

METHODS AND COMPOSITIONS FOR PREDICTING RESPONSE TO ERIBULIN

RELATED APPLICATIONS

5 This application claims priority to U.S. Provisional Application No. 61/454426, filed March 18, 2011, the entire contents of which are hereby incorporated by reference herein.

BACKGROUND OF THE INVENTION

10 Cancer is a term used to describe a wide variety of diseases that are each characterized by the uncontrolled growth of a particular type of cell. It begins in a tissue containing such a cell and, if the cancer has not spread to any additional tissues at the time of diagnosis, may be treated by, for example, surgery, radiation, or another type of localized therapy. However, when there is evidence that cancer has metastasized from its tissue of origin, different approaches to treatment are typically used. Indeed, because it
15 is not possible to determine the extent of metastasis, systemic approaches to therapy are usually undertaken when any evidence of spread is detected. These approaches involve the administration of chemotherapeutic drugs that interfere with the growth of rapidly dividing cells, such as cancer cells.

 Halichondrin B is a structurally complex, macrocyclic compound that was
20 originally isolated from the marine sponge *Halichondria okadai*, and subsequently was found in *Axinella sp.*, *Phakellia carteri*, and *Lissodendoryx sp.* A total synthesis of halichondrin B was published in 1992 (Aicher *et al.*, *J. Am. Chem. Soc.* 114:3162-3164, 1992). Halichondrin B has been shown to inhibit tubulin polymerization, microtubule assembly, beta-tubulin crosslinking, GTP and vinblastine binding to tubulin, and
25 tubulin-dependent GTP hydrolysis *in vitro*. This molecule has also been shown to have anti-cancer properties *in vitro* and *in vivo*. Halichondrin B analogs having anti-cancer activities are described in U.S. Pat. No. 6,214,865 B1.

 In particular, eribulin mesylate, a Halichondrin B analog, has been developed as an anticancer drug. Recently, eribulin mesylate was approved for the treatment of
30 patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease, wherein prior therapy may have included an anthracycline and/or a taxane in either the adjuvant or metastatic setting. The ability to predict in advance of treatment whether a cancer patient is likely to be responsive to an anti-cancer agent can guide selection of appropriate treatment, and
35 is beneficial to patients. Accordingly, there is a need for methods for and compositions

useful in, assessing or predicting responsiveness to eribulin in patients having cancer and, in particular, breast cancer.

SUMMARY OF THE INVENTION

5 The invention is based, at least in part, on the observation that a low level of expression, *e.g.*, the absence of expression, of the biomarkers identified herein is indicative of responsiveness to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate). Specifically, the absence of expression or a low level of expression of these biomarkers, including, for example, one or more of
10 those biomarkers set forth in Table 1, in a subject is indicative that the subject will be responsive to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate).

 Accordingly, in one aspect, the present invention provides a method for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt
15 thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer, by assaying a sample derived from the subject to determine the level of expression in the sample of a biomarker selected from the group of biomarkers listed in Table 1, wherein a low level of expression of the biomarker is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), will be effective
20 in treating the subject having breast cancer. In another aspect, the present invention provides a method for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer, by determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1 in a sample derived from the
25 subject, wherein a low level of expression of the biomarker is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), will be effective in treating the subject having breast cancer. In a further aspect, the present invention provides a method for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to
30 treat a subject having breast cancer, by determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1 in a sample derived from the subject, and predicting that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), will be effective in treating a subject having breast cancer when there is a low level of expression of the biomarker in the
35 sample. In one embodiment of the foregoing aspects of the invention, the methods may further include obtaining a sample from a subject.

In yet another aspect, the present invention provides a method for determining the sensitivity of a breast tumor, for example, derived from a subject having breast cancer, to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), by determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1 in the tumor, wherein a low level of expression of the biomarker in the tumor indicates that the tumor is sensitive to treatment with eribulin, or an analog thereof. In yet another aspect, the present invention provides a method for determining the sensitivity of a breast tumor, for example, derived from a subject having breast cancer, to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), by determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1 in the tumor, and identifying the tumor as being sensitive to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), when the biomarker is expressed in the tumor at a low level.

