTGTGTGCCTTAT TTACACTTTATTGTCTCCCGCTTCTCAGATAGTTTTGATGTGTTGTAC AGTGGAATATCTTAGATACTTTTTGGAAAGTATTTACATAAGTTATA TCACAATTAAAATGTTGAATTTAA	
RAD50 NM_005732.3	TTTCCCGGCGTGCCCCAGGAGAGCGGCGTGGACGCGTGCGGGCCTA GAGGCCCACGTGATCCGCAGGGCGGCCGAGGCAGGAAGCTGTGAGT GCGCGGTTGCGGGGTCGCATTGTGGCTACGGCTTTGCGTCCCCGGCG GGCAGCCCCAGGCTGGTCCCCGCCTCCGCTCTCCCCACCGGCGGGGA AAGCAGCTGGTGTGGGAGGAAAGGCTCCATCCCCCGCCCCCTCTCTC CCGCTGTTGGCTGGCAGGATCTTTTGGCAGTCCTGTGGCCTCGCTCC CCGCCCGGATCCTCCTGACCCTGAGATTCGCGGGTCTCACGTCCCGT GCACGCCTTGCTTCGGCCTCAGTTAAGCCTTTGTGGACTCCAGGTCC CTGGTGAGATTAGAAACGTTTGCAAACATGTCCCGGATCGAAAAGA TGAGCATTCTGGGCGTGCGGAGTTTTGGAATAGAGGACAAAGATAA GCAAATTATCACTTTCTTCAGCCCCCTTACAATTTTGGTTGGACCCAA TGGGGCGGGAAAGACGACCATCATTGAATGTCTAAAATATATTTGTA CTGGAGATTTCCCTCCTGGAACCAAAGGAAATACATTTGTACACGAT CCCAAGGTTGCTCAAGAAACAGATGTGAGAGCCCAGATTCGTCTGC AATTTCGTGATGTCAATGGAGAACTTATAGCTGTGCAAAGATCTATG GTGTGTACTCAGAAAAGCAAAAAGACAGAATTTAAAACTCTGGAAG GAGTCATTACTAGAACAAAGCATGGTGAAAAGGTCAGTCTGAGCTC TAAGTGTGCAGAAATTGACCGAGAAATGATCAGTTCTCTTGGGGTTT CCAAGGCTGTGCTAAATAATGTCATTTTCTGTCATCAAGAAGATTCT AATTGGCCTTTAAGTGAAGGAAAGGCTTTGAAGCAAAAGTTTGATG AGATTTTTTCAGCAACAAGATACATTAAAGCCTTAGAAACACTTCGG CAGGTACGTCAGACACAAGGTCAGAAAGTAAAAGAATATCAAATGG AACTAAAATATCTGAAGCAATATAAGGAAAAAGCTTGTGAGATTCG TGATCAGATTACAAGTAAGGAAGCCCAGTTAACATCTTCAAAGGAA ATTGTCAAATCCTATGAGAATGAACTTGATCCATTGAAGAATCGTCT	212

	AAAAGAAATTGAACATAATCTCTCTAAAATAATGAAACTTGACAAT GAAATTAAAGCCTTGGATAGCCGAAAGAAGCAAATGGAGAAAGATA ATAGTGAACTGGAAGAGAAAATGGAAAAGGTTTTTCAAGGGACTGA TGAGCAACTAAATGACTTATATCACAATCACCAGAGAACAGTAAGG GAGAAAGAAAGGAAATTGGTAGACTGTCATCGTGAACTGGAAAAAC TAAATAAAGAATCTAGGCTTCTCAATCAGGAAAAATCAGAACTGCTT GTTGAACAGGGTCGTCTACAGCTGCAAGCAGATCGCCATCAAGAAC ATATCCGAGCTAGAGATTCATTAATTCAGTCTTTGGCAACACAGCTA GAATTGGATGGCTTTGAGCGTGGACCATTCAGTGAAAGACAGATTA AAAATTTTCACAAACTTGTGAGAGAGAGACAAGAAGGGGAAGCAAA AACTGCCAACCAACTGATGAATGACTTTGCAGAAAAAGAGACTCTG AAACAAAAACAGATAGATGAGATAAGAGATAAGAAAACTGGACTG GGAAGAATAATTGAGTTAAAATCAGAAATCCTAAGTAAGAAGCAGA ATGAGCTGAAAAATGTGAAGTATGAATTACAGCAGTTGGAAGGATC TTCAGACAGGATTCTTGAACTGGACCAGGAGCTCATAAAAGCTGAA CGTGAGTTAAGCAAGGCTGAGAAAAACAGCAATGTAGAAACCTTAA AAATGGAAGTAATAAGTCTCCAAAATGAAAAAGCAGACTTAGACAG GACCCTGCGTAAACTTGACCAGGAGATGGAGCAGTTAAACCATCAT ACAACAACACGTACCCAAATGGAGATGCTGACCAAAGACAAAGCTG ACAAAGATGAACAAATCAGAAAAATAAAATCTAGGCACAGTGATGA ATTAACCTCACTGTTGGGATATTTTCCCAACAAAAAACAGCTTGAAG ACTGGCTACATAGTAAATCAAAAGAAATTAATCAGACCAGGGACAG ACTTGCCAAATTGAACAAGGAACTAGCTTCATCTGAGCAGAATAAA AATCATATAAATAATGAACTAAAAAGAAAGGAAGAGCAGTTGTCCA GTTACGAAGACAAGCTGTTTGATGTTTGTGGTAGCCAGGATTTTGAA AGTGATTTAGACAGGCTTAAAGAGGAAATTGAAAAATCATCAAAAC AGCGAGCCATGCTGGCTGGAGCCACAGCAGTTTACTCCCAGTTCATT ACTCAGCTAACAGACGAAAACCAGTCATGTTGCCCCGTTTGTCAGAG AGTTTTTCAGACAGAGGCTGAGTTACAAGAAGTCATCAGTGATTTGC AGTCTAAACTGCGACTTGCTCCAGATAAACTCAAGTCAACAGAATCA GAGCTAAAAAAAAAGGAAAAGCGGCGTGATGAAATGCTGGGACTTG TGCCCATGAGGCAAAGCATAATTGATTTGAAGGAGAAGGAAATACC AGAATTAAGAAACAAACTGCAGAATGTCAATAGAGACATACAGCGC CTAAAGAACGACATAGAAGAACAAGAAACACTCTTGGGTACAATAA TGCCTGAAGAAGAAAGTGCCAAAGTATGCCTGACAGATGTTACAAT TATGGAGAGGTTCCAGATGGAACTTAAAGATGTTGAAAGAAAAATT GCACAACAAGCAGCTAAGCTACAAGGAATAGACTTAGATCGAACTG TCCAACAAGTCAACCAGGAGAAACAAGAGAAACAGCACAAGTTAG ACACAGTTTCTAGTAAGATTGAATTGAATCGTAAGCTTATACAGGAC CAGCAGGAACAGATTCAACATCTAAAAAGTACAACAAATGAGCTAA AATCTGAGAAACTTCAGATATCCACTAATTTGCAACGTCGTCAGCAA CTGGAGGAGCAGACTGTGGAATTATCCACTGAAGTTCAGTCTTTGTA CAGAGAGATAAAGGATGCTAAAGAGCAGGTAAGCCCTTTGGAAACA ACATTGGAAAAGTTCCAGCAAGAAAAAGAAGAATTAATCAACAAAA AAAATACAAGCAACAAAATAGCACAGGATAAACTGAATGATATTAA AGAGAAGGTTAAAAATATTCATGGCTATATGAAAGACATTGAGAAT TATATTCAAGATGGGAAAGACGACTATAAGAAGCAAAAAGAAACTG AACTTAATAAAGTAATAGCTCAACTAAGTGAATGCGAGAAACACAA AGAAAAGATAAATGAAGATATGAGACTCATGAGACAAGATATTGAT ACACAGAAGATACAAGAAAGGTGGCTACAAGATAACCTTACTTTAA GAAAAAGAAATGAGGAACTAAAAGAAGTTGAAGAAGAAAGAAAAC AACATTTGAAGGAAATGGGTCAAATGCAGGTTTTGCAAATGAAAAG TGAACATCAGAAGTTGGAAGAGAACATAGACAATATAAAAAGAAAT CATAATTTGGCATTAGGGCGACAGAAAGGTTATGAAGAAGAAATTA TTCATTTTAAGAAAGAACTTCGAGAACCACAATTTCGGGATGCTGAG GAAAAGTATAGAGAAATGATGATTGTTATGAGGACAACAGAACTTG	

	TGAACAAGGATCTGGATATTTATTATAAGACTCTTGACCAAGCAATA ATGAAATTTCACAGTATGAAAATGGAAGAAATCAATAAAATTATAC GTGACCTGTGGCGAAGTACCTATCGTGGACAAGATATTGAATACATA GAAATACGGTCTGATGCCGATGAAAATGTATCAGCTTCTGATAAAAG GCGGAATTATAACTACCGAGTGGTGATGCTGAAGGGAGACACAGCC TTGGATATGCGAGGACGATGCAGTGCTGGACAAAAGGTATTAGCCT CACTCATCATTCGCCTGGCCCTGGCTGAAACGTTCTGCCTCAACTGT GGCATCATTGCCTTGGATGAGCCAACAACAAATCTTGACCGAGAAA ACATTGAATCTCTTGCACATGCTCTGGTTGAGATAATAAAAAGTCGC TCACAGCAGCGTAACTTCCAGCTTCTGGTAATCACTCATGATGAAGA TTTTGTGGAGCTTTTAGGACGTTCTGAATATGTGGAGAAATTCTACA GGATTAAAAAGAACATCGATCAGTGCTCAGAGATTGTGAAATGCAG TGTTAGCTCCCTGGGATTCAATGTTCATTAAAAATATCCAAGATTTA AATGCCATAGAAATGTAGGTCCTCAGAAAGTGTATAATAAGAAACT TATTTCTCATATCAACTTAGTCAATAAGAAAATATATTCTTTCAAAG GAACATTGTGTCTAGGATTTTGGATGTTGAGAGGTTCTAAAATCATG AAACTTGTTTCACTGAAAATTGGACAGATTGCCTGTTTCTGATTTGCT GCTCTTCATCCCATTCCAGGCAGCCTCTGTCAGGCCTTCAGGGTTCA GCAGTACAGCCGAGACTCGACTCTGTGCCTCCCTCCCCAGTGCAAAT GCATGCTTCTTCTCAAAGCACTGTTGAGAAGGAGATAATTACTGCCT TGAAAATTTATGGTTTTGGTATTTTTTTAAATCATAGTTAAATGTTAC CTCTGAATTTACTTCCTTGCATGTGGTTTGAAAAACTGAGTATTAATA TCTGAGGATGACCAGAAATGGTGAGATGTATGTTTGGCTCTGCTTTT AACTTTATAAATCCAGTGACCTCTCTCTCTGGGACTTGGTTTCCCCAA CTAAAATTTGAAGTAGTTGAATGGGGTCTCAAAGTTTGACAGGAACC TTAAGTAATCATCTAAGTCAGTACCCACCACCTTCTTCTCCTACATAT CCCTTCCAGATGGTCATCCAGACTCAGAGCTCTCTCTACAGAGAGGA AATTCTCCACTGTGCACACCCACCTTTGGAAAGCTCTGACCACTTGA GGCCTGATCTGCCCATCGTGAAGAAGCCTGTAACACTCCTCTGCGTC TATCCTGTGTAGCATACTGGCTTCACCATCAATCCTGATTCCTCTCTA AGTGGGCATTGCCATGTGGAAGGCAAGCCAGGCTCACTCACAGAGT CAAGGCCTGCTCCCTGTAGGGTCCAACCAGACCTGGAAGAACAGGC CTCTCCATTTGCTCTTCAGATGCCACTTCTAAGAAAAGCCTAATCAC AGTTTTTCCTGGAATTGCCAGCTGACATCTTGAATCCTTCCATTCCAC ACAGAATGCAACCAAGTCACACGCTTTTGAATTATGCTTTGTAGAGT TTTGTCATTCAGAGTCAGCCAGGACCATACCGGGTCTTGATTCAGTC ACATGGCATGGTTTTGTGCCATCTGTAGCTATAATGAGCATGTTTGC CTAGACAGCTTTTCTCAACTGGGTCCAGAAGAGAATTAAGCCCTAAG GTCCTAAGGCATCTATCTGTGCTAGGTTAAATGGTTGGCCCCCAAAG ATAGACAGGTCCTGATTTCTAGAACCCGTGACTGTTACTTTATACAG CAAAGGAAACTTTGCAGATGTGATTAAAGCTAAGGACCTTAAGACA GAGTATCCTGGGGGTGGTGGTGGGGTGGGGGGGGGTCCTAAATGTA ATCACGAGTAAGATTAAGAGCAAATCAATTCTAGTCATATATTAAAC ATCCACAATAACCAAGATATTTTTATCCCAAGAATGCAAGATTTCAG AAAATGAAAAATCTGTTGATAAATCCATCACTATAATAAAACCGAA GGTGAAAAAAAATTCTGAAAAAATTCTAGCAGCTATATTTGATAAAAT TCAACATCTCCTAGCTTTAGCAAACTCACAGTTTTGCAAATAATATTT TCTTAATGTTATCTGTTGCTAAATCAAAATTAAACAGTCATCTTAACT GCAAAATAAAACATTTCTCAGTAAATATTAAAGCCAGTTACCTTCTA TCAACATGTTAATGAAAGTGCTAGTTGTTGCAGCAAAGAATAACAA AGGCAATACACGATCAATATAGGCAGTGAAACAAAAGTATCATTTG CAAGTTAAAACAGACTTCCCAATTTTAAATCTGGTTTCCCCCTGAAT ATGTGGCATCCTTGGCAGCACTTCTGAGAGTGGCTGCTTTCATTCCA AGAAGCCCATGGGTTTGGAGGTGGGATAGGTGCCTTTCTGGCTTCTC ATTGCTGCTTCTAGATCAGTCTCCAAATATCCCCCTTCCCCACATTGG AATGAATAGCCATCACAGCATGGATGGAGGTTAGAATGAGCCAGAC	

	TGCCTGGGCTCAAATCCTAGCACACCACTCACTAGCTGGGGACCTTG AGCAAGTTATTTGTCCTGTTTTCTGTTTCCTTATATGTAAAAGTGGGT AAAATGGTACATATTTTGTAGGGTTGTTATGAAGATTGAATGACATT ATTTACAAACTGCTTAGAACTGCTTGCCACCTACTAAATACTGTGTA AGTGTTCAAGAAAAAGCTGTCTTCATTTCA	
RB1 NM_000321.2	GCTCAGTTGCCGGGCGGGGGAGGGCGCGTCCGGTTTTTCTCAGGGG ACGTTGAAATTATTTTTGTAACGGGAGTCGGGAGAGGACGGGGCGT GCCCCGACGTGCGCGCGCGTCGTCCTCCCCGGCGCTCCTCCACAGCT CGCTGGCTCCCGCCGCGGAAAGGCGTCATGCCGCCCAAAACCCCCC GAAAAACGGCCGCCACCGCCGCCGCTGCCGCCGCGGAACCCCCGGC ACCGCCGCCGCCGCCCCCTCCTGAGGAGGACCCAGAGCAGGACAGC GGCCCGGAGGACCTGCCTCTCGTCAGGCTTGAGTTTGAAGAAACAG AAGAACCTGATTTTACTGCATTATGTCAGAAATTAAAGATACCAGAT CATGTCAGAGAGAGAGCTTGGTTAACTTGGGAGAAAGTTTCATCTGT GGATGGAGTATTGGGAGGTTATATTCAAAAGAAAAAGGAACTGTGG GGAATCTGTATCTTTATTGCAGCAGTTGACCTAGATGAGATGTCGTT CACTTTTACTGAGCTACAGAAAAACATAGAAATCAGTGTCCATAAAT TCTTTAACTTACTAAAAGAAATTGATACCAGTACCAAAGTTGATAAT GCTATGTCAAGACTGTTGAAGAAGTATGATGTATTGTTTGCACTCTT CAGCAAATTGGAAAGGACATGTGAACTTATATATTTGACACAACCC AGCAGTTCGATATCTACTGAAATAAATTCTGCATTGGTGCTAAAAGT TTCTTGGATCACATTTTTATTAGCTAAAGGGGAAGTATTACAAATGG AAGATGATCTGGTGATTTCATTTCAGTTAATGCTATGTGTCCTTGACT ATTTTATTAAACTCTCACCTCCCATGTTGCTCAAAGAACCATATAAA ACAGCTGTTATACCCATTAATGGTTCACCTCGAACACCCAGGCGAGG TCAGAACAGGAGTGCACGGATAGCAAAACAACTAGAAAATGATACA AGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATATAGATGA GGTGAAAAATGTTTATTTCAAAAATTTTATACCTTTTATGAATTCTCT TGGACTTGTAACATCTAATGGACTTCCAGAGGTTGAAAATCTTTCTA AACGATACGAAGAAATTTATCTTAAAAATAAAGATCTAGATGCAAG ATTATTTTTGGATCATGATAAAACTCTTCAGACTGATTCTATAGACA GTTTTGAAACACAGAGAACACCACGAAAAAGTAACCTTGATGAAGA GGTGAATGTAATTCCTCCACACACTCCAGTTAGGACTGTTATGAACA CTATCCAACAATTAATGATGATTTTAAATTCAGCAAGTGATCAACCT TCAGAAAATCTGATTTCCTATTTTAACAACTGCACAGTGAATCCAAA AGAAAGTATACTGAAAAGAGTGAAGGATATAGGATACATCTTTAAA GAGAAATTTGCTAAAGCTGTGGGACAGGGTTGTGTCGAAATTGGATC ACAGCGATACAAACTTGGAGTTCGCTTGTATTACCGAGTAATGGAAT CCATGCTTAAATCAGAAGAAGAACGATTATCCATTCAAAATTTTAGC AAACTTCTGAATGACAACATTTTTCATATGTCTTTATTGGCGTGCGCT CTTGAGGTTGTAATGGCCACATATAGCAGAAGTACATCTCAGAATCT TGATTCTGGAACAGATTTGTCTTTCCCATGGATTCTGAATGTGCTTAA TTTAAAAGCCTTTGATTTTTACAAAGTGATCGAAAGTTTTATCAAAG CAGAAGGCAACTTGACAAGAGAAATGATAAAACATTTAGAACGATG TGAACATCGAATCATGGAATCCCTTGCATGGCTCTCAGATTCACCTT TATTTGATCTTATTAAACAATCAAAGGACCGAGAAGGACCAACTGAT CACCTTGAATCTGCTTGTCCTCTTAATCTTCCTCTCCAGAATAATCAC ACTGCAGCAGATATGTATCTTTCTCCTGTAAGATCTCCAAAGAAAAA AGGTTCAACTACGCGTGTAAATTCTACTGCAAATGCAGAGACACAA GCAACCTCAGCCTTCCAGACCCAGAAGCCATTGAAATCTACCTCTCT TTCACTGTTTTATAAAAAAGTGTATCGGCTAGCCTATCTCCGGCTAA ATACACTTTGTGAACGCCTTCTGTCTGAGCACCCAGAATTAGAACAT ATCATCTGGACCCTTTTCCAGCACACCCTGCAGAATGAGTATGAACT CATGAGAGACAGGCATTTGGACCAAATTATGATGTGTTCCATGTATG GCATATGCAAAGTGAAGAATATAGACCTTAAATTCAAAATCATTGTA ACAGCATACAAGGATCTTCCTCATGCTGTTCAGGAGACATTCAAACG	213