In further aspects of the invention, methods are provided for treating a subject having breast cancer. The methods include identifying a subject having breast cancer in which a biomarker selected from the group of biomarkers listed in Table 1 is expressed at a low level, and administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), to the subject. In yet a further aspect, the present invention provides methods of treating a subject having breast cancer, by assaying a sample derived from the subject to determine the level of expression in the sample of a biomarker selected from the group of biomarkers listed in Table 1, and administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), to the subject when a low level of expression of the biomarker is detected in the sample. In one embodiment of the foregoing aspects of the invention, the methods may further include obtaining a sample from a subject.

In further aspects of the invention, methods are provided for treating a subject having breast cancer that is sensitive to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof. The methods include identifying a subject having breast cancer that is sensitive to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, (*e.g.*, a breast cancer in which a biomarker selected from the group of biomarkers listed in Table 1 is expressed at a low level), and administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), to the subject. In yet a further aspect, the present invention provides methods of treating a subject having breast cancer that is sensitive to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, by

assaying a sample derived from the subject to determine the level of expression in the sample of a biomarker selected from the group of biomarkers listed in Table 1, and administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), to the subject when a low level of expression of the biomarker is detected in the sample. In one embodiment of the foregoing aspects of the invention, the methods may further include obtaining a sample from a subject.

In various embodiments, the subject has not been previously treated with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate). Alternatively, the subject has been previously treated with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof. In certain embodiments, the breast cancer is an Estrogen Receptor (ER) negative breast cancer and/or a Progesterone Receptor (PR) negative breast cancer and/or a Her-2 negative breast cancer.

In various embodiments, the level of expression of at least 2, at least 3, at least 4 or at least 5 biomarkers selected from the group of biomarkers listed in Table 1 is determined.

In particular embodiments, a predictive gene signature comprising a sub-combination of 2 or more biomarkers selected from the group of biomarkers listed in Table 1 is used. In various embodiments, the level of expression of at least 2, at least 3, at least 4 or at least 5 biomarkers selected from the group of biomarkers listed in Table 1 is determined. For example, the predictive gene signature may include at least 2 biomarkers, *e.g.*, DYSF and EDIL3; GNAT1 and ERGIC3; KRT24 and PAPLN; MANSC1 and PDGFB; PCDH1 and PDGFB; or PHOSPHO2 and PSENEN. In another embodiment, the predictive gene signature may include at least 3 biomarkers, *e.g.*, COL7A1, YTHDF1 and ZIC5; CKLF, IL10 and TUBB6; CDC20, CFL1 and TMEM79; HYAL2, NCBP1 and SNX11; or CEP152, NCBP1 and SATB1. In another embodiment, the predictive gene signature may include at least 4 biomarkers, *e.g.*, APBB2, CCL26, PSENEN and SATB1; ANG, JAM3, KLHL17 and PAPLN; ITFG3, MAD2L1BP, NMU and PDGFB; SPTA1, TYROBP, SNX11 and PSENEN; GRAMD4, GNAT1, TMIGD2 and YTHDF1; or GRAMD4, HYAL2, PHOSPHO2 and TUBB6. In another embodiment, the predictive gene signature may include at least 5 biomarkers, *e.g.*, CCL26, CDC20, ERGIC3, EDIL3 and PCDH1; DYSF, NMU, PHOSPHO2, PSENEN and SNX11; APBB2, CKLF, CYP4F3, TUBB6 and YTHDF1; or CEP152, MAD2L1BP, SPTA1, TMEM79 and ZIC5.

In particular embodiments, the predictive gene signature may include 2 or more of biomarkers ABI3, ANG, APBB2, CCL26, CDC20, CEP152, CFL1, CKLF, COL7A1,