	TGTTTTGATCAAAGAAGAGGAGTATGATTCTATTATAGTATTCTATA ACTCGGTCTTCATGCAGAGACTGAAAACAAATATTTTGCAGTATGCT TCCACCAGGCCCCCTACCTTGTCACCAATACCTCACATTCCTCGAAG CCCTTACAAGTTTCCTAGTTCACCCTTACGGATTCCTGGAGGGAACA TCTATATTTCACCCCTGAAGAGTCCATATAAAATTTCAGAAGGTCTG CCAACACCAACAAAAATGACTCCAAGATCAAGAATCTTAGTATCAA TTGGTGAATCATTCGGGACTTCTGAGAAGTTCCAGAAAATAAATCAG ATGGTATGTAACAGCGACCGTGTGCTCAAAAGAAGTGCTGAAGGAA GCAACCCTCCTAAACCACTGAAAAAACTACGCTTTGATATTGAAGGA TCAGATGAAGCAGATGGAAGTAAACATCTCCCAGGAGAGTCCAAAT TTCAGCAGAAACTGGCAGAAATGACTTCTACTCGAACACGAATGCA AAAGCAGAAAATGAATGATAGCATGGATACCTCAAACAAGGAAGA GAAATGAGGATCTCAGGACCTTGGTGGACACTGTGTACACCTCTGGA TTCATTGTCTCTCACAGATGTGACTGTATAACTTTCCCAGGTTCTGTT TATGGCCACATTTAATATCTTCAGCTCTTTTTGTGGATATAAAATGTG CAGATGCAATTGTTTGGGTGATTCCTAAGCCACTTGAAATGTTAGTC ATTGTTATTTATACAAGATTGAAAATCTTGTGTAAATCCTGCCATTTA AAAAGTTGTAGCAGATTGTTTCCTCTTCCAAAGTAAAATTGCTGTGC TTTATGGATAGTAAGAATGGCCCTAGAGTGGGAGTCCTGATAACCCA GGCCTGTCTGACTACTTTGCCTTCTTTTGTAGCATATAGGTGATGTTT GCTCTTGTTTTTATTAATTTATATGTATATTTTTTTAATTTAACATGAA CACCCTTAGAAAATGTGTCCTATCTATCTTCCAAATGCAATTTGATTG ACTGCCCATTCACCAAAATTATCCTGAACTCTTCTGCAAAAATGGAT ATTATTAGAAATTAGAAAAAAATTACTAATTTTACACATTAGATTTT ATTTTACTATTGGAATCTGATATACTGTGTGCTTGTTTTATAAAATTT TGCTTTTAATTAAATAAAAGCTGGAAGCAAAGTATAACCATATGATA CTATCATACTACTGAAACAGATTTCATACCTCAGAATGTAAAAGAAC TTACTGATTATTTTCTTCATCCAACTTATGTTTTTAAATGAGGATTAT TGATAGTACTCTTGGTTTTTATACCATTCAGATCACTGAATTTATAAA GTACCCATCTAGTACTTGAAAAAGTAAAGTGTTCTGCCAGATCTTAG GTATAGAGGACCCTAACACAGTATATCCCAAGTGCACTTTCTAATGT TTCTGGGTCCTGAAGAATTAAGATACAAATTAATTTTACTCCATAAA CAGACTGTTAATTATAGGAGCCTTAATTTTTTTTTCATAGAGATTTGT CTAATTGCATCTCAAAATTATTCTGCCCTCCTTAATTTGGGAAGGTTT GTGTTTTCTCTGGAATGGTACATGTCTTCCATGTATCTTTTGAACTGG CAATTGTCTATTTATCTTTTATTTTTTTAAGTCAGTATGGTCTAACACT GGCATGTTCAAAGCCACATTATTTCTAGTCCAAAATTACAAGTAATC AAGGGTCATTATGGGTTAGGCATTAATGTTTCTATCTGATTTTGTGCA AAAGCTTCAAATTAAAACAGCTGCATTAGAAAAAGAGGCGCTTCTC CCCTCCCCTACACCTAAAGGTGTATTTAAACTATCTTGTGTGATTAAC TTATTTAGAGATGCTGTAACTTAAAATAGGGGATATTTAAGGTAGCT TCAGCTAGCTTTTAGGAAAATCACTTTGTCTAACTCAGAATTATTTTT AAAAAGAAATCTGGTCTTGTTAGAAAACAAAATTTTATTTTGTGCTC ATTTAAGTTTCAAACTTACTATTTTGACAGTTATTTTGATAACAATGA CACTAGAAAACTTGACTCCATTTCATCATTGTTTCTGCATGAATATCA TACAAATCAGTTAGTTTTTAGGTCAAGGGCTTACTATTTCTGGGTCTT TTGCTACTAAGTTCACATTAGAATTAGTGCCAGAATTTTAGGAACTT CAGAGATCGTGTATTGAGATTTCTTAAATAATGCTTCAGATATTATT GCTTTATTGCTTTTTTGTATTGGTTAAAACTGTACATTTAAAATTGCT ATGTTACTATTTTCTACAATTAATAGTTTGTCTATTTTAAAATAAATT AGTTGTTAAGAGTCTTAA	

[70] ***Breast Cancer***

[71] Subjects with breast cancer tumors that fit in the Luminal A or Basal-like subtype,

classified by gene expression analysis, were surprisingly found to have a significantly decreased rate of local recurrence and significantly increased rate of breast cancer specific survival when treated with a post-mastectomy breast cancer treatment that included radiation.

[72] Classifying breast cancer tumors by intrinsic subtype and treating patients with radiation only when this treatment provides increased therapeutic efficacy to offset the added cost and side effects can improve the clinical outcome and quality of life of thousands of patients.

[73] For the purposes of the present disclosure, "breast cancer" includes, for example, those conditions classified by biopsy or histology as malignant pathology. The clinical delineation of breast cancer diagnoses is well known in the medical arts. One of skill in the art will appreciate that breast cancer refers to any malignancy of the breast tissue, including, for example, carcinomas and sarcomas. Particular embodiments of breast cancer include ductal carcinoma *in situ* (DCIS), lobular carcinoma *in situ* (LCIS), or mucinous carcinoma. Breast cancer also refers to infiltrating ductal carcinoma (IDC), lobular neoplasia or infiltrating lobular carcinoma (ILC). In most embodiments of the disclosure, the subject of interest is a human patient suspected of or actually diagnosed with breast cancer.

[74] Breast cancer includes all forms of cancer of the breast. Breast cancer can include primary epithelial breast cancers. Breast cancer can include cancers in which the breast is involved by other tumors such as lymphoma, sarcoma or melanoma. Breast cancer can include carcinoma of the breast, ductal carcinoma of the breast, lobular carcinoma of the breast, undifferentiated carcinoma of the breast, cystosarcoma phyllodes of the breast, angiosarcoma of the breast, and primary lymphoma of the breast. Breast cancer can include Stage I, II, IIIA, IIIB, IIIC and IV breast cancer. Ductal carcinoma of the breast can include invasive carcinoma, invasive carcinoma *in situ* with predominant intraductal component, inflammatory breast cancer, and a ductal carcinoma of the breast with a histologic type selected from the group consisting of comedo, mucinous (colloid), medullary, medullary with lymphcytic infiltrate, papillary, scirrhous, and tubular. Lobular carcinoma of the breast can include invasive lobular carcinoma with predominant *in situ* component, invasive lobular carcinoma, and infiltrating lobular carcinoma. Breast cancer can include Paget's disease, Paget's disease with intraductal carcinoma, and Paget's disease with invasive ductal carcinoma. Breast cancer can include breast neoplasms having histologic and ultrastructual heterogeneity (*e.g.*, mixed cell types).

[75] A breast cancer that is to be treated can include familial breast cancer. A breast cancer that is to be treated can include sporadic breast cancer. A breast cancer that is to be treated can arise in a male subject. A breast cancer that is to be treated can arise in a female subject. A breast cancer that is to be treated can arise in a premenopausal female subject or a postmenopausal female subject. A breast cancer that is to be treated can be in a pre-mastectomy female subject or a post-mastectomy female patient.

[76] A breast cancer that is to be treated can include a localized tumor of the breast. A breast cancer that is to be treated can include a tumor of the breast that is associated with a negative sentinel lymph node (SLN) biopsy. A breast cancer that is to be treated can include a tumor of the breast that is associated with a positive sentinel lymph node (SLN) biopsy. A breast cancer that is to be treated can include a tumor of the breast that is associated with one or more positive axillary lymph nodes, where the axillary lymph nodes have been staged by any applicable method. A breast cancer that is to be treated can include a tumor of the breast that has been typed as having nodal negative status (*e.g.*, node-negative) or nodal positive status (*e.g.*, node-positive). A breast cancer that is to be treated can include a tumor of the breast that has been typed as being hormone receptor negative (*e.g.*, estrogen receptor-negative) or hormone receptor positive status (*e.g.*, estrogen receptor-positive). A breast cancer that is to be treated can include a tumor of the breast that has metastasized to other locations in the body. A breast cancer that is to be treated can be classified as having metastasized to a location selected from the group consisting of bone, lung, liver, lymph nodes, and brain. A breast cancer that is to be treated can be classified according to a characteristic selected from the group consisting of metastatic, localized, regional, local-regional, locally advanced, distant, multicentric, bilateral, ipsilateral, contralateral, newly diagnosed, recurrent, and inoperable.

[77] For the purposes of the present disclosure, "a breast cancer treatment comprising radiation" is a breast cancer treatment that includes radiation therapy, radiation treatment or radiation exposure. A "breast cancer treatment comprising radiation" can also be a breast cancer treatment that includes other anti-cancer or chemotherapeutic agents.

[78] For the purposes of the present disclosure, "a breast cancer treatment not comprising radiation" is a breast cancer treatment that does not include any radiation therapy, radiation treatment or radiation exposure. These treatments can contain other anti-cancer or chemotherapeutic agents.

[79] By "prolong" is meant an increase in time relative to a reference, standard, or control condition. Time may be increased anywhere from 0.01% to 10,000%, *e.g.*, 0.01%, 0.05%, 0.1%, 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 100%, 200%, 300%, 400%, 500%, 600%, 700%, 800%, 900%, 1,000%, 2,000%, 3,000%, 4,000%, 5,000%, 6,000%, 7,000%, 8,000%, 9,000%, and 10,000%.

[80] The amount of radiation used in radiation therapy (*e.g.*, photon radiation therapy) is measured in gray (Gy), and varies depending on the type and stage of cancer being treated. The total dose of radiation therapy can be between about 20 to about 80 Gy. A dose for a solid epithelial tumor ranges can be from about 60 to about 80 Gy. A dose for lymphomas can be from about 20 Gy to about 40 Gy. Preventative (adjuvant) doses can be about 40 Gy to about 60 Gy. Preferably, about 45 Gy to about 60 Gy. Preferably, radiation therapy is administered in about 1.5 Gy to about 2.0 Gy fractions.

[81] The total dose is fractionated (spread out over time), which permits normal cells time to recover, while tumor cells are generally less efficient in repair between fractions. Fractionation also allows tumor cells that were in a relatively radio-resistant phase of the cell cycle during one treatment to cycle into a sensitive phase of the cycle before the next fraction is given. One fractionation schedule for adults can be about 1.8 to about 2.0 Gy per day, five days a week. One fractionation schedule for children can be about 1.5 to about 1.8 Gy per day.

[82] Accelerated Partial Breast Irradiation (APBI) is another fraction schedule use to treat breast cancer. APBI can be performed with either brachytherapy or with external beam radiation. APBI normally involves two high-dose fractions per day for five days, compared to whole breast irradiation, in which a single, smaller fraction is given five times a week over a six-to-seven-week period.

[83] Classes of anti-cancer or chemotherapeutic agents can include anthracycline agents, alkylating agents, nucleoside analogs, platinum agents, taxanes, vinca agents, anti-estrogen drugs, aromatase inhibitors, ovarian suppression agents, endocrine/hormonal agents, bisphophonate therapy agents and targeted biological therapy agents.

[84] Specific anti-cancer or chemotherapeutic agents can include cyclophosphamide, fluorouracil (or 5-fluorouracil or 5-FU), methotrexate, thiotepa, carboplatin, cisplatin, anthracyclines, gemcitabine, taxanes, paclitaxel, protein-bound paclitaxel, docetaxel, vinorelbine, tamoxifen, raloxifene, toremifene, fulvestrant, irinotecan, ixabepilone, temozolmide, topotecan,

vincristine, vinblastine, eribulin, mutamycin, capecitabine, capecitabine, anastrozole, exemestane, letrozole, leuprolide, abarelix, buserlin, goserelin, megestrol acetate, risedronate, pamidronate, ibandronate, alendronate, denosumab, zoledronate, trastuzumab, tykerb or bevacizumab, or combinations thereof; one such combination is CMF which includes cyclophosphamide, methotrexate, and fluorouracil.

[85] *Description of Intrinsic Subtype Biology*

[86] Luminal subtypes: The most common subtypes of breast cancer are the luminal subtypes, Luminal A and Luminal B. Prior studies suggest that Luminal A comprises approximately 30% to 40% and Luminal B approximately 20% of all breast cancers, but they represent over 90 % of hormone receptor positive breast cancers (Nielsen *et al. Clin. Cancer Res.*, 16(21):5222-5232 (2009)). The gene expression pattern of these subtypes resembles the luminal epithelial component of the breast. These tumors are characterized by high expression of estrogen receptor (ER), progesterone receptor (PR), and genes associated with ER activation, such as *LIV1*, *GATA3*, and *cyclin D1*, as well as expression of luminal cytokeratins 8 and 18 (Lisa Carey & Charles Perou (2009). "Gene Arrays, Prognosis, and Therapeutic Interventions". Jay R. Harris *et al.* (4th ed.), "Diseases of the breast" (pp. 458-472). Philadelphia, PA: Lippincott Williams & Wilkins).

[87] Luminal A: Luminal A (LumA) breast cancers exhibit low expression of genes associated with cell cycle activation and the *ERBB2* cluster resulting in a better prognosis than Luminal B. The Luminal A subgroup has the most favorable prognosis of all subtypes and is enriched for endocrine therapy-responsive tumors.

[88] Luminal B: Luminal B (LumB) breast cancers also express ER and ER-associated genes. Genes associated with cell cycle activation are highly expressed and this tumor type can be HER2(+) (~20%) or HER2(-). The prognosis is unfavorable (despite ER expression) and endocrine therapy responsiveness is generally diminished relative to LumA.

[89] HER2-enriched: The HER2-enriched subtype is generally ER-negative and is HER2-positive in the majority of cases with high expression of the *ERBB2* cluster, including ERBB2 and GRB7. Genes associated with cell cycle activation are highly expressed and these tumors have a poor outcome.

[90] Basal-like: The Basal-like subtype is generally ER-negative, is almost always clinically HER2-negative and expresses a suite of "Basal" biomarkers including the basal epithelial cytokeratins (CK) and epidermal growth factor receptor (*EGFR*). Genes associated with cell cycle activation are highly expressed.

[91] *Clinical variables*

[92] The methods described herein, *e.g.*, the PAM50 or NANO46 classification models, may be further combined with information on clinical variables (also referred to herein as "clinicopathological variables") to generate a continuous risk of recurrence (ROR) predictor. As described herein, a number of clinical and prognostic breast cancer factors are known in the art and are used to predict treatment outcome and the likelihood of disease recurrence. Such factors include, for example, lymph node involvement, tumor size, histologic grade, estrogen and progesterone hormone receptor status, *HER2* levels, and tumor ploidy. In one embodiment, risk of recurrence (ROR) score is provided for a subject diagnosed with or suspected of having breast cancer. This score uses an above-described classification model, *e.g.*, the PAM50 or NANO46 classification models, in combination with clinical factors of lymph node status (N) and tumor size (T). Assessment of clinical variables is based on the American Joint Committee on Cancer (AJCC) standardized system for breast cancer staging. In this system, primary tumor size is categorized on a scale of 0-4 (T0: no evidence of primary tumor; T1: < 2 cm; T2: > 2 cm to < 5 cm; T3: > 5 cm; T4: tumor of any size with direct spread to chest wall or skin). Lymph node status is classified as N0-N3 (N0: regional lymph nodes are free of metastasis; N1: metastasis to movable, same-side axillary lymph node(s); N2: metastasis to same-side lymph node(s) fixed to one another or to other structures; N3: metastasis to same-side lymph nodes beneath the breastbone). Methods of identifying breast cancer patients and staging the disease are well known and may include manual examination, biopsy, review of patient's and/or family history, and imaging techniques, such as mammography, magnetic resonance imaging (MRI), and positron emission tomography (PET).

[93] *Sample Source*

[94] In one embodiment of the present disclosure, breast cancer subtype is assessed through the evaluation of expression patterns, or profiles, of the intrinsic genes listed in Table 1 in one or

more subject samples and/or fluorescence *in situ* hybridization (FISH) analysis or immunohistochemistry (IHC) performed to ascertain the *HER2* status of the cancer. As used herein, the term "subject" or "subject sample", refers to an individual regardless of health and/or disease status. A subject can be a subject, a study participant, a control subject, a screening subject, or any other class of individual from whom a sample is obtained and assessed in the context of the disclosure. Accordingly, a subject can be diagnosed with breast cancer, can present with one or more symptoms of breast cancer, or a predisposing factor, such as a family (genetic) or medical history (medical) factor, for breast cancer, can be undergoing treatment or therapy for breast cancer, or the like. As such, the subject is a subject in need of treatment for breast cancer, detection of breast cancer, classification of a cancer, screening of likelihood of effectiveness of a treatment, and prediction of local-regional relapse free or breast cancer specific survival in response to a treatment. Alternatively, a subject can be healthy with respect to any of the aforementioned factors or criteria. It will be appreciated that the term "healthy" as used herein, is relative to breast cancer status, as the term "healthy" cannot be defined to correspond to any absolute evaluation or status. Thus, an individual defined as healthy with reference to any specified disease or disease criterion, can in fact be diagnosed with any other one or more diseases, or exhibit any other one or more disease criterion, including one or more cancers other than breast cancer. However, the healthy controls are preferably free of any cancer.

[95] As used herein, a "subject in need thereof" is a subject having breast cancer or presenting with one or more symptoms of breast cancer, or a subject having an increased risk of developing breast cancer relative to the population at large. Preferably, a subject in need thereof has breast cancer. The breast cancer can be primary breast cancer, locally advanced breast cancer or metastatic breast cancer. A "subject" includes a mammal. The mammal can be any mammal, *e.g.*, a human, a primate, a bird, a mouse, a rat, a fowl, a dog, a cat, a cow, a horse, a goat, a camel, a sheep and a pig. Preferably, the mammal is a human. The subject can be a male or a female.

[96] In particular embodiments, the methods and kits for predicting breast cancer intrinsic subtypes or *HER2* status (*e.g.*, for predicting local-regional relapse free or breast cancer specific survival in a subject, for screening for the likelihood of the effectiveness of a post-mastectomy breast cancer treatment, and for treating breast cancer in a subject) include collecting a biological sample comprising a cancer cell or tissue, such as a breast tissue sample or a primary breast

tumor tissue sample. By "biological sample" is intended any sampling of cells, tissues, or bodily fluids in which expression of an intrinsic gene can be detected. Examples of such biological samples include, but are not limited to, biopsies and smears. Bodily fluids useful in the present disclosure include blood, lymph, urine, saliva, nipple aspirates, gynecological fluids, or any other bodily secretion or derivative thereof. Blood can include whole blood, plasma, serum, or any derivative of blood. In some embodiments, the biological sample includes breast cells, particularly breast tissue from a biopsy, such as a breast tumor tissue sample. Biological samples may be obtained from a subject by a variety of techniques including, for example, by scraping or swabbing an area, by using a needle to aspirate cells or bodily fluids, or by removing a tissue sample (*i.e.*, biopsy). Methods for collecting various biological samples are well known in the art. In some embodiments, a breast tissue sample is obtained by, for example, fine needle aspiration biopsy, core needle biopsy, or excisional biopsy. Fixative and staining solutions may be applied to the cells or tissues for preserving the specimen and for facilitating examination. Biological samples, particularly breast tissue samples, may be transferred to a glass slide for viewing under magnification. In one embodiment, the biological sample is a formalin fixed paraffin embedded (FFPE) breast tissue sample, particularly a primary breast tumor sample. In various embodiments, the tissue sample is obtained from a pathologist-guided tissue core sample.

[97] *Expression Profiling*

[98] In various embodiments, the present disclosure provides methods for classifying, prognosticating, or monitoring breast cancer in subjects. In this embodiment, data obtained from analysis of intrinsic gene expression is evaluated using one or more pattern recognition algorithms. *See*, as examples, U.S. Patent Application Publication Nos. 2011/0145176 and 2013/0337444. Such analysis methods may be used to form a predictive model, which can be used to classify test data. For example, one convenient and particularly effective method of classification employs multivariate statistical analysis modeling, first to form a model (a "predictive mathematical model") using data ("modeling data") from samples of known subtype (*e.g.*, from subjects known to have a particular breast cancer intrinsic subtype: LumA, LumB, Basal-like, HER2-enriched, or normal-like), and second to classify an unknown sample (*e.g.*, "test sample") according to subtype. Pattern recognition methods have been used widely to characterize many different types of problems ranging, for example, over linguistics,

fingerprinting, chemistry and psychology. In the context of the methods described herein, pattern recognition is the use of multivariate statistics, both parametric and non-parametric, to analyze data, and hence to classify samples and to predict the value of some dependent variable based on a range of observed measurements. There are two main approaches. One set of methods is termed "unsupervised" and these simply reduce data complexity in a rational way and also produce display plots which can be interpreted by the human eye. However, this type of approach may not be suitable for developing a clinical assay that can be used to classify samples derived from subjects independent of the initial sample population used to train the prediction algorithm.

[99] The other approach is termed "supervised" whereby a training set of samples with known class or outcome is used to produce a mathematical model which is then evaluated with independent validation data sets. Here, a "training set" of intrinsic gene expression data is used to construct a statistical model that predicts correctly the "subtype" of each sample. This training set is then tested with independent data (referred to as a test or validation set) to determine the robustness of the computer-based model. These models are sometimes termed "expert systems," but may be based on a range of different mathematical procedures. Supervised methods can use a data set with reduced dimensionality (for example, the first few principal components), but typically use unreduced data, with all dimensionality. In all cases the methods allow the quantitative description of the multivariate boundaries that characterize and separate each subtype in terms of its intrinsic gene expression profile. It is also possible to obtain confidence limits on any predictions, for example, a level of probability to be placed on the goodness of fit. The robustness of the predictive models can also be checked using cross-validation, by leaving out selected samples from the analysis.

[100] The PAM50 or NANO46 classification models described herein (and as described in U.S. Patent Application Publication Nos. 2011/0145176 and 2013/0337444) is based on the gene expression profile for a plurality of subject samples using the 50 or 46, respectively, intrinsic genes listed in Table 1. The plurality of samples includes a sufficient number of samples derived from subjects belonging to each subtype class. By "sufficient samples" or "representative number" in this context is intended a quantity of samples derived from each subtype that is sufficient for building a classification model that can reliably distinguish each subtype from all others in the group. A supervised prediction algorithm is developed based on the profiles of

objectively-selected prototype samples for "training" the algorithm. The samples are selected and subtyped using an expanded intrinsic gene set according to the methods disclosed in International Patent Publication WO 2007/061876 and U.S. Patent Publication No. 2009/0299640. Alternatively, the samples can be subtyped according to any known assay for classifying breast cancer subtypes. After stratifying the training samples according to subtype, a centroid-based prediction algorithm is used to construct centroids based on the expression profile of all or some of the intrinsic gene set described in Table 1.

[101] In one embodiment, the prediction algorithm is the nearest centroid methodology related to that described in Narashiman and Chu (2002) *PNAS* 99:6567-6572. In the present disclosure, the method computes a standardized centroid for each subtype. This centroid is the average gene expression for each gene in each subtype (or "class") divided by the within-class standard deviation for that gene. Nearest centroid classification takes the gene expression profile of a new sample, and compares it to each of these class centroids. Subtype prediction is done by calculating the Spearman's rank correlation of each test case to the five centroids, and assigning a sample to a subtype based on the nearest centroid.

[102] *Detection of intrinsic gene expression*

[103] Any methods available in the art for detecting expression of the intrinsic genes listed in Table 1 are encompassed herein. By "detecting expression" is intended determining the quantity or presence of an RNA transcript or its expression product of an intrinsic gene. Methods for detecting expression of the intrinsic genes of the disclosure, that is, gene expression profiling, include methods based on hybridization analysis of polynucleotides, methods based on sequencing of polynucleotides, immunohistochemistry methods, and proteomics-based methods. The methods generally detect expression products (*e.g.*, mRNA) of the intrinsic genes listed in Table 1. In preferred embodiments, PCR-based methods, such as reverse transcription PCR (RT-PCR) (Weis *et al.*, *TIG* 8:263- 64, 1992), and array-based methods such as microarray (Schena *et al.*, *Science* 270:467- 70, 1995) are used. By "microarray" is intended an ordered arrangement of hybridizable array elements, such as, for example, polynucleotide probes, on a substrate. The term "probe" refers to any molecule that is capable of selectively binding to a specifically intended target biomolecule, for example, a nucleotide transcript or a protein encoded by or corresponding to an intrinsic gene. Probes can be synthesized by one of skill in

the art, or derived from appropriate biological preparations. Probes may be specifically designed to be labeled. Examples of molecules that can be utilized as probes include, but are not limited to, RNA, DNA, proteins, antibodies, and organic molecules.

[104] Many expression detection methods use isolated RNA. The starting material is typically total RNA isolated from a biological sample, such as a tumor or tumor cell line, and corresponding normal tissue or cell line, respectively. If the source of RNA is a primary tumor, RNA (*e.g.*, mRNA) can be extracted, for example, from frozen or archived paraffin-embedded and fixed (*e.g.*, formalin-fixed) tissue samples (*e.g.*, pathologist-guided tissue core samples).

[105] General methods for RNA extraction are well known in the art and are disclosed in standard textbooks of molecular biology, including Ausubel *et al.*, ed., "Current Protocols in Molecular Biology", John Wiley & Sons, New York 1987-1999. Methods for RNA extraction from paraffin embedded tissues are disclosed, for example, in Rupp and Locker, *Lab Invest.* 56:A67, (1987); and De Andres *et al. Biotechniques* 18:42-44, (1995). In particular, RNA isolation can be performed using a purification kit, a buffer set and protease from commercial manufacturers, such as Qiagen (Valencia, CA), according to the manufacturer's instructions. For example, total RNA from cells in culture can be isolated using Qiagen RNeasy mini-columns. Other commercially available RNA isolation kits include Masterpure™ Complete DNA and RNA Purification Kit (Epicentre®, Madison, WI.) and Paraffin Block RNA Isolation Kit (Ambion®, Austin, TX). Total RNA from tissue samples can be isolated, for example, using RNA Stat-60 (Tel-Test, Friendswood, TX). RNA prepared from a tumor can be isolated, for example, by cesium chloride density gradient centrifugation. Additionally, large numbers of tissue samples can readily be processed using techniques well known to those of skill in the art, such as, for example, the single-step RNA isolation process of Chomczynski (U.S. Pat. No. 4,843,155).

[106] Isolated RNA can be used in hybridization or amplification assays that include, but are not limited to, PCR analyses and probe arrays. One method for the detection of RNA levels involves contacting the isolated RNA with a nucleic acid molecule (probe) that can hybridize to the mRNA encoded by the gene being detected. The nucleic acid probe can be, for example, a full-length cDNA, or a portion thereof, such as an oligonucleotide of at least 7, 15, 30, 60, 100, 250, or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to an intrinsic gene of the present disclosure, or any derivative DNA or RNA.

Hybridization of an mRNA with the probe indicates that the intrinsic gene in question is being expressed. The term "stringent conditions" is as well-known in the art and as described, at least, in books, publications and patent documents listed herein.

[107] In one embodiment, the mRNA is immobilized on a solid surface and contacted with a probe, for example by running the isolated mRNA on an agarose gel and transferring the mRNA from the gel to a membrane, such as nitrocellulose. In an alternative embodiment, the probes are immobilized on a solid surface and the mRNA is contacted with the probes, for example, in an Agilent (Santa Clara, CA) gene chip array. A skilled artisan can readily adapt known mRNA detection methods for use in detecting the level of expression of the intrinsic genes of the present disclosure.

[108] An alternative method for determining the level of intrinsic gene expression product in a sample involves the process of nucleic acid amplification, for example, by RT-PCR (U.S. Pat. No. 4,683,202), ligase chain reaction (Barany, *PNAS USA* 88: 189-93, (1991)), self-sustained sequence replication (Guatelli *et al.*, *PNAS USA* 87: 1874-78, (1990)), transcriptional amplification system (Kwoh *et al.*, *PNAS USA* 86: 1173-77, (1989)), Q-Beta Replicase (Lizardi *et al.*, *Bio/Technology* 6:1197, (1988)), rolling circle replication (U.S. Pat. No. 5,854,033), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

[109] In particular aspects of the disclosure, intrinsic gene expression can assessed by quantitative RT-PCR. Numerous different PCR or quantitative real-time PCR (qPCR) protocols are known in the art and exemplified herein and can be directly applied or adapted for use using the presently-described methods and kits for the detection and/or quantification of the intrinsic genes listed in Table 1. Generally, in PCR, a target polynucleotide sequence is amplified by reaction with at least one oligonucleotide primer or a pair of oligonucleotide primers. The primer(s) hybridize to a complementary region of the target nucleic acid and a DNA polymerase extends the primer(s) to amplify the target sequence. Under conditions sufficient to provide polymerase-based nucleic acid amplification products, a nucleic acid fragment of one size dominates the reaction products (the target polynucleotide sequence which is the amplification product). The amplification cycle is repeated to increase the concentration of the single target

polynucleotide sequence. The reaction can be performed in any thermocycler commonly used for PCR. However, preferred are cyclers with real time fluorescence measurement capabilities, for example, Smartcycler® (Cepheid, Sunnyvale, CA), ABI Prism 7700® (Applied Biosystems®, Foster City, CA.), Rotor- Gene™ (Corbett Research, Sydney, Australia), Lightcycler® (Roche Diagnostics Corp, Indianapolis, IN.), iCycler® (Biorad Laboratories, Hercules, CA.) and MX4000® (Stratagene, La Jolla, CA.).

[110] In another embodiment of the disclosure, microarrays are used for expression profiling. Microarrays are particularly well suited for this purpose because of the reproducibility between different experiments. DNA microarrays provide one method for the simultaneous measurement of the expression levels of large numbers of genes. Each array consists of a reproducible pattern of capture probes attached to a solid support. Labeled RNA or DNA is hybridized to complementary probes on the array and then detected by laser scanning. Hybridization intensities for each probe on the array are determined and converted to a quantitative value representing relative gene expression levels. *See*, for example, U.S. Pat. Nos. 6,040,138, 5,800,992 and 6,020,135, 6,033,860, and 6,344,316. High-density oligonucleotide arrays are particularly useful for determining the gene expression profile for a large number of RNAs in a sample.

[111] In a preferred embodiment, the nCounter® Analysis System (NanoString Technologies, Seattle, WA) is used to detect intrinsic gene expression. The basis of the nCounter® Analysis System is the unique code assigned to each nucleic acid target to be assayed (International Patent Application Publication No. WO 08/124847, U.S. Patent No. 8,415,102 and Geiss *et al. Nature Biotechnology*. 2008. 26(3): 317-325). The code is composed of an ordered series of colored fluorescent spots which create a unique barcode for each target to be assayed. A pair of probes is designed for each DNA or RNA target, a biotinylated capture probe and a reporter probe carrying the fluorescent barcode. This system is also referred to, herein, as the nanoreporter code system.

[112] Specific reporter and capture probes are synthesized for each target. The reporter probe can comprise at a least a first label attachment region to which are attached one or more label monomers that emit light constituting a first signal; at least a second label attachment region, which is non-over-lapping with the first label attachment region, to which are attached one or more label monomers that emit light constituting a second signal; and a first target-specific

sequence. Preferably, each sequence specific reporter probe comprises a target specific sequence capable of hybridizing to no more than one gene of Table 1 and optionally comprises at least three, or at least four label attachment regions, said attachment regions comprising one or more label monomers that emit light, constituting at least a third signal, or at least a fourth signal, respectively. The capture probe can comprise a second target-specific sequence; and a first affinity tag. In some embodiments, the capture probe can also comprise one or more label attachment regions. Preferably, the first target-specific sequence of the reporter probe and the second target-specific sequence of the capture probe hybridize to different regions of the same gene of Table 1 to be detected. Reporter and capture probes are all pooled into a single hybridization mixture, the "probe library". Preferably, the probe library comprises a probe pair (a capture probe and reporter) for each of the genes in Table 1. Preferably, the probe library comprises a probe pair (a capture probe and reporter) for each of the NANO46 genes as described above. Preferably, the probe library comprises a probe pair (a capture probe and reporter) for each of the housekeeping genes and other genes described herein, *e.g.*, *Her2*.

[113] The relative abundance of each target is measured in a single multiplexed hybridization reaction. The method comprises contacting a biological sample with a probe library, the library comprising a probe pair for each of the at least 40 genes in Table 1, *e.g.*, each of the NANO46 or PAM50 genes, and/or the housekeeping genes and other genes described herein, such that the presence of each target in the sample creates a probe pair – target complex. The complex is then purified. More specifically, the sample is combined with the probe library, and hybridization occurs in solution. After hybridization, the tripartite hybridized complexes (probe pairs and target) are purified in a two-step procedure using magnetic beads linked to oligonucleotides complementary to universal sequences present on the capture and reporter probes. This dual purification process allows the hybridization reaction to be driven to completion with a large excess of target-specific probes, as they are ultimately removed, and, thus, do not interfere with binding and imaging of the sample. All post hybridization steps are handled robotically on a custom liquid-handling robot (Prep Station, NanoString Technologies).

[114] Purified reactions are deposited by the Prep Station into individual flow cells of a sample cartridge, bound to a streptavidin-coated surface *via* the capture probe, electrophoresed to elongate the reporter probes, and immobilized. After processing, the sample cartridge is transferred to a fully automated imaging and data collection device (Digital Analyzer,

NanoString Technologies). The expression level of a target is measured by imaging each sample and counting the number of times the code for that target is detected. For each sample, typically 600 fields-of-view (FOV) are imaged (1376 X 1024 pixels) representing approximately 10 mm^2 of the binding surface. Typical imaging density is 100-1200 counted reporters per field of view depending on the degree of multiplexing, the amount of sample input, and overall target abundance. Data is output in simple spreadsheet format listing the number of counts per target, per sample.

[115] This system can be used along with nanoreporters. Additional disclosure regarding nanoreporters can be found in International Publication No. WO 07/076129 and WO 07/076132, and US Patent Publication No. 2010/0015607 and 2010/0261026. Further, the term nucleic acid probes and nanoreporters can include the rationally designed (*e.g.*, synthetic sequences) described in International Publication No. WO 2010/019826 and US Patent Publication No. 2010/0047924.

[116] *Data processing*

[117] It is often useful to pre-process gene expression data, for example, by addressing missing data, translation, scaling, normalization, and weighting. Multivariate projection methods, such as principal component analysis (PCA) and partial least squares analysis (PLS), are so-called scaling sensitive methods. By using prior knowledge and experience about the type of data studied, the quality of the data prior to multivariate modeling can be enhanced by scaling and/or weighting. Adequate scaling and/or weighting can reveal important and interesting variation hidden within the data, and therefore make subsequent multivariate modeling more efficient. Scaling and weighting may be used to place the data in the correct metric, based on knowledge and experience of the studied system, and therefore reveal patterns already inherently present in the data.

[118] If possible, missing data, for example gaps in column values, should be avoided. However, if necessary, such missing data may be replaced or "filled" with, for example, the mean value of a column ("mean fill"); a random value ("random fill"); or a value based on a principal component analysis ("principal component fill").

[119] "Translation" of the descriptor coordinate axes can be useful. Examples of such translation include normalization and mean centering. "Normalization" may be used to remove

sample-to-sample variation. For microarray data, the process of normalization aims to remove systematic errors by balancing the fluorescence intensities of the two labeling dyes. The dye bias can come from various sources including differences in dye labeling efficiencies, heat and light sensitivities, as well as scanner settings for scanning two channels. Some commonly used methods for calculating normalization factor include: (i) global normalization that uses all genes on the array; (ii) housekeeping genes normalization that uses constantly expressed housekeeping/invariant genes; and (iii) internal controls normalization that uses known amount of exogenous control genes added during hybridization (Quackenbush, *Nat. Genet.* 32 (Suppl.), 496-501 (2002)). In one embodiment, the intrinsic genes disclosed herein can be normalized to control housekeeping genes. For example, the housekeeping genes described in U.S. Patent Publication 2008/0032293 can be used for normalization. Exemplary housekeeping genes include *MRPL19*, *PSMC4*, *SF3A1*, *PUM1*, *ACTB*, *GAPD*, *GUSB*, *RPLPO*, and *TFRC*. It will be understood by one of skill in the art that the methods disclosed herein are not bound by normalization to any particular housekeeping genes, and that any suitable housekeeping gene(s) known in the art can be used.

[120] Many normalization approaches are possible, and they can often be applied at any of several points in the analysis. In one embodiment, microarray data is normalized using the LOWESS method, which is a global locally weighted scatterplot smoothing normalization function. In another embodiment, qPCR data is normalized to the geometric mean of set of multiple housekeeping genes.

[121] "Mean centering" may also be used to simplify interpretation. Usually, for each descriptor, the average value of that descriptor for all samples is subtracted. In this way, the mean of a descriptor coincides with the origin, and all descriptors are "centered" at zero. In "unit variance scaling," data can be scaled to equal variance. Usually, the value of each descriptor is scaled by 1/StDev, where StDev is the standard deviation for that descriptor for all samples. "Pareto scaling" is, in some sense, intermediate between mean centering and unit variance scaling. In Pareto scaling, the value of each descriptor is scaled by 1/sqrt(StDev), where StDev is the standard deviation for that descriptor for all samples. In this way, each descriptor has a variance numerically equal to its initial standard deviation. The Pareto scaling may be performed, for example, on raw data or mean centered data.

[122] "Logarithmic scaling" may be used to assist interpretation when data have a positive

skew and/or when data spans a large range, *e.g.*, several orders of magnitude. Usually, for each descriptor, the value is replaced by the logarithm of that value. In "equal range scaling," each descriptor is divided by the range of that descriptor for all samples. In this way, all descriptors have the same range, that is, 1. However, this method is sensitive to presence of outlier points. In "autoscaling," each data vector is mean centered and unit variance scaled. This technique is very useful because each descriptor is then weighted equally, and large and small values are treated with equal emphasis. This can be important for genes expressed at very low, but still detectable, levels.

[123] In one embodiment, data is collected for one or more test samples and classified using the at least 40 genes of Table 1 as described herein, e.g., the PAM50 or NANO46 classification models. When comparing data from multiple analyses (*e.g.*, comparing expression profiles for one or more test samples to the centroids constructed from samples collected and analyzed in an independent study), it will be necessary to normalize data across these data sets. In one embodiment, Distance Weighted Discrimination (DWD) is used to combine these data sets together (Benito *et al.* (2004) *Bioinformatics* 20(1): 105-114). DWD is a multivariate analysis tool that is able to identify systematic biases present in separate data sets and then make a global adjustment to compensate for these biases; in essence, each separate data set is a multi-dimensional cloud of data points, and DWD takes two points clouds and shifts one such that it more optimally overlaps the other.

[124] The methods described herein may be implemented and/or the results recorded using any device capable of implementing the methods and/or recording the results. Examples of devices that may be used include but are not limited to electronic computational devices, including computers of all types. When the methods described herein are implemented and/or recorded in a computer, the computer program that may be used to configure the computer to carry out the steps of the methods may be contained in any computer readable medium capable of containing the computer program. Examples of computer readable medium that may be used include but are not limited to diskettes, CD-ROMs, DVDs, ROM, RAM, non-transitory computer-readable media, and other memory and computer storage devices. The computer program that may be used to configure the computer to carry out the steps of the methods and/or record the results may also be provided over an electronic network, for example, over the internet, an intranet, or other network.

[125] *Calculation of risk of recurrence*

[126] Provided herein are methods for predicting breast cancer outcome within the context of the intrinsic subtype and optionally other clinical variables. Outcome may refer to overall or disease-specific survival, event-free survival, or outcome in response to a particular treatment or therapy. In particular, the methods may be used to predict the likelihood of long-term, disease-free survival. "Predicting the likelihood of survival of a breast cancer patient" is intended to assess the risk that a patient will die as a result of the underlying breast cancer. "Long-term, disease-free survival" is intended to mean that the patient does not die from or suffer a recurrence of the underlying breast cancer within a period of at least five years, or at least ten or more years, following initial diagnosis or treatment.

[127] In embodiments, outcome is predicted based on classification of a subject according to cancer subtype. This classification is based on expression profiling using the at least 40 intrinsic genes listed in Table 1. In addition to providing a subtype assignment, the at least 40 intrinsic genes listed in Table 1, *e.g.*, the PAM50 or NANO46 genes, provide measurements of the similarity of a test sample to all four subtypes which is translated into a Risk of Recurrence (ROR) score that can be used in any patient population regardless of disease status and treatment options. The intrinsic subtypes and ROR also have value in the prediction of pathological complete response in women treated with, for example, neoadjuvant taxane and anthracycline chemotherapy (Rouzier *et al.*, *J Clin Oncol* 23:8331-9 (2005)). Thus, in various embodiments of the present disclosure, a risk of recurrence (ROR) model is used to predict outcome. Using these risk models, subjects can be stratified into low, medium, and high risk of recurrence groups. Calculation of ROR can provide prognostic information to guide treatment decisions and/or monitor response to therapy.

[128] In some embodiments described herein, the prognostic performance of the intrinsic subtypes defied by expression profiles of the at least 40 genes listed in Table 1, *e.g.*, the PAM50- or NANO46-defined intrinsic subtypes, and/or other clinical parameters is assessed utilizing a Cox Proportional Hazards Model Analysis, which is a regression method for survival data that provides an estimate of the hazard ratio and its confidence interval. The Cox model is a well-recognized statistical technique for exploring the relationship between the survival of a patient and particular variables. This statistical method permits estimation of the hazard (*i.e.*, risk) of

individuals given their prognostic variables (*e.g.*, intrinsic gene expression profile with or without additional clinical factors, as described herein). The "hazard ratio" is the risk of death at any given time point for patients displaying particular prognostic variables. *See* generally Spruance *et al.*, *Antimicrob. Agents & Chemo.* 48:2787-92 (2004).

[129] The classification models described herein, *e.g.*, the PAM50 or NANO46 classification models, can be trained for risk of recurrence using subtype distances (or correlations) alone, or using subtype distances with clinical variables as discussed *supra*. In one embodiment, the risk score for a test sample is calculated using intrinsic subtype distances alone using the following equation (Equation 2):

[130] ROR = 0.05*Basal + 0.1 1*HER2 + -0.25*LumA + 0.07*LumB + -0.1 1*Normal,

where the variables "Basal," "HER2," "LumA," "LumB," and "Normal" are the distances to the centroid for each respective classifier when the expression profile from a test sample is compared to centroids constructed using the gene expression data deposited with the National Center for Biotechnology Information Gene Expression Omnibus (GEO); as examples with accession number GSE2845 or GSE10886.

[131] Risk score can also be calculated using a combination of breast cancer subtype and the clinical variables tumor size (T) and lymph nodes status (N) using the following equation (Equation 3):

[132] ROR (full) = 0.05*Basal + 0.1*HER2 + -0.19*LumA + 0.05*LumB + - 0.09*Normal + 0.16*T + 0.08*N,

where the variables "Basal," "HER2," "LumA," and "LumB" are as described *supra* and when comparing test expression profiles to centroids constructed using the gene expression data deposited with GEO; as examples with accession number GSE2845 or GSE10886.

[133] In yet another embodiment, risk score for a test sample is calculated using intrinsic subtype distances alone using the following equation (Equation 4):

[134] ROR-S = 0.05*Basal + 0.12*HER2 + -0.34*LumA + 0.0.23*LumB,

where the variables "Basal," "HER2," "LumA," and "LumB" are as described *supra* and the test expression profiles are compared to centroids constructed using the gene expression data deposited with GEO; as examples with accession number GSE2845 or GSE10886.

[135] In yet another embodiment, risk score can also be calculated using a combination of breast cancer subtype and the clinical variable tumor size (T) using the following equation (Equation 5):

[136] ROR-C = 0.05*Basal + 0.11*HER2 + -0.23*LumA + 0.09*LumB + 0.17*T,

where the variables "Basal," "HER2," "LumA," and "LumB" are as described *supra* and the test expression profiles are compared to centroids constructed using the gene expression data deposited with GEO; as examples with accession number GSE2845 or GSE10886.

[137] In yet another embodiment, risk score for a test sample is calculated using intrinsic subtype distances in combination with the proliferation signature ("Prolif") using the following equation (Equation 6):

[138] ROR-P = -0.001*Basal + 0.7*HER2 + -0.95*LumA + 0.49*LumB + 0.34*Prolif,

where the variables "Basal," "HER2," "LumA," "LumB" and "Prolif" are as described *supra* and the test expression profiles are compared to centroids constructed using the gene expression data deposited with GEO; as examples with accession number GSE2845 or GSE10886.

[139] In yet another embodiment, risk score can also be calculated using a combination of breast cancer subtype, proliferation signature and the clinical variable tumor size (T) using the ROR-PT described in conjunction with **Table 5**, *supra*.

[140] *Detection of Subtypes*

[141] Immunohistochemistry (IHC) for estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki67 can be performed concurrently on serial sections with the standard streptavidin–biotin complex method with 3,3′-diaminobenzidine as the chromogen. Staining for ER, PR, and HER2 interpretation can be performed as described previously (Cheang *et al.*, *Clin Cancer Res.* 2008;14(5):1368–1376.), however any method known in the art may be used.

[142] For example, a Ki67 antibody (clone SP6; ThermoScientific™, Fremont, CA) can be applied at a 1:200 dilution for 32 minutes, by following the Ventana Benchmark automated immunostainer (Ventana®, Tucson, AZ) standard Cell Conditioner 1 (CC1, a proprietary buffer) protocol at 98°C for 30 minutes. An ER antibody (clone SP1; ThermoFisher Scientific™) can be used at 1:250 dilution with 10-minute incubation, after an 8-minute microwave antigen retrieval

in 10 mM sodium citrate (pH 6.0). Ready-to-use PR antibody (clone 1E2; Ventana®) can be used by following the CC1 protocol as above. HER2 staining can be done with a SP3 antibody (ThermoFisher Scientific™) at a 1:100 dilution after antigen retrieval in 0.05 M Tris buffer (pH 10.0) with heating to 95°C in a steamer for 30 minutes. For HER2 fluorescent *in situ* hybridization (FISH) assay, slides can be hybridized with probes to LSI (locus-specific identifier) HER2/neu and to centromere 17 by use of the PathVysion HER-2 DNA Probe kit (Abbott Molecular, Abbott Park, IL) according to manufacturer's instructions, with modifications to pretreatment and hybridization as previously described (Brown LA, Irving J, Parker R, *et al.* "Amplification of EMSY, a novel oncogene on 11q13, in high grade ovarian surface epithelial carcinomas". *Gynecol Oncol.* 2006;100(2):264–270). Slides can then be counterstained with 4′,6-diamidino-2-phenylindole. Stained material can be visualized on a Zeiss Axioplan epifluorescent microscope, and signals analyzed with a Metafer image acquisition system (Metasystems, Altlussheim, Germany). Biomarker expression from immunohistochemistry assays can then be scored by two pathologists, who are blinded to the clinicopathological characteristics and outcome and who used previously established and published criteria for biomarker expression levels that had been developed on other breast cancer cohorts.

[143] Tumors are considered positive for ER or PR if immunostaining is observed in more than 1% of tumor nuclei, as described previously. Tumors are considered positive for HER2 if immunostaining is scored as 3+ according to HercepTest™ (Dako, Carpinteria, CA) criteria, with an amplification ratio for fluorescent *in situ* hybridization of 2.0 or more being the cut point that can be used to segregate immunohistochemistry equivocal tumors (scored as 2+) (Yaziji, *et al.*, *JAMA*, 291(16):1972–1977 (2004)). Ki67 can be visually scored for percentage of tumor cell nuclei with positive immunostaining above the background level.

[144] Other methods can also be used to detect the HER2+ subtype. These techniques include enzyme-linked immunosorbent assay (ELISA), Western blots, Northern blots, or fluorescence-activated cell sorting (FACS) analysis.

[145] *Kits*

[146] The present disclosure also describes kits useful for classifying breast cancer intrinsic subtypes and/or providing prognostic information to identify breast cancers that are more or less

responsive to radiation. These kits comprise a set of reporter/capture probes and/or primers specific for the genes listed in Table 1, and/or housekeeping genes, and/or other genes described herein. The kits can further include instructions for detecting the aforementioned genes and classifying breast cancer intrinsic subtypes and/or providing prognostic information to identify breast cancers that are more responsive to radiation. The kits may include instructions for recommended treatments based on a classified breast cancer intrinsic subtype. The kits may also contain reagents sufficient to facilitate detection and/or quantitation of *HER2,* in order to classify cells as HER2+. Preferably, the kit comprises a set of reporter/capture probes and/or primers specific for at least 10, at least 15, at least 20, at least 25, at least 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or all 50 genes listed in Table 1. The kit may further comprise a non-transitory computer readable medium.

[147] In embodiments of the present disclosure, the capture probes are immobilized on an array. By "array" is intended a solid support or a substrate with peptide or nucleic acid probes attached to the support or substrate. Arrays typically comprise a plurality of different capture probes that are coupled to a surface of a substrate in different, known locations. The arrays of the disclosure comprise a substrate having a plurality of capture probes that can specifically bind an intrinsic gene expression product. The number of capture probes on the substrate varies with the purpose for which the array is intended. The arrays may be low-density arrays or high-density arrays and may contain 4 or more, 8 or more, 12 or more, 16 or more, 32 or more addresses, but will minimally comprise capture probes for at least 10, at least 15, at least 20, at least 25, or at least 46 of the intrinsic genes or all 50 intrinsic genes listed in Table 1. The array may include capture probes for the housekeeping genes and/or other genes listed herein.

[148] Techniques for the synthesis of these arrays using mechanical synthesis methods are described in, *e.g.*, U.S. Patent No. 5,384,261. The array may be fabricated on a surface of virtually any shape or even a multiplicity of surfaces. Arrays may be probes (*e.g.*, nucleic-acid binding probes) on beads, gels, polymeric surfaces, fibers such as fiber optics, glass or any other appropriate substrate, see U.S. Pat. Nos. 5,770,358, 5,789,162, 5,708,153, 6,040,193 and 5,800,992. Arrays may be packaged in such a manner as to allow for diagnostics or other manipulation on the device. *See,* for example, U.S. Pat. Nos. 5,856,174 and 5,922,591.

[149] In embodiments, the kit comprises a set of oligonucleotide primers sufficient for the detection and/or quantitation of each of the intrinsic genes listed in Table 1. Preferably, the kit

comprises a set of oligonucleotide primers sufficient for the detection and/or quantitation of at least 10, at least 15, at least 20, at least 25, at least 46 of the intrinsic genes or all 50 intrinsic genes listed in Table 1 and/or for the detection and/or quantitation of the housekeeping genes and/or other genes listed herein. The oligonucleotide primers may be provided in a lyophilized or reconstituted form, or may be provided as a set of nucleotide sequences. In certain embodiments, the primers are provided in a microplate format, where each primer set occupies a well (or multiple wells, as in the case of replicates) in the microplate. The microplate may further comprise primers sufficient for the detection of one or more housekeeping genes (*e.g.*, eight) as discussed herein. The kit may further comprise reagents and instructions sufficient for the amplification of expression products from the genes listed in Table 1 and/or for the amplification of expression products from the housekeeping genes and/or other genes listed herein.

[150] In order to facilitate ready access, *e.g.*, for comparison, review, recovery, and/or modification, the molecular signatures/expression profiles are typically recorded in a database. Most typically, the database is a relational database accessible by a computational device, although other formats, *e.g.*, manually accessible indexed files of expression profiles as photographs, analogue or digital imaging readouts, and spreadsheets can be used. Regardless of whether the expression patterns initially recorded are analog or digital in nature, the expression patterns, expression profiles (collective expression patterns), and molecular signatures (correlated expression patterns) are stored digitally and accessed *via* a database. Typically, the database is compiled and maintained at a central facility, with access being available locally and/or remotely.

[151] In certain embodiments, the kit also includes a substance that is used to find the expression level of *HER2*. This substance can be an antibody or a nucleic acid probe. These substances can be used to detect *HER2* using FISH, IHC, ELISA, Western blots, Northern blots, or FACS analysis. Optionally, the kit also includes reagents that allows for the detection of the detecting substance and the quantitation of *HER2* expression in a sample.

EXAMPLES

Example 1.

[152] *Background*: Luminal A (LumA) tumors are associated with good prognosis, but with substantial risk for late loco-regional relapses. Here was tested the predictive value of intrinsic subtypes as defined by research-based PAM50 classifier, for predicting adjuvant radiation therapy benefit among pre-menopausal women with node positive tumors from a post mastectomy randomized adjuvant radiation trials with more than 20 years follow-up.

[153] *Methods*: Formalin fixed paraffin embedded tissues (FFPE) (n = 145) were collected from the British Columbia trial and gene expression profiles were done using Nanostring nCounter® for FFPE samples. Tumors were classified into subtypes (Luminal A (LumA), Luminal B (LumB), HER2-enriched (HER2-E), Basal-like (BLBC) and Normal-like) based on the PAM50 classifier. Kaplan-Meier analysis and the log-rank test were used to test the differences in local-regional relapse free survival (LRFS) and breast cancer specific survival (BCSS).

[154] RNA can be extracted from Formalin-fixed, Paraffin-embedded (FFPE) tissue that has been diagnosed as having a carcinoma of the breast. A Pathologist reviews a hematoxylin and eosin stain (H & E) stained slide to identify the tissue area containing sufficient tumor tissue content for the test. Unstained slide mounted tissue sections are processed by macro-dissecting the identified tumor area on each slide to remove any adjacent normal tissue. RNA is then isolated from the tumor tissue, and DNA is removed from the sample.

[155] Total RNA was extracted using the High Pure RNA Paraffin Kit (Roche Applied Science, Indianapolis, IN, cat# 03270289001), according to the manufacturer's protocol. RNA yield and purity were assessed using the NanoDrop ND-1000 Spectrophotometer (NanoDrop Technologies, Rockland, DE). RNA samples used in downstream analysis met pre-specified quality criteria of an initial concentration of total RNA ≥ 12.5 ng/µl, a minimum total yield of 250ng, and a purity ratio in the range 1.7-2.5.

[156] Gene expression was measured on the NanoString nCounter® Analysis System which delivers direct, multiplexed measurements through digital readouts of the relative abundance of hundreds of mRNA transcripts. In brief, the expression of the fifty target genes of Table 1 (PAM50) as well as normalizing "housekeeping" genes (for example *MRPL19*, *PSMC4*, *SF3A1*,

PUM1, *ACTB*, *GAPDH*, *GUSB*, *RPLPO*, and *TFRC*) were measured in a single hybridization reaction without the use of any enzymatic reactions. An nCounter® CodeSet with gene-specific probe-pairs to the PAM50 targets as well as exogenous positive and negative controls was hybridized in solution to 125-500ng total RNA (nominally 250ng). After overnight hybridization, the samples were processed using the NanoString nCounter® Prep Station and Digital Analyzer according to the instructions and kits provided by NanoString Technologies. Data from each sample were qualified using prospectively defined quality control metrics for the positive and negative controls included in each reaction.

[157] Intrinsic subtype classification of qualified patient samples was based upon the PAM50 gene expression signature. Reporter-code-count files, containing the digital abundance or "counts" of each target mRNA molecule for every sample, were sent to NanoString Technologies for PAM50 subtype calling using a prospectively defined and locked proprietary algorithm. Assignment of subtypes was performed in a blinded fashion, by researchers with no access to information regarding the clinical parameters or outcomes.

[158] *Results*: In this trial, patients received adjuvant CMF (cyclophosphamide, methotrexate, and fluorouracil) and were randomized to with or without post mastectomy radiation therapy (RT) groups. Patients with estrogen receptor positive tumor, as defined by the dextran charcoal biochemical assay, were randomized selected to receive oophorectomy and 42 of them were included in this correlative science study. Figure 1A shows loco-regional relapse for subjects whose tumor samples are classified as Luminal A, with or without radiation therapy. Figure 1B shows breast cancer specific survival (BCSS) for subjects whose tumor samples are classified as Luminal A, with or without radiation therapy. Figure 2A shows loco-regional relapse for subjects whose tumor samples are classified as Luminal B, with or without radiation therapy. Figure 2B shows breast cancer specific survival (BCSS) for subjects whose tumor samples are classified as Luminal B, with or without radiation therapy. Figure 3A shows loco-regional relapse for subjects whose tumor samples are classified as HER2-enriched, with or without radiation therapy. Figure 3B shows breast cancer specific survival (BCSS) for subjects whose tumor samples are classified as HER2-enriched, with or without radiation therapy. Figure 4A shows loco-regional relapse for subjects whose tumor samples are classified as Basal-like, with or without radiation therapy. Figure 4B shows breast cancer specific survival (BCSS) for subjects whose tumor samples are classified as Basal-like, with or without radiation therapy.

[159] Figure 5 shows a subpopulation treatment effect pattern plot (STEPP) showing 10-year breast cancer specific survival (BCSS) to the Spearman's correlation to Basal-like tumors average expression profile.

[160] Figure 6A shows loco-regional relapse for subjects who are classified as low risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy. Figure 6B shows breast cancer specific survival (BCSS) for subjects who are classified as low risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy. Figure 7A shows loco-regional relapse for subjects who are classified as moderate/intermediate risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy. Figure 7B shows breast cancer specific survival (BCSS) for subjects who are classified as moderate/intermediate risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy. Figure 8A shows loco-regional relapse for subjects who are classified as high risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy. Figure 8B shows breast cancer specific survival (BCSS) for subjects who are classified as high risk based on their Risk of Recurrence Score (subtypes centroid based), ROR-S, with or without radiation therapy.

[161] These results demonstrate improved breast cancer specific survival (BCSS) for tumor samples classified as Basal-like subtype and have classified as ROR-S high risk and also demonstrate improved loco-regional relapse survival for tumor samples classified as Luminial A subtype and classified as ROR-S low risk.

[162] Example 2.

[163] Herein an aim was to investigate the predictive value of additional genomic profiles (continuous measurements instead of subgroup analysis) for loco-regional recurrences (LRR) and breast cancer survival (BCSS) in node-positive, pre-menopausal breast cancer patients randomized to adjuvant chemoradiation or chemotherapy alone, in the British Columbia trial.

[164] Methods: In the British Columbia trial, 318 patients received adjuvant cyclophosphamide, methotrexate, fluorouracil (CMF) and were randomized to with or without postmastectomy RT groups. From 145 formalin fixed paraffin embedded tissues, expression profiling of 66 genes was done with the Nanostring nCounter® Subpopulation Treatment Effect

Pattern Plot analysis and permutation tests were used to examine treatment effects on LRR and BCSS events for the absolute difference (Kaplan-Meier) and relative effectiveness (Hazard Ratio) terms. For each tumor, the research-based PAM50 proliferation score, a Spearman's correlation to each of the four intrinsic subtypes (*i.e.,* a quantitative measurement of similarity to the average expression profiles of a typical HER2-Enriched, Basal-like, Luminal A and Luminal B), Risk of Recurrence scores (ROR) and a 13-gene VEGF-signature score (VEGF-s) were calculated as previously described (Parker *et al*, *J. Clin. Oncol.*, 27(8):1160-7 (2009); Hu *et al BMC Medicine*, 7:9 2009). Expression level of DNA repair genes (*RAD17* and *RAD50*) and tumor suppressor *RB1* were also measured.

[165] Results: Overall, patients in the RT arm (n= 69) were significantly associated with better LRR and BCSS than the non-RT-treated arm (n = 76). No significant treatment-effect heterogeneity was detected for VEGF-s, *RAD17* and *RAD50* expressions. On the other hand, patients with lower *RB1* expression levels and higher proliferation scores had better LRR survival when assigned the RT (*See*, Table 9) respectively. The patters of treatment efficacy on LRR and BCSS were most heterogeneous for the varying levels of risk of recurrence scores particularly for patients with higher ROR-C (*i.e.*, intrinsic subtypes centroids and tumor size) (*See*, Table 9) had poorest prognosis, but may benefit from adjuvant RT.

[166] **Table 9**. Subpopulation treatment effect pattern plot analysis of the treatment effect of RT versus no RT as measured by 10-year and 20-yr LRR and BCSS. KM = Kaplan –Meier. HR = Hazard Ratio.

Covariate	**Treatment-covariate interaction test**	**LRR (n = 145)**		**BCSS (n = 145)**	
		10-yr	**20-yr**	**10-yr**	**20-yr**
RB-1	KM based p-value	0.08	0.03	0.49	0.4
	HR based p-value	0.03	0.03	0.41	0.41
Proliferation Score	KM based p-value	0.02	0.06	0.17	0.6
	HR based p-value	0.06	0.06	0.24	0.24
ROR-C	KM based p-value	0.01	0.35	< 0.0001	0.06
	HR based p-value	0.21	0.2	0.02	0.02

ROR-PC	KM based p-value	0.02	0.11	0.09	0.36
	HR based p-value	0.1	0.09	0.04	0.06

[167] Conclusion: *RB1*, proliferation score and risk of recurrence signatures predict LRR and BCSS benefit for adjuvant radiation therapy in this study. The clinical utility of these biomarkers as predictors for adjuvant radiation therapy requires confirmation in a second independent trial.

What is claimed is:

1. A method of predicting local-regional relapse free survival or breast cancer specific survival in a subject having breast cancer comprising:

(a) obtaining a biological sample from the subject; and

(b) assaying the biological sample to determine whether the biological sample is classified as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype, wherein the subtype is determined using a measurement of at least 40 of the genes listed in Table 1,

wherein if the biological sample is classified as a Luminal A or Basal-like subtype, a post-mastectomy breast cancer treatment comprising radiation is more likely to prolong local-regional relapse free survival or breast cancer specific survival of the subject and wherein if the biological sample is classified as a Luminal B or HER2-enriched subtype, a post-mastectomy breast cancer treatment comprising radiation is not likely to prolong local-regional relapse free survival or breast cancer specific survival of the subject.

2. A method of screening for the likelihood of the effectiveness of a post-mastectomy breast cancer treatment comprising radiation in a subject in need thereof comprising:

(a) obtaining a biological sample from the subject; and

(b) assaying the biological sample to determine whether the biological sample is classified as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype, wherein the subtype is determined using a measurement of at least 40 of the genes listed in Table 1;

wherein if the biological sample is classified as a Luminal A or Basal-like subtype, a post-mastectomy breast cancer treatment comprising radiation is more likely to be effective in the subject and wherein if the biological sample is classified as a Luminal B or HER2-enriched subtype, the post-mastectomy breast cancer treatment comprising radiation is not likely to be effective in the subject.

3. A method of treating breast cancer in a subject in need thereof comprising:

(a) obtaining a biological sample from the subject;

(b) assaying the biological sample to determine whether the biological sample is classified as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype, wherein the

subtype is determined using a measurement of at least 40 of the genes listed in Table 1; and

(c) administering a breast cancer treatment to the subject, wherein if the biological sample is classified as a Luminal A or Basal-like subtype, the subject is administered a post-mastectomy breast cancer treatment comprising radiation and wherein if the biological sample is classified as a Luminal B or HER2-enriched subtype, the subject is administered a breast cancer treatment not comprising radiation, thereby treating breast cancer in the subject.

4. The method of any of the preceding claims, wherein assaying includes detecting expression levels of at the least the following 24 genes from the at least 40 of the genes listed in Table 1: FOXA1, MLPH, ESR1, FOXC1, CDC20, ANLN, MAPT, ORC6L, CEP55, MKI67, UBE2C, KNTC2, EXO1, PTTG1, MELK, BIRC5, GPR160, RRM2, SRFP1, NAT1, KIF2C, CXXC5, MIA and BCL2.

5. The method of any of the preceding claims, wherein expression levels of at least CCNE1, CDC6, CDCA1, CENPF, TYMS, and UBE2T are additionally detected.

6. The method of any of the preceding claims, wherein assaying includes generating a gene expression profile based on said expression of said genes for the biological sample.

7. The method of any of the preceding claims, wherein assaying includes comparing the gene expression profile for the biological sample to centroids constructed from gene expression data for the at least 40 of the genes listed in Table 1 for the Luminal A, Luminal B, HER2-enriched or Basal-like subtypes.

8. The method of any of the preceding claims, wherein assaying includes utilizing a supervised algorithm and calculating the distance of the gene expression profile for the biological sample to each of the centroids.

9. The method of any of the preceding claims, wherein assaying includes classifying the biological sample as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype based upon the nearest centroid.

10. The method of any of the preceding claims, wherein assaying includes detecting expression levels of *HER2*.

11. The method of any of the preceding claims, wherein assaying includes detecting expression levels of at least 46 of the genes listed in Table 1.

12. The method of any of the preceding claims, wherein assaying includes detecting expression levels of the NANO46 gene set.

13. The method of any of the preceding claims, wherein assaying includes detecting expression levels of all 50 genes listed in Table 1.

14. The method of any of the preceding claims, wherein the biological sample is selected from the group consisting of a cell, tissue and bodily fluid;

wherein the tissue is obtained from a biopsy and wherein the bodily fluid is selected from the group consisting of blood, lymph, urine, saliva and nipple aspirate.

15. The method of any of the preceding claims, wherein the tissue is obtained from a biopsy.

16. The method of any of the preceding claims, wherein the bodily fluid is selected from the group consisting of blood, lymph, urine, saliva and nipple aspirate.

17. The method of any of the preceding claims, wherein the biological sample is a formalin fixed paraffin embedded tissues (FFPE) sample.

18. The method of any of the preceding claims, wherein the biological sample is an estrogen receptor positive tumor.

19. The method of any of the preceding claims, wherein the breast cancer is primary breast cancer.

20. The method of any of the preceding claims, wherein the breast cancer is locally advanced or metastatic breast cancer.

21. The method of any of the preceding claims, wherein assaying the biological sample to determine whether the biological sample is classified as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype includes RNA expression profiling, immunohistochemistry (IHC) or fluorescence *in situ* hybridization (FISH).

22. The method of any of the preceding claims, wherein the subject is pre-menopausal.

23. The method of any of the preceding claims, wherein the subject has node-positive breast cancer.

24. The method of any of the preceding claims, wherein if the biological sample is an estrogen receptor positive tumor, optionally, the subject is further subjected to oophorectomy.

25. The method of claim 3, wherein the breast cancer treatment comprising radiation further comprises one or more anti-cancer agents selected from the group consisting of anthracycline agents, alkylating agents, nucleoside analogs, platinum agents, taxanes, vinca agents, anti-estrogen drugs, aromatase inhibitors, ovarian suppression agents, endocrine/hormonal agents, bisphophonate therapy agents and targeted biological therapy agents;

wherein specific anti-cancer or chemotherapeutic agents are selected from the group include cyclophosphamide, fluorouracil (or 5-fluorouracil or 5-FU), methotrexate, thiotepa, carboplatin, cisplatin, gemcitabine, anthracycline, taxanes, paclitaxel, protein-bound paclitaxel, docetaxel, vinorelbine, tamoxifen, raloxifene, toremifene, fulvestrant, irinotecan, ixabepilone, temozolmide, topotecan, vincristine, vinblastine, eribulin, mutamycin, capecitabine, capecitabine, anastrozole, exemestane, letrozole, leuprolide, abarelix, buserlin, goserelin, megestrol acetate, risedronate, pamidronate, ibandronate, alendronate, denosumab, zoledronate, trastuzumab, tykerb and bevacizumab, or combinations thereof.

26. The method of claim 25, wherein the anti-cancer agent is cyclophosphamide, fluorouracil (or 5-fluorouracil or 5-FU), methotrexate, or combinations thereof.

27. The method of claim 1, further comprising

determining a proliferation score based on the expression of a subset of proliferation genes in the genes listed in Table 1,

calculating a risk of recurrence (ROR) score using a weighted sum of the classified subtype, proliferation score and optionally one or more clinicopathological variables selected from the group consisting of tumor size, nodal status and histological grade; and

determining whether the subject has a low or high risk of recurrence based on the ROR score, wherein if the subject has a low risk of recurrence a treatment comprising radiation is more likely to prolong local-regional relapse free survival or if the subject has a high risk of recurrence a treatment comprising radiation is more likely to prolong breast cancer specific survival of the subject.

28. The method of claim 2, further comprising

determining a proliferation score based on the expression of a subset of proliferation genes in the genes listed in Table 1,

calculating a risk of recurrence (ROR) score using a weighted sum of the classified subtype, proliferation score and optionally one or more clinicopathological variables selected from the group consisting of tumor size, nodal status and histological grade; and

determining whether the subject has a low or high risk of recurrence based on the ROR score, wherein if the subject has a low risk of recurrence a treatment comprising radiation is more likely to be effective in prolonging local-regional relapse free survival or if the subject has a high risk of recurrence a treatment comprising radiation is more likely to be effective prolonging breast cancer specific survival of the subject.

29. The method of claim 3, further comprising

determining a proliferation score based on the expression of a subset of proliferation genes in the genes listed in Table 1,

calculating a risk of recurrence (ROR) score using a weighted sum of the classified

subtype, proliferation score and optionally one or more clinicopathological variables selected from the group consisting of tumor size, nodal status and histological grade; and

determining whether the subject has a low or high risk of recurrence based on the ROR score, wherein if the subject has a low risk of recurrence administering a treatment comprising radiation to prolong local-regional relapse free survival or if the subject has a high risk of recurrence administering a treatment comprising radiation to prolong breast cancer specific survival of the subject.

30. The method of any of claims 27, 28 or 29, wherein determining a proliferation signature based on the expression of a subset of proliferation genes in the gene list of Table 1 comprises determining the expression of each of the genes selected from *ANLN, CCNE1, CDC20, CDC6, CDCA1, CENPF, CEP55, EXO1, KIF2C, KNTC2, MELK, MKI67, ORC6L, PTTG1, RRM2, TYMS, UBE2C* and *UBE2T*.

31. A kit for predicting local-regional relapse free survival or breast cancer specific survival in a subject having breast cancer comprising

reagents sufficient for the detection of at least 40 of the genes listed in Table 1; and

instructions for performing an assay to determine whether a biological sample from said subject is classified as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype, by using said reagents to measure of at least 40 of the genes listed in Table 1, wherein if the biological sample is classified as a Luminal A or Basal-like subtype, a post-mastectomy breast cancer treatment comprising radiation is more likely to prolong local-regional relapse free survival or breast cancer specific survival of the subject and wherein if the biological sample is classified as a Luminal B or HER2-enriched subtype, a post-mastectomy breast cancer treatment comprising radiation is not likely to prolong local-regional relapse free survival or breast cancer specific survival of the subject.

32. A kit for screening for the likelihood of the effectiveness of a post-mastectomy breast cancer treatment comprising radiation in a subject in need thereof comprising

reagents sufficient for the detection of at least 40 of the genes listed in Table 1; and

instructions for performing an assay to determine whether a biological sample from said

subject is classified as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype, by using said reagents to measure of at least 40 of the genes listed in Table 1, wherein if the biological sample is classified as a Luminal A or Basal-like subtype, a post-mastectomy breast cancer treatment comprising radiation is more likely to be effective in the subject and wherein if the biological sample is classified as a Luminal B or HER2-enriched subtype, a post-mastectomy breast cancer treatment comprising radiation is not likely to be effective in the subject.

33. A kit for treating breast cancer in a subject in need thereof comprising

reagents sufficient for the detection of at least 40 of the genes listed in Table 1;

instructions for performing an assay to determine whether a biological sample from said subject is classified as a Luminal A, Luminal B, HER2-enriched or Basal-like subtype, by using said reagents to measure of at least 40 of the genes listed in Table 1; and

instructions for administering a post-mastectomy breast cancer treatment comprising radiation if the biological sample is classified as a Luminal A or Basal like subtype and instructions for administering a post-mastectomy breast cancer treatment not comprising radiation if the biological sample is classified as a Luminal B or HER2-enriched subtype.

34. The kit of claim 31, further comprising

reagents sufficient for the detection of the proliferation genes selected from *ANLN, CCNE1, CDC20, CDC6, CDCA1, CENPF, CEP55, EXO1, KIF2C, KNTC2, MELK, MKI67, ORC6L, PTTG1, RRM2, TYMS, UBE2C* and *UBE2T,*

instructions for performing an assay to determine a proliferation score based on the expression of the proliferation genes,

instructions for calculating a risk of recurrence score using a weighted sum of the classified subtype, proliferation score and optionally one or more clinicopathological variables selected from the group consisting of tumor size, nodal status and histological grade; and

instructions for determining whether the subject has a low or high risk of recurrence based on the risk of recurrence score, wherein if the subject has a low risk of recurrence a treatment comprising radiation is more likely to prolong local-regional relapse free survival or if the subject has a high risk of recurrence a treatment comprising radiation is more likely to prolong breast cancer specific survival of the subject.

35. The kit of claim 32, further comprising

reagents sufficient for the detection of the proliferation genes selected from *ANLN, CCNE1, CDC20, CDC6, CDCA1, CENPF, CEP55, EXO1, KIF2C, KNTC2, MELK, MKI67, ORC6L, PTTG1, RRM2, TYMS, UBE2C* and *UBE2T*.

instructions for performing an assay to determine a proliferation score based on the expression of the proliferation genes,

instructions for calculating a risk of recurrence score using a weighted sum of the classified subtype, proliferation score and optionally one or more clinicopathological variables selected from the group consisting of tumor size, nodal status and histological grade; and

instructions for determining whether the subject has a low or high risk of recurrence based on the risk of recurrence score, wherein if the subject has a low risk of recurrence a treatment comprising radiation is more likely to be effective in prolonging local-regional relapse free survival or if the subject has a high risk of recurrence a treatment comprising radiation is more likely to be effective prolonging breast cancer specific survival of the subject.

36. The kit of claim 33, further comprising

reagents sufficient for the detection of the proliferation genes selected from *ANLN, CCNE1, CDC20, CDC6, CDCA1, CENPF, CEP55, EXO1, KIF2C, KNTC2, MELK, MKI67, ORC6L, PTTG1, RRM2, TYMS, UBE2C* and *UBE2T*,

instructions for performing an assay to determine a proliferation score based on the expression of the proliferation genes,

instructions for calculating a risk of recurrence score using a weighted sum of the classified subtype, proliferation score and optionally one or more clinicopathological variables selected from the group consisting of tumor size, nodal status and histological grade; and

instructions for determining whether the subject has a low or high risk of recurrence based on the risk of recurrence score, wherein if the subject has a low risk of recurrence administering a treatment comprising radiation to prolong local-regional relapse free survival or if the subject has a high risk of recurrence administering a treatment comprising radiation to prolong breast cancer specific survival of the subject.

37. The kit of any of claims 31 to 36, wherein the kit provides reagents sufficient for the detection of at least 46 of the genes listed in Table 1.

Figure 1A

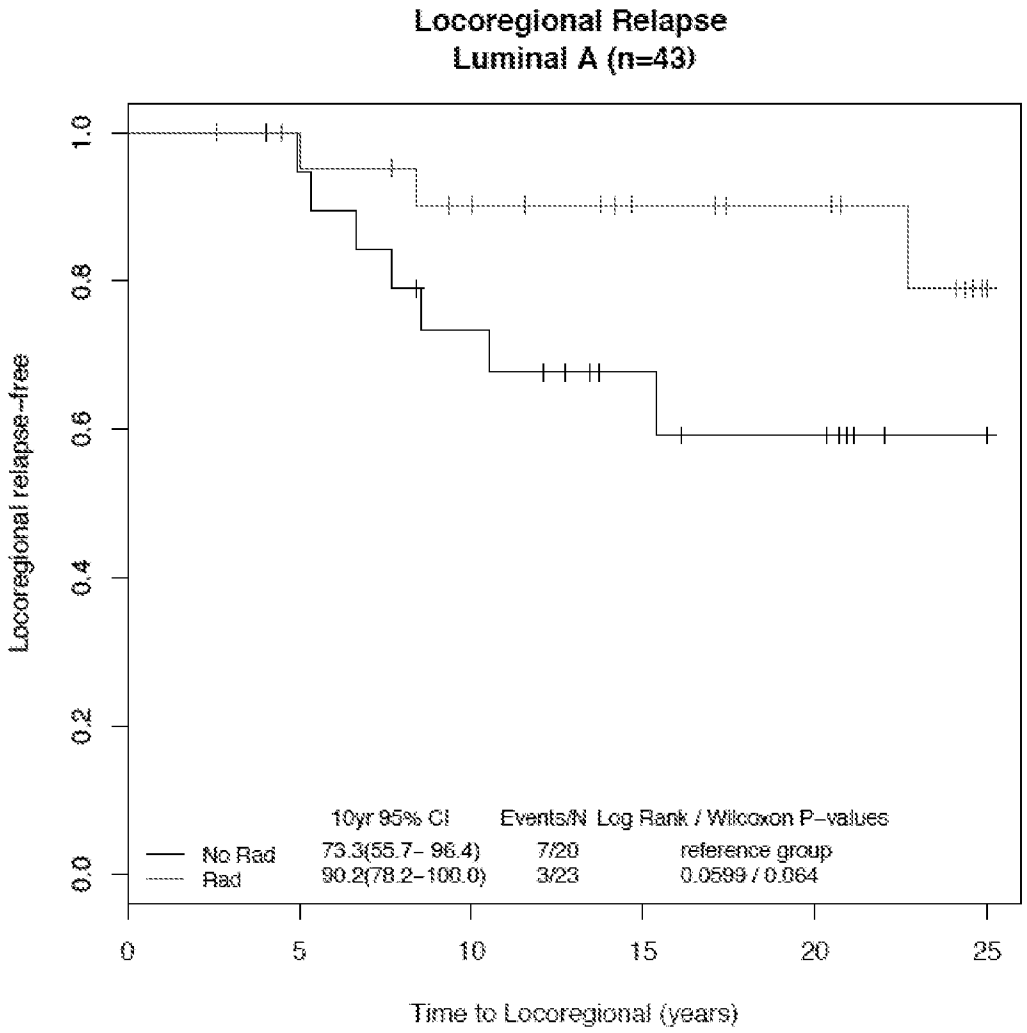

Locoregional Relapse
Luminal A (n=43)
Locoregional relapse-free
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
25
Time to Locoregional (years)
10yr 95% CI
Events/N
Log Rank / Wilcoxon P-values
No Rad
Rad
73.3(55.7- 96.4)
90.2(78.2-100.0)
7/20
3/23
reference group
0.0599 / 0.064

Figure 1B

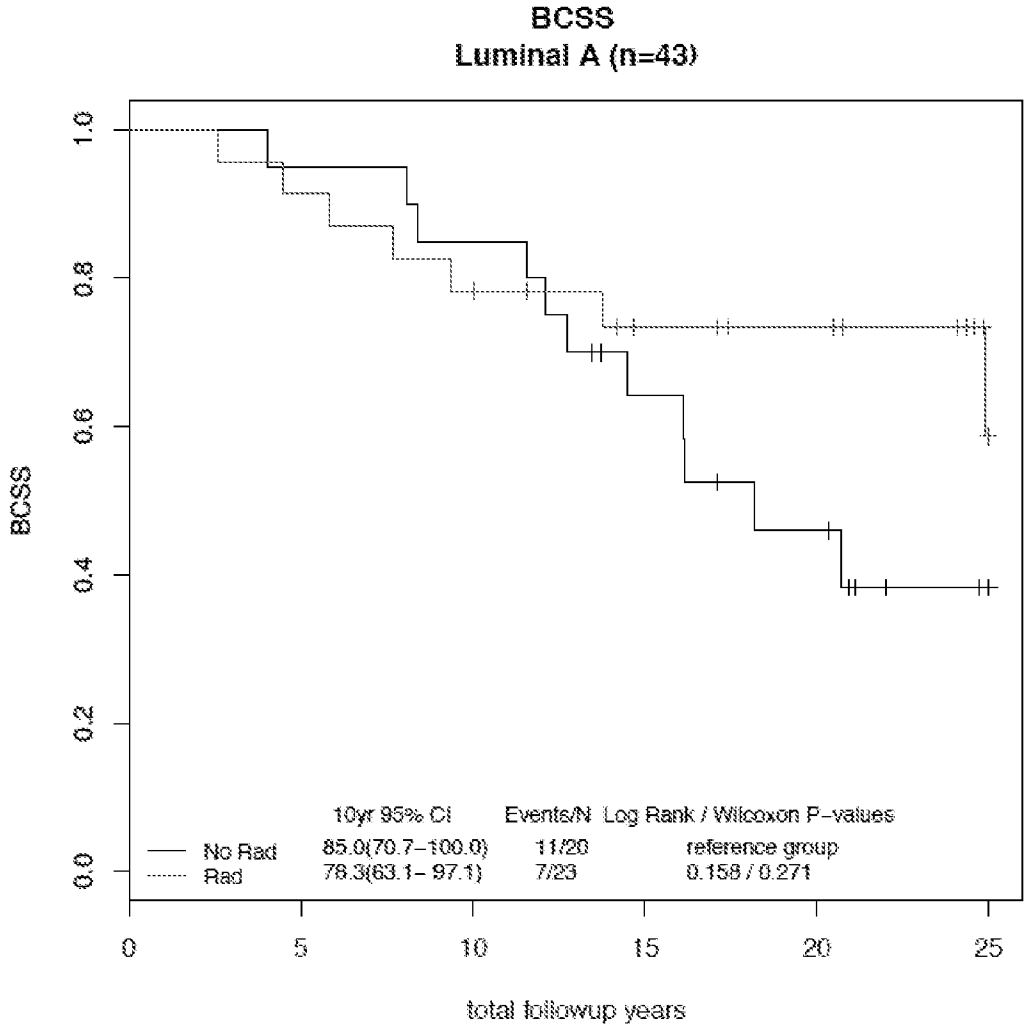

BCSS
Luminal A (n=43)
BCSS
1.0
0.8
0.6
0.4
0.2
0.0
10yr 95% CI
Events/N
Log Rank / Wilcoxon P-values
No Rad
85.0(70.7-100.0)
11/20
reference group
Rad
78.3(63.1- 97.1)
7/23
0.158 / 0.271
0
5
10
15
20
25
total followup years

Figure 2A

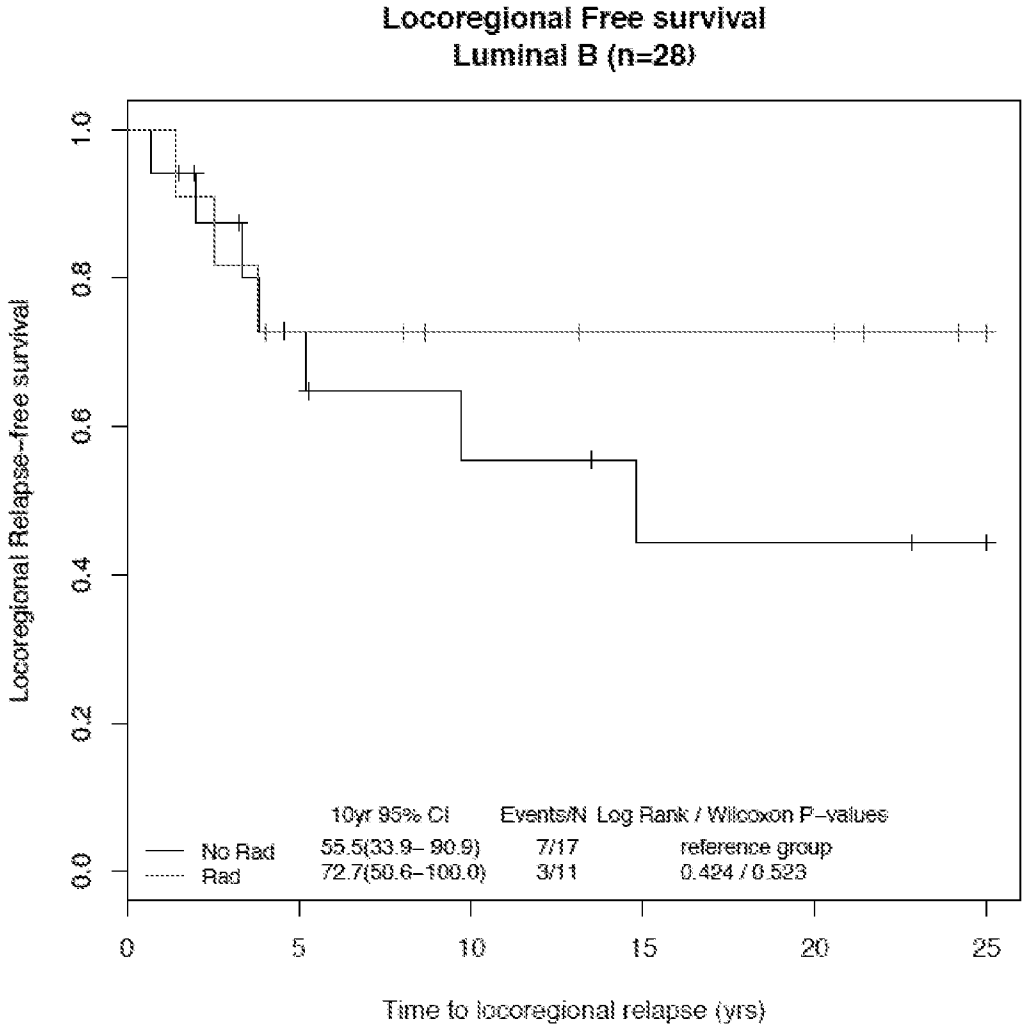

Locoregional Free survival
Luminal B (n=28)
Locoregional Relapse-free survival
0.0
0.2
0.4
0.6
0.8
1.0
10yr 95% CI
Events/N
Log Rank / Wilcoxon P-values
No Rad
55.5(33.9- 90.9)
7/17
reference group
Rad
72.7(50.6-100.0)
3/11
0.424 / 0.523
0
5
10
15
20
25
Time to locoregional relapse (yrs)

Figure 2B

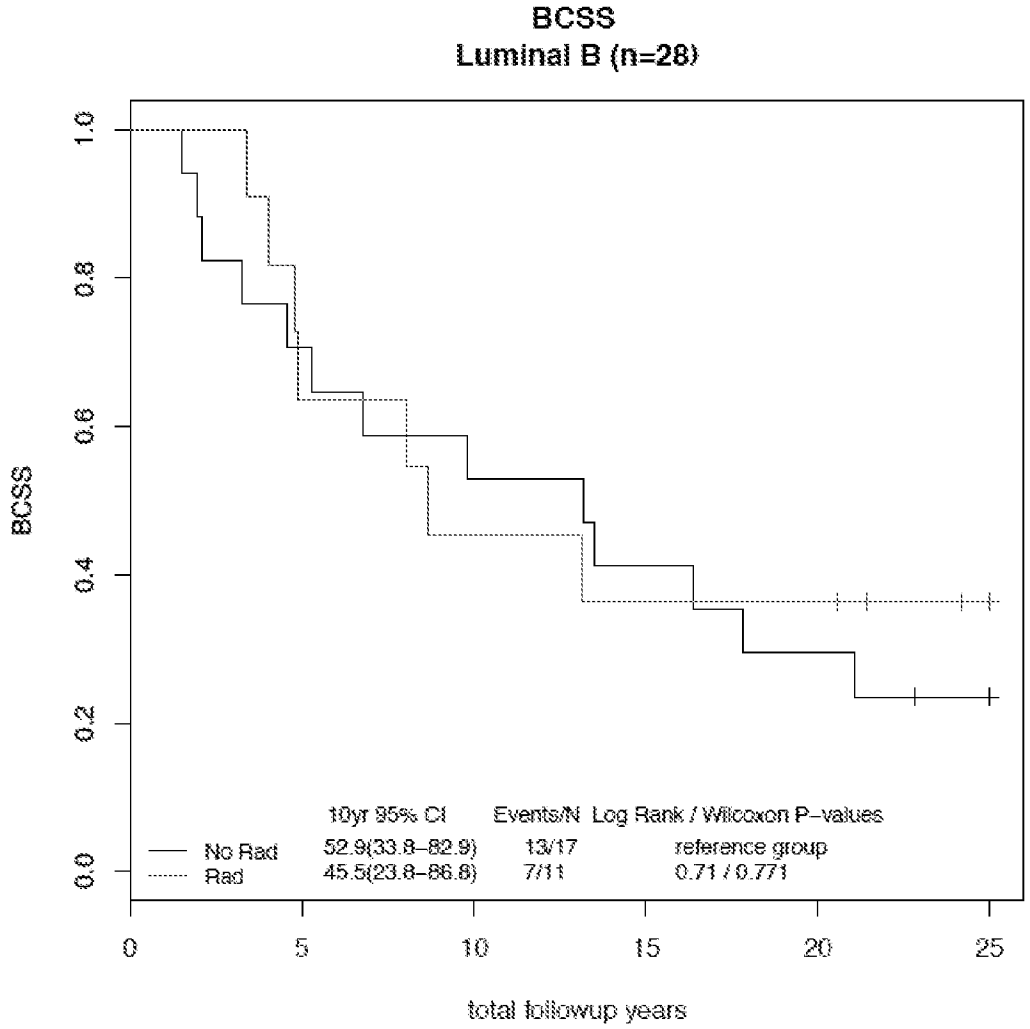

BCSS
Luminal B (n=28)
BCSS
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
25
total followup years
10yr 95% CI
Events/N
Log Rank / Wilcoxon P-values
No Rad
52.9(33.8–82.9)
13/17
reference group
Rad
45.5(23.8–86.8)
7/11
0.71 / 0.771

Figure 3A

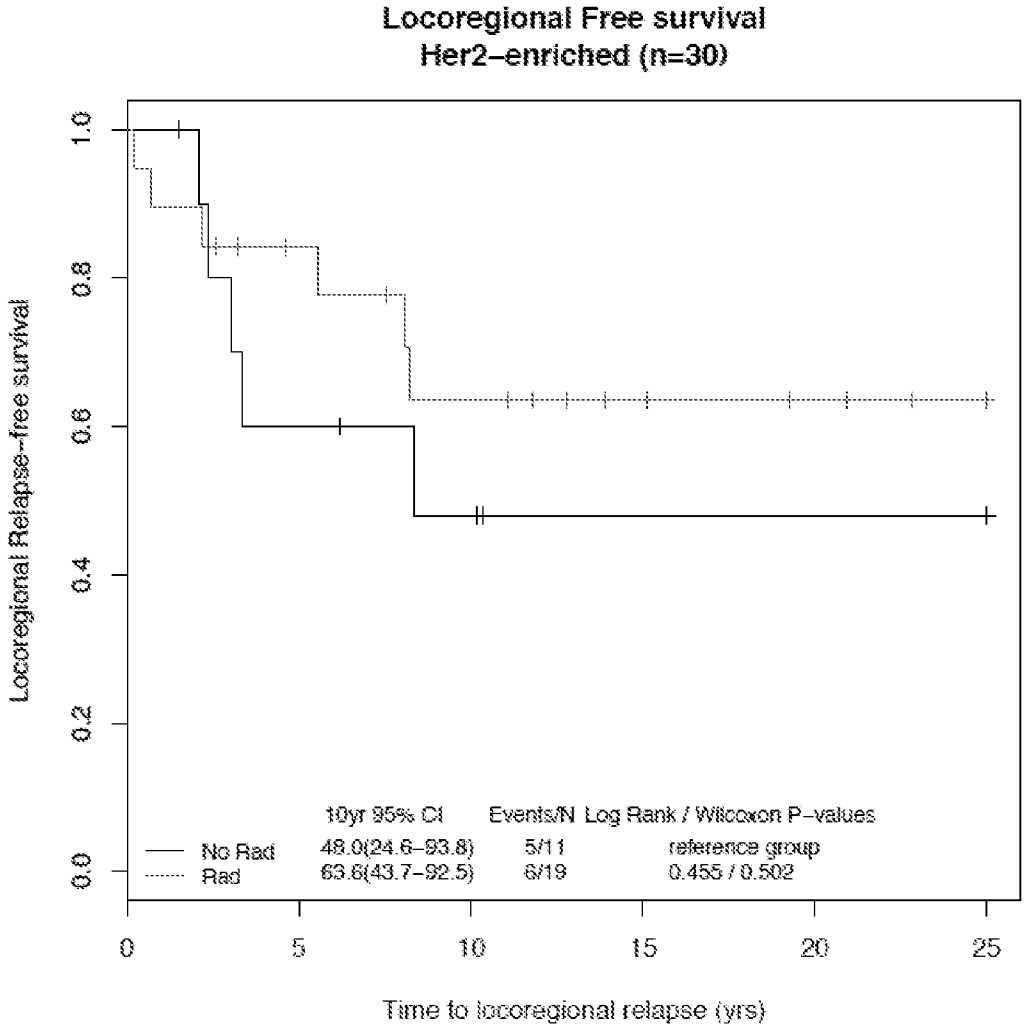

Locoregional Free survival
Her2−enriched (n=30)
Locoregional Relapse−free survival
0.0
0.2
0.4
0.6
0.8
1.0
10yr 95% CI
Events/N
Log Rank / Wilcoxon P−values
No Rad
48.0(24.6−93.8)
5/11
reference group
Rad
63.6(43.7−92.5)
6/19
0.455 / 0.502
0
5
10
15
20
25
Time to locoregional relapse (yrs)

Figure 3B

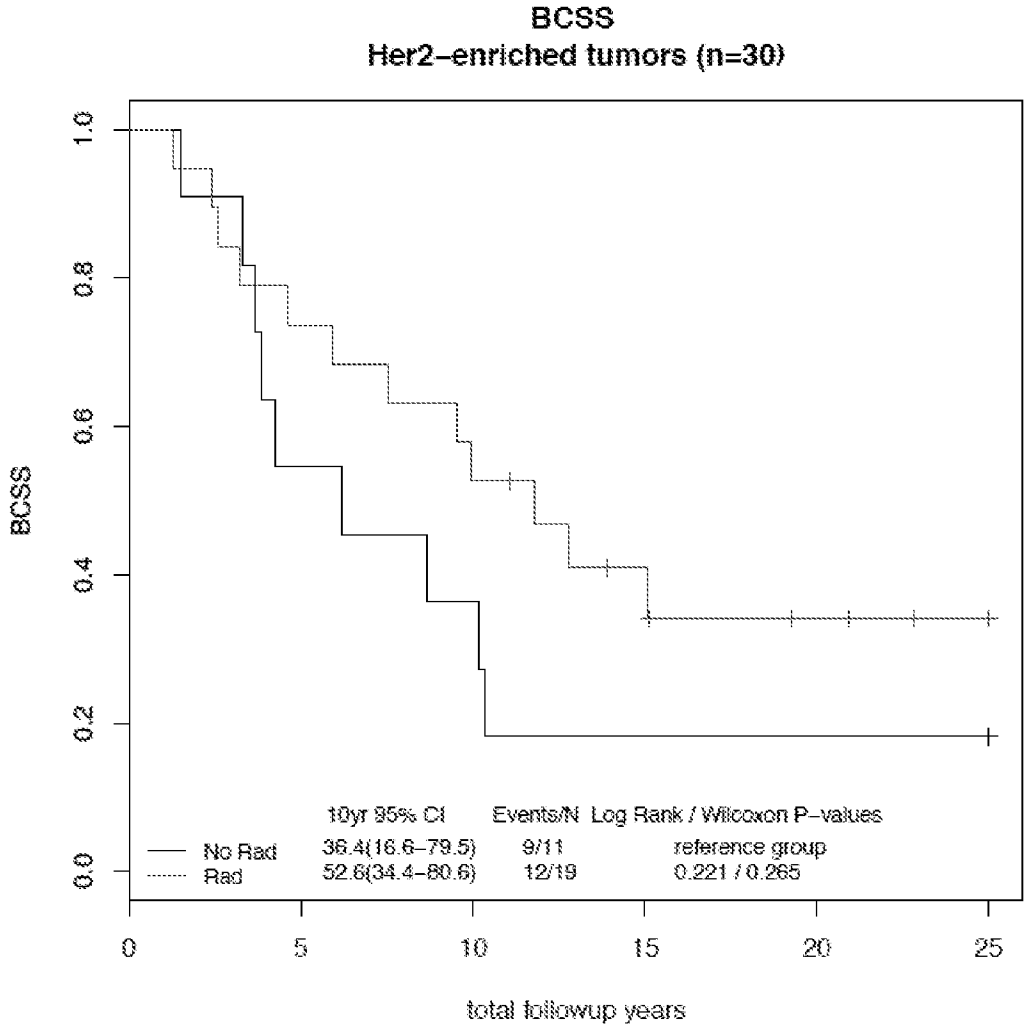

BCSS
Her2−enriched tumors (n=30)
BCSS
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
25
total followup years
10yr 95% CI
Events/N
Log Rank / Wilcoxon P−values
No Rad
Rad
36.4(16.6−79.5)
52.6(34.4−80.6)
9/11
12/19
reference group
0.221 / 0.265

Figure 4A

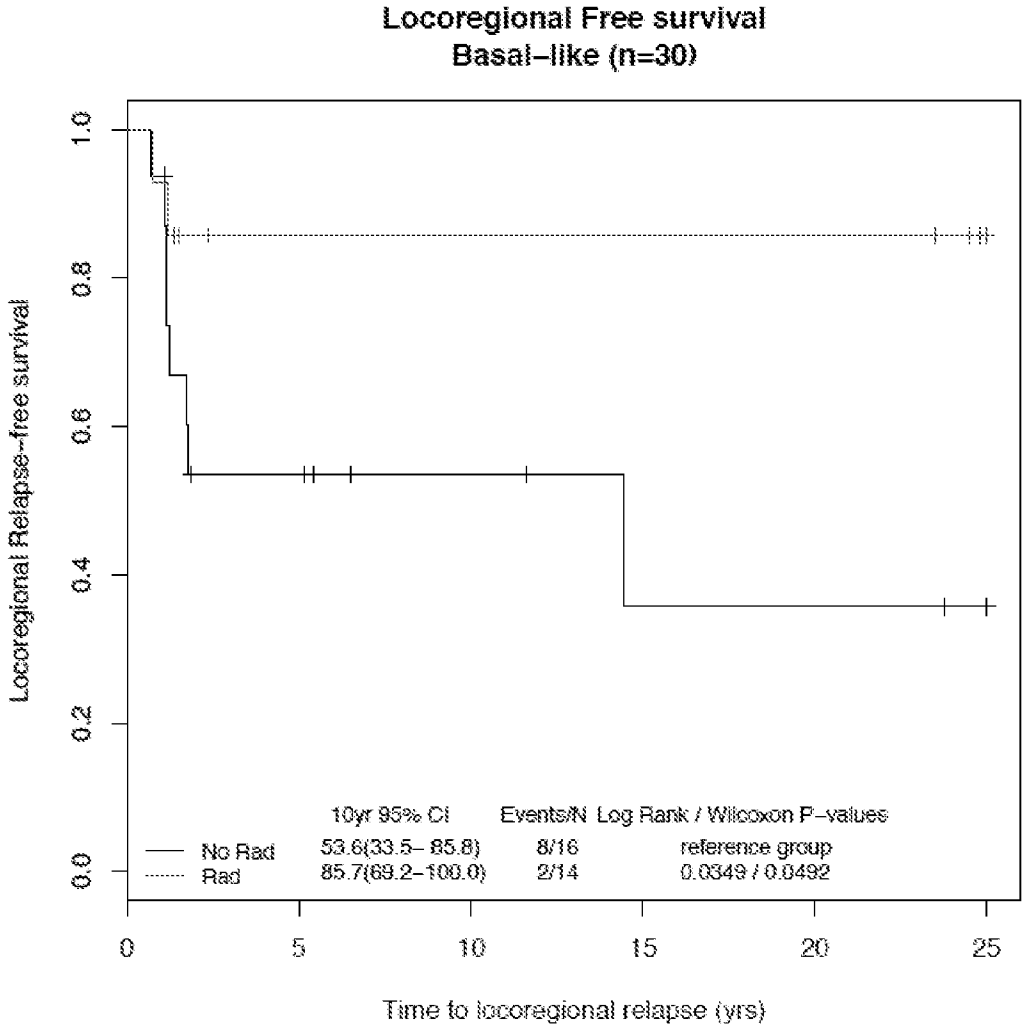

Locoregional Free survival
Basal–like (n=30)
Locoregional Relapse–free survival
1.0
0.8
0.6
0.4
0.2
0.0
10yr 95% CI
Events/N
Log Rank / Wilcoxon P–values
No Rad
53.6(33.5– 85.8)
8/16
reference group
Rad
85.7(69.2–100.0)
2/14
0.0349 / 0.0492
0
5
10
15
20
25
Time to locoregional relapse (yrs)

Figure 4B

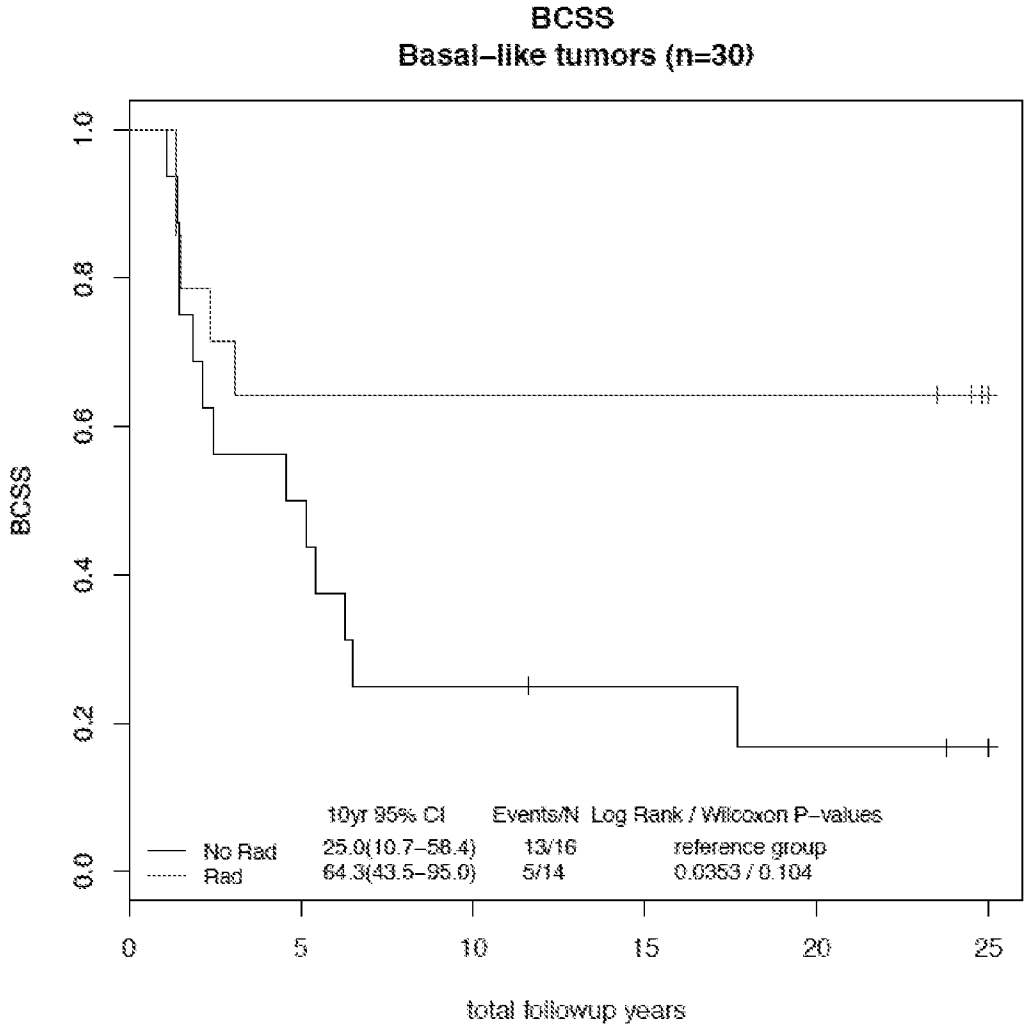

BCSS
Basal–like tumors (n=30)
BCSS
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
total followup years
10yr 95% CI
Events/N
Log Rank / Wilcoxon P–values
No Rad
Rad
25.0(10.7–58.4)
64.3(43.5–95.0)
13/16
5/14
reference group
0.0353 / 0.104

Figure 5

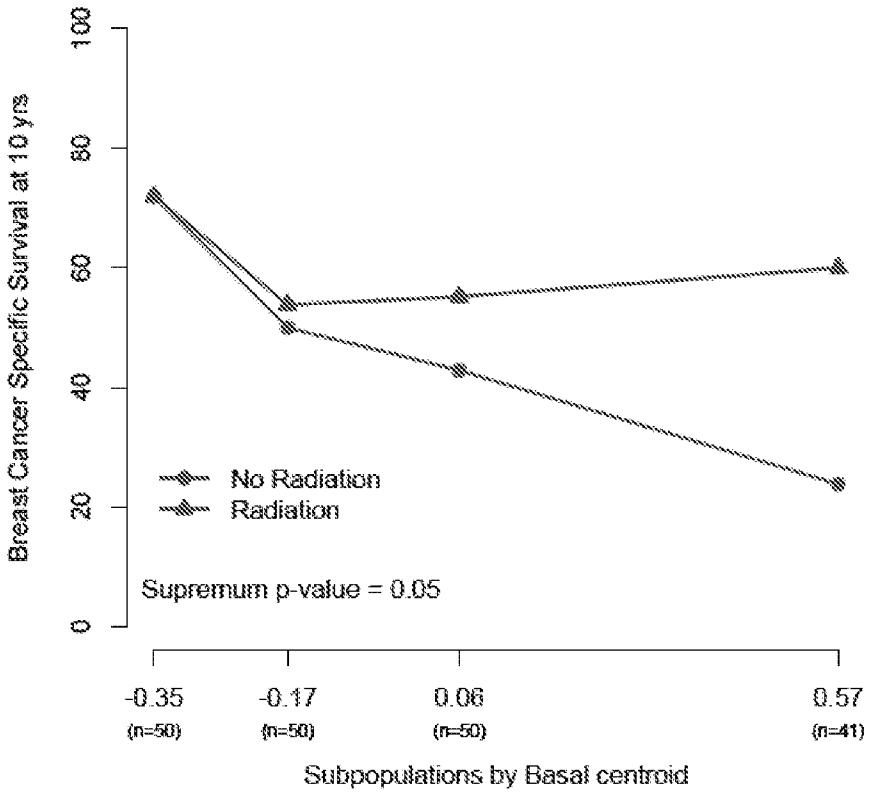

Breast Cancer Specific Survival at 10 yrs
0
20
40
60
80
100
No Radiation
Radiation
Supremum p-value = 0.05
-0.35
(n=50)
-0.17
(n=50)
0.06
(n=50)
0.57
(n=41)
Subpopulations by Basal centroid

Figure 6A

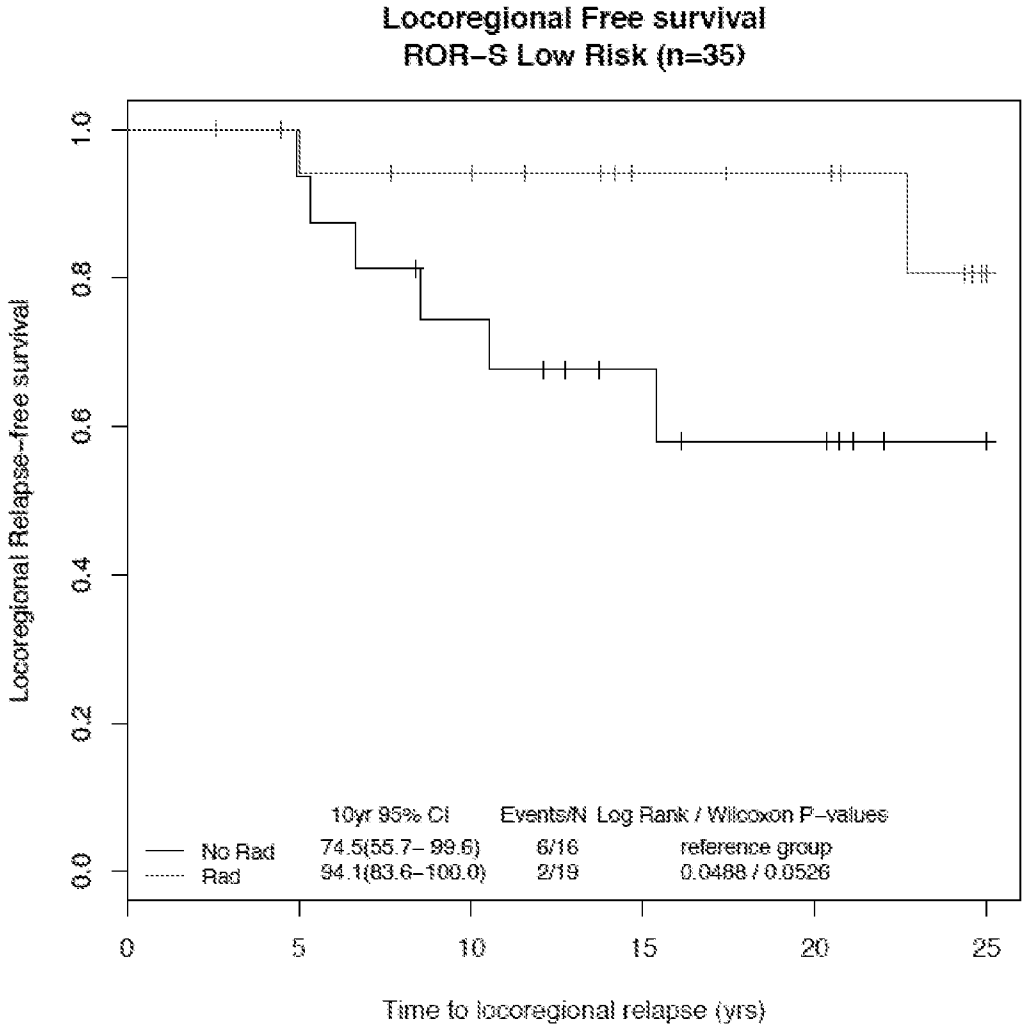

Locoregional Free survival
ROR-S Low Risk (n=35)
Locoregional Relapse-free survival
0.0
0.2
0.4
0.6
0.8
1.0
10yr 95% CI
Events/N
Log Rank / Wilcoxon P-values
No Rad
74.5(55.7- 99.6)
6/16
reference group
Rad
94.1(83.6-100.0)
2/19
0.0488 / 0.0526
0
5
10
15
20
25
Time to locoregional relapse (yrs)

Figure 6B

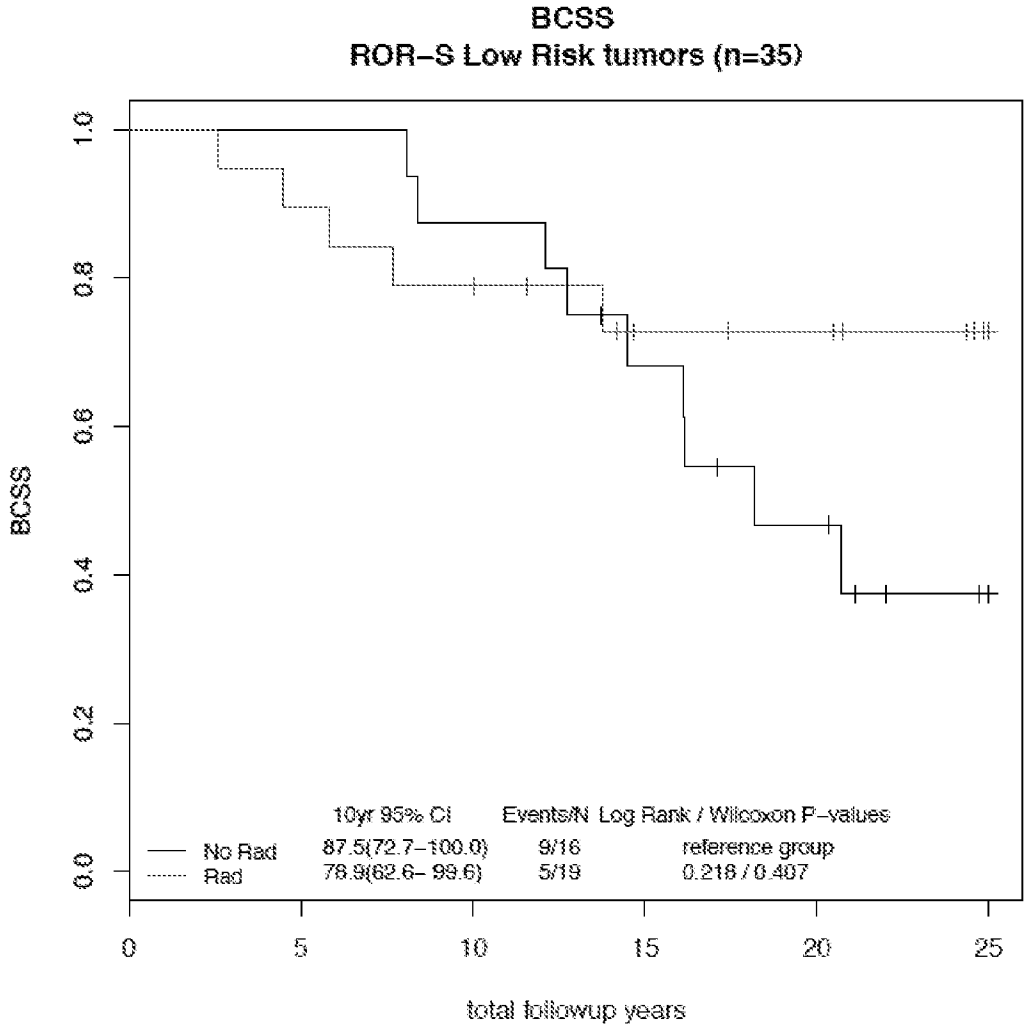

BCSS
ROR−S Low Risk tumors (n=35)
BCSS
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
total followup years
10yr 95% CI
Events/N
Log Rank / Wilcoxon P−values
No Rad
87.5(72.7−100.0)
9/16
reference group
Rad
78.9(62.6− 99.6)
5/19
0.218 / 0.407

Figure 7A

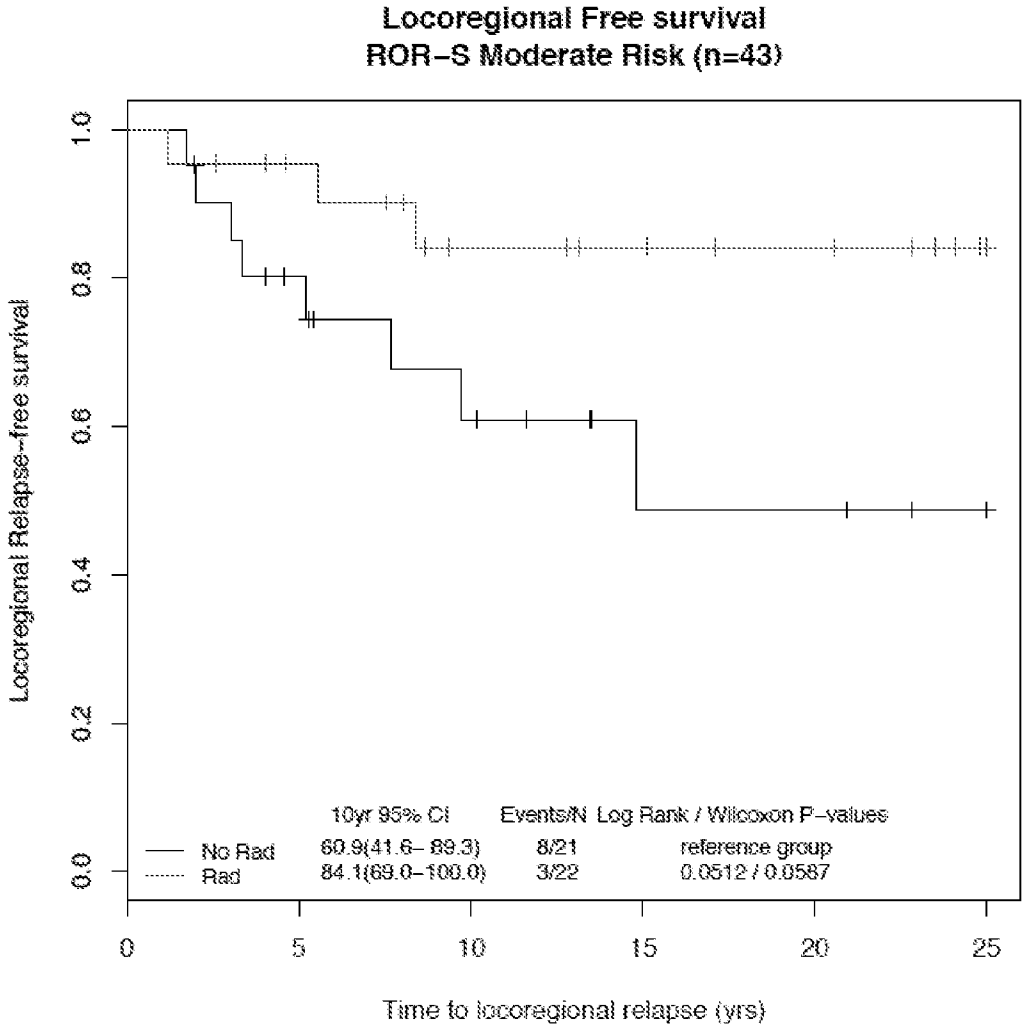

Locoregional Free survival
ROR-S Moderate Risk (n=43)
Locoregional Relapse-free survival
1.0
0.8
0.6
0.4
0.2
0.0
10yr 95% CI
Events/N
Log Rank / Wilcoxon P-values
No Rad
60.9(41.6- 89.3)
8/21
reference group
Rad
84.1(69.0-100.0)
3/22
0.0512 / 0.0587
0
5
10
15
20
25
Time to locoregional relapse (yrs)

Figure 7B

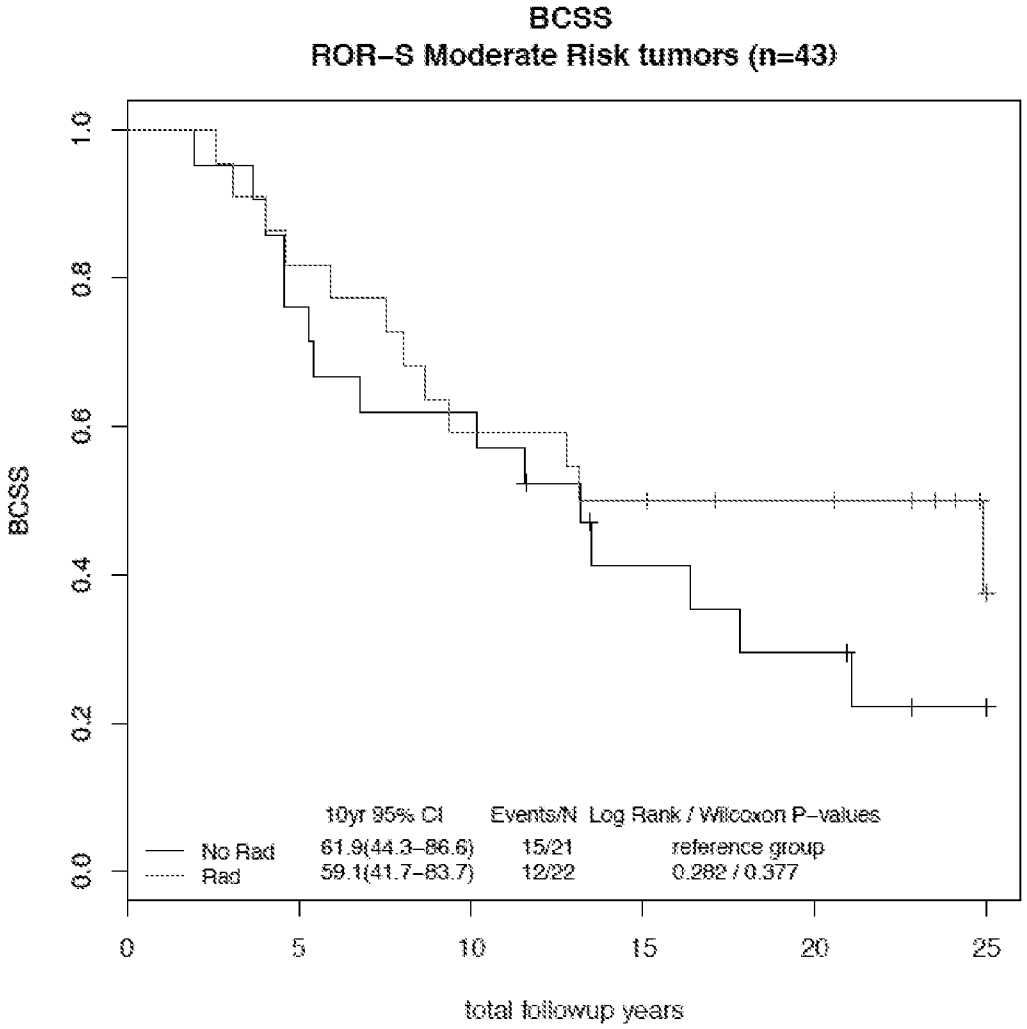

BCSS
ROR-S Moderate Risk tumors (n=43)
BCSS
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
total followup years
10yr 95% CI
Events/N
Log Rank / Wilcoxon P-values
No Rad
61.9(44.3-86.6)
15/21
reference group
Rad
59.1(41.7-83.7)
12/22
0.282 / 0.377

Figure 8A

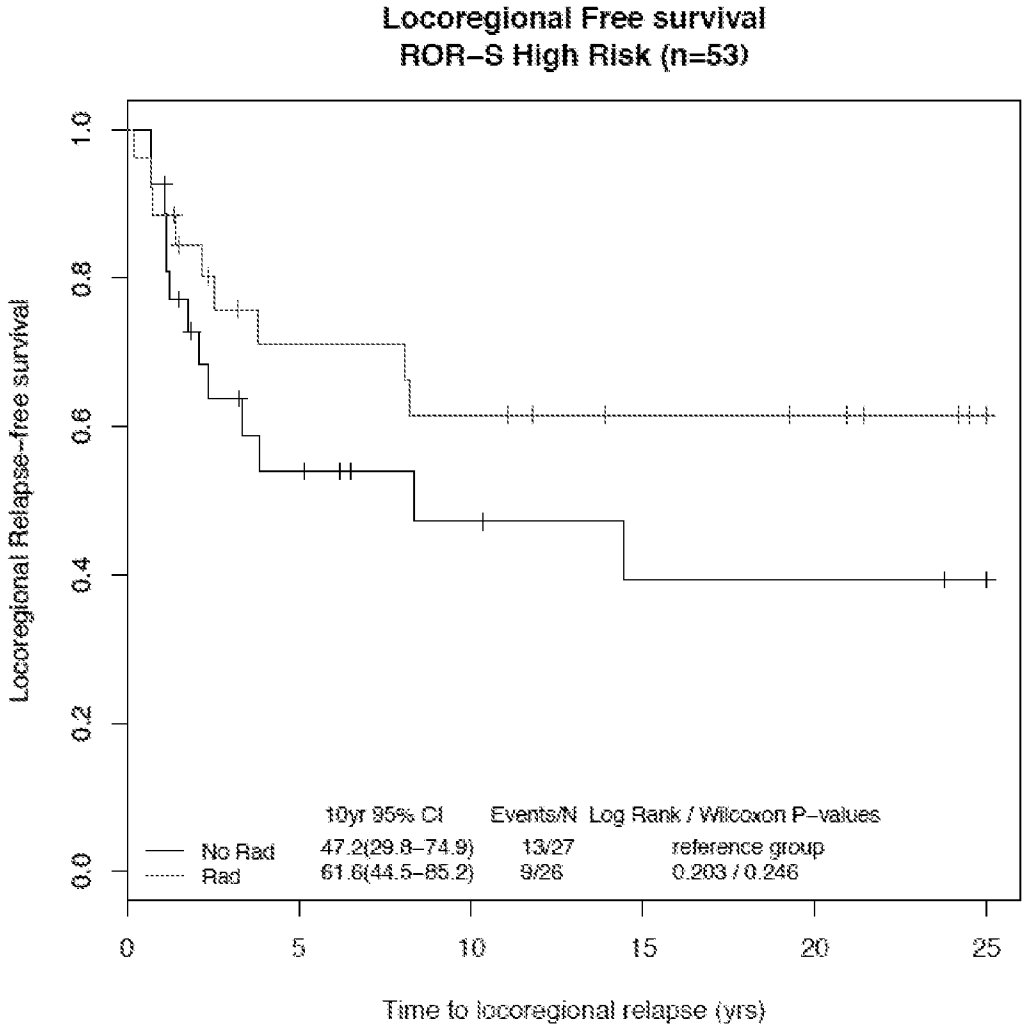

Locoregional Free survival
ROR-S High Risk (n=53)
Locoregional Relapse-free survival
0.0
0.2
0.4
0.6
0.8
1.0
10yr 95% CI
Events/N
Log Rank / Wilcoxon P-values
No Rad
47.2(29.8-74.9)
13/27
reference group
Rad
61.6(44.5-85.2)
9/26
0.203 / 0.246
0
5
10
15
20
25
Time to locoregional relapse (yrs)

Figure 8B

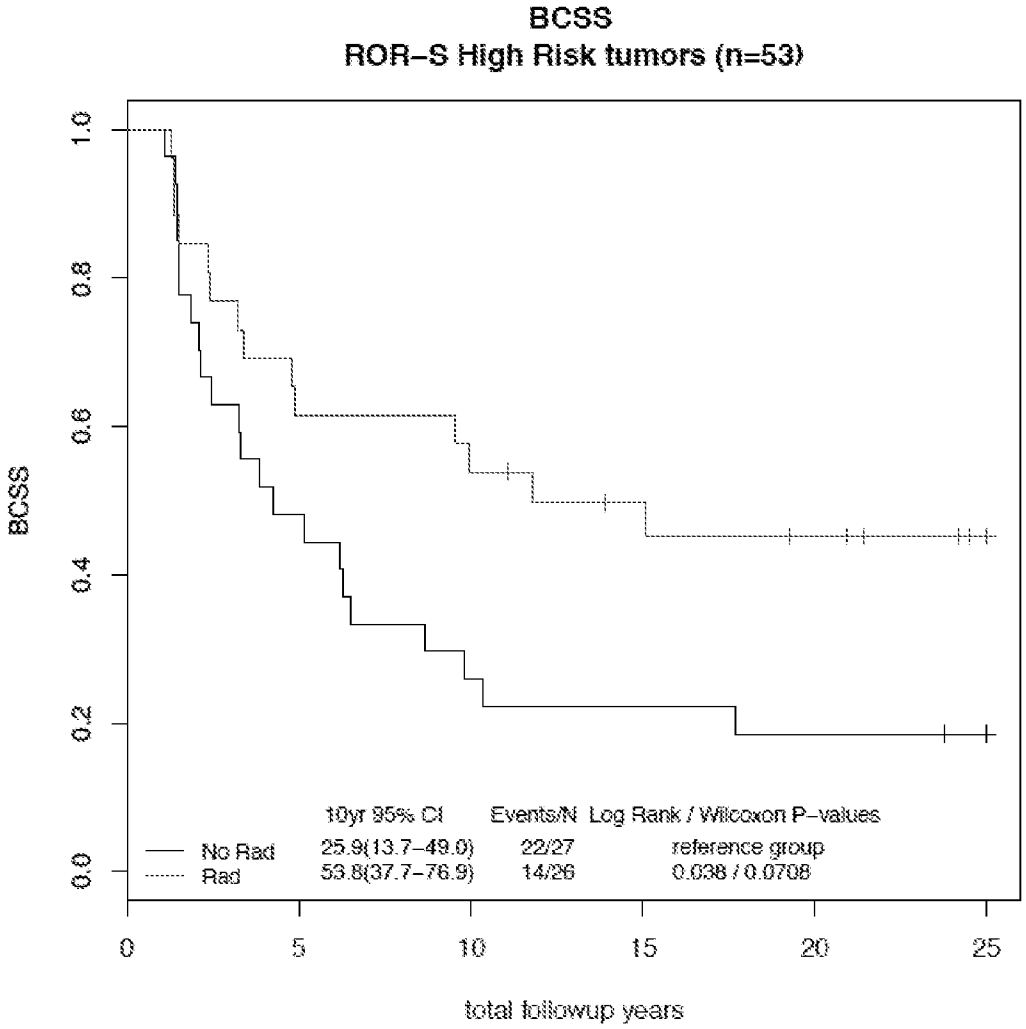

BCSS
ROR–S High Risk tumors (n=53)
BCSS
1.0
0.8
0.6
0.4
0.2
0.0
10yr 95% CI
Events/N
Log Rank / Wilcoxon P–values
No Rad
25.9(13.7–49.0)
22/27
reference group
Rad
53.8(37.7–76.9)
14/26
0.038 / 0.0708
0
5
10
15
20
25
total followup years

Figure 9

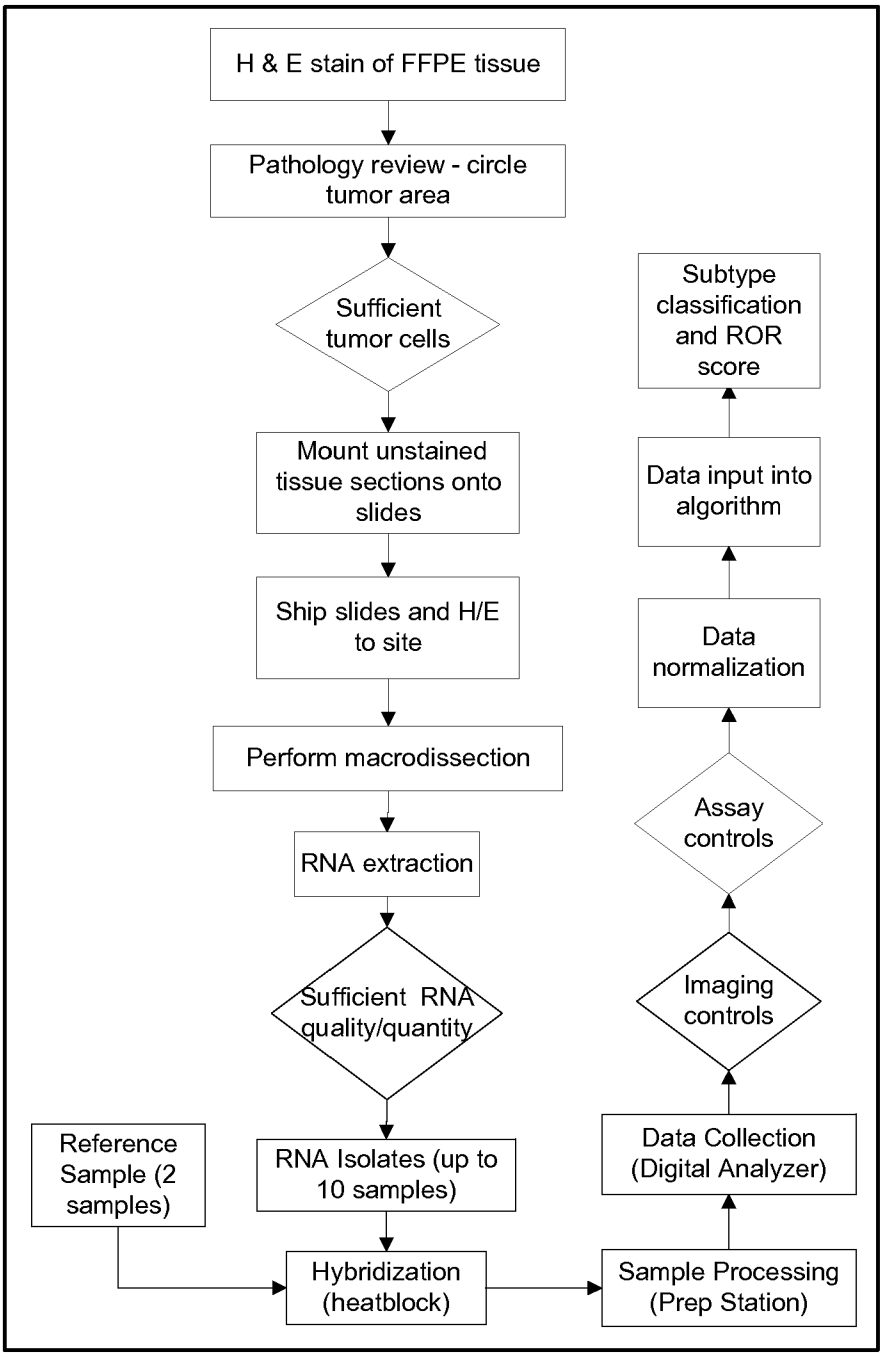
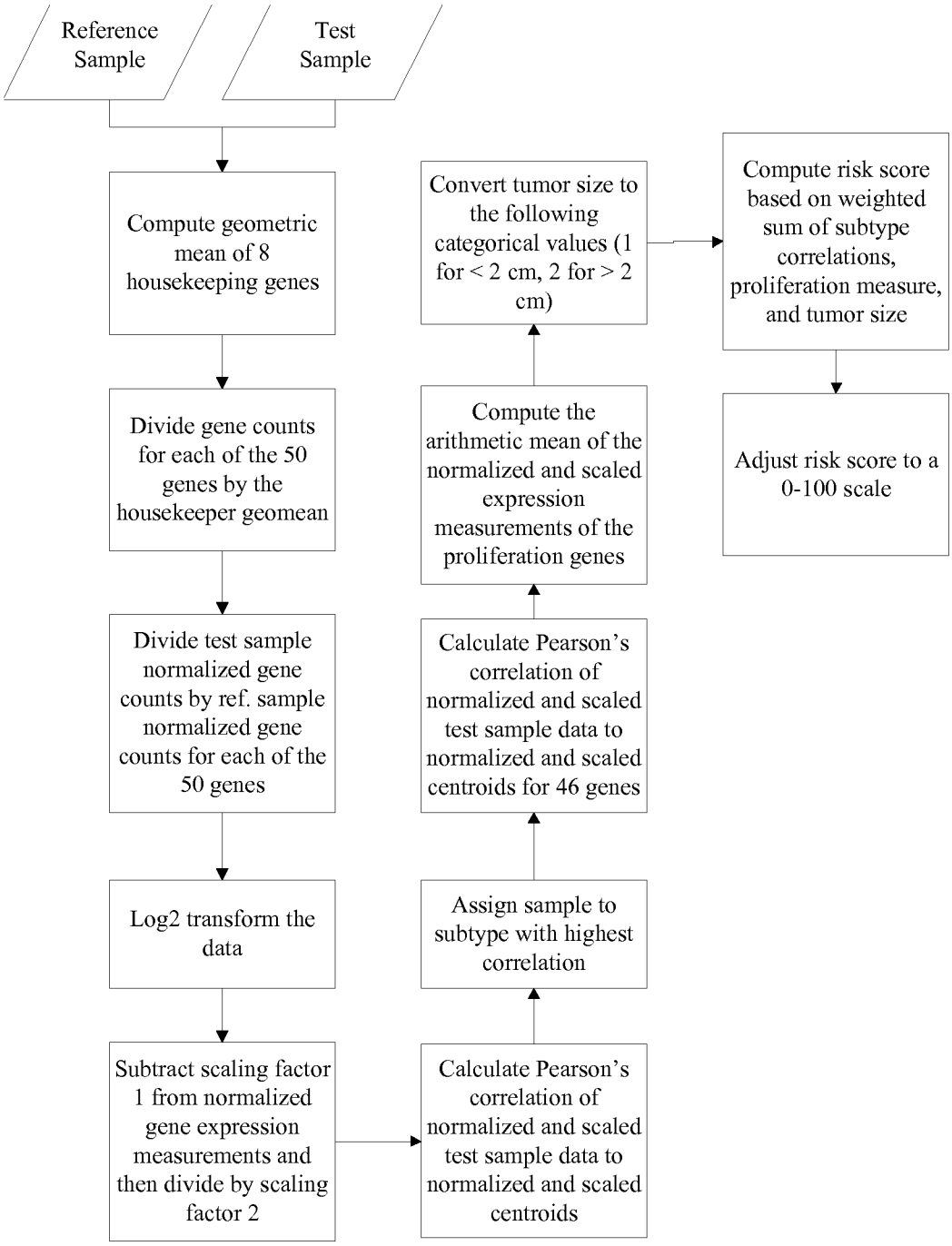

H & E stain of FFPE tissue
Pathology review - circle tumor area
Sufficient tumor cells
Mount unstained tissue sections onto slides
Ship slides and H/E to site
Perform macrodissection
RNA extraction
Sufficient RNA quality/quantity
Reference Sample (2 samples)
RNA Isolates (up to 10 samples)
Hybridization (heatblock)
Sample Processing (Prep Station)
Data Collection (Digital Analyzer)
Imaging controls
Assay controls
Data normalization
Data input into algorithm
Subtype classification and ROR score

Figure 10


Reference Sample
Test Sample
Compute geometric mean of 8 housekeeping genes
Divide gene counts for each of the 50 genes by the housekeeper geomean
Divide test sample normalized gene counts by ref. sample normalized gene counts for each of the 50 genes
Log2 transform the data
Subtract scaling factor 1 from normalized gene expression measurements and then divide by scaling factor 2
Calculate Pearson's correlation of normalized and scaled test sample data to normalized and scaled centroids
Assign sample to subtype with highest correlation
Calculate Pearson's correlation of normalized and scaled test sample data to normalized and scaled centroids for 46 genes
Compute the arithmetic mean of the normalized and scaled expression measurements of the proliferation genes
Convert tumor size to the following categorical values (1 for < 2 cm, 2 for > 2 cm)
Compute risk score based on weighted sum of subtype correlations, proliferation measure, and tumor size
Adjust risk score to a 0-100 scale

SEQUENCE LISTING

<110> British Columbia Cancer Agency Branch
The University of North Carolina at Chapel Hill
Washington University
University of Utah
University of Utah Research Foundation
Cheang, Maggie
Nielsen, Torsten
Perou, Charles
Ellis, Matthew
Bernard, Philip

<120> METHODS AND KITS FOR PREDICTING OUTCOME AND METHODS AND KITS FOR TREATING BREAST CANCER WITH RADIATION THERAPY

<130> NATE-022001WO (321329-2204)

<150> US 61/875,373
<151> 2013-09-09

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<151> 2014-05-09

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<170> PatentIn version 3.5

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<212> DNA
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<400> 154

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gagaagcggg agtggatctg aaataaaatc caggaatctg ggggtcctca gacggagcca 180

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<213> Homo sapi ens

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