CYP4F3, DYSF, GNAT1, GRAMD4, HYAL2, IL10, ITFG3, JAM3, KLHL17, KRT24, MAD2L1BP, MANSC1, MOBKL1B, NCBP1, NMU, PCDH1, PHOSPHO2, SPTA1, TMIGD2, TYROBP, ZIC5, ERGIC3, PDGFB, PSENEN, SATB1, SNX11, TMEM79 and YTHDF1, *e.g.*, ABI3 and ANG; APBB2 and CCL26; GNAT1 and GRAMD4; IL10 and ITFG3; MACSC1 and MOBKL1B; NMU and PCDH1; or TYROBP and ZIC5. In other embodiments, the predictive gene signature includes at least 3 of the previously recited biomarkers, *e.g.*, ABI3, ANG and APBB2; CCL26, CKLF and COL7A1; DYSF, GNAT1 and HYAL2; JAM3, KLHL17 and KRT24; NCBP1, NMU and PCDH1; SPTA1, TMIGD2 and TYROBP; or ZIC5, MAD2L1BP and CDC20. In other

embodiments, the predictive gene signature includes at least 4 of the previously recited biomarkers, *e.g.*, ABI3, ANG, APBB2 and CCL26; CEP152, CFL1, CKLF and COL7A1; KRT24, MANSC1, MOBKL1B and SPTA1; TYROBP, TMIGD2, PHOSPHO2 and NMU; ABI3, GNAT1, KLHL17 and SPTA1; or CEP152, HYAL2, PCDH1 and TMIGD2. In yet further embodiments, the predictive gene signature

includes at least 5 of the previously recited biomarkers, *e.g.*, CKLF, COL7A1, GRAMD4, JAM3 and PCDH1; APBB2, CEP152, DYSF, IL10 and TYROBP; CYP4F3, HYAL2, ITFG3, KLHL17 and KRT24; NCBP1, SPTA1, TMIGD2, IL10 and JAM3; or CCL26, PHOSPHO2, SPTA1, TMIGD2 and ZIC5.

In other embodiments, the predictive gene signature may include 2 or more of biomarkers ERGIC3, PDGFB, PSENEN, SATB1, SNX11, TMEM79 or YTHDF1, or any sub-combination thereof, *e.g.*, ERGIC3 and PDGFB; ERGIC3 and PSENEN; ERGIC3 and SATB1; ERGIC3 and SNX11; ERGIC3 and TMEM79; ERGIC3 and YTHDF1; PDGFB and PSENEN; PDGFB and SATB1; PDGFB and SNX11; PDGFB and TMEM79; PDGFB and YTHDF1; PSENEN and SATB1; PSENEN and SNX11; PSENEN and TMEM79; PSENEN and YTHDF1; SATB1 and SNX11; SATB1 and TMEM79; SATB1 and YTHDF1; SNX11 and TMEM79; SNX11 and YTHDF1; or TMEM79 and YTHDF1. In other embodiments, the predictive gene signature includes at least 3 biomarkers, for example, ERGIC3, PDGFB and PSENEN; SATB1, SNX11 and TMEM79; SNX11, TMEM79 and YTHDF1; or ERGIC3, PDGFB and SATB1. In further embodiments, the predictive gene signature includes at least 4 biomarkers, for example, ERGIC3, PDGFB, PSENEN and SATB1; SNX11, TMEM79, YTHDF1 and ERGIC3; or ERGIC3, PDGFB, PSENEN and YTHDF1. In further embodiments, the predictive gene signature includes at least 5 biomarkers, for example, ERGIC3, PDGFB, PSENEN, SATB1 and SNX11; ERGIC3, PDGFB, PSENEN, SATB1 and TMEM79; or PSENEN, SATB1, SNX11, TMEM79 and YTHDF1. In yet further embodiments, the predictive gene signature includes at least 6 biomarkers, for example, ERGIC3, PDGFB, PSENEN, SATB1, SNX11 and TMEM79; PDGFB, PSENEN, SATB1, SNX11,

TMEM79 and YTHDF1; or ERGIC3, PSENEN, SATB1, SNX11, TMEM79 and YTHDF1. In yet another embodiment, the predictive gene signature includes 7 biomarkers, for example, ERGIC3, PDGFB, PSENEN, SATB1, SNX11, TMEM79 and YTHDF1.

5 In various embodiments, the biomarker is not one or more of SPTA1, PAPLN, PCDH1, TMIGD2 and/or KRT24. In a particular embodiment, the biomarker is not SPTA1, PAPLN, PCDH1, TMIGD2 and KRT24. In one embodiment, the biomarker is not SPTA1. In another embodiment, the biomarker is not PAPLN. In another embodiment, the biomarker is not PCDH1. In another embodiment, the biomarker is not
10 TMIGD2. In yet another embodiment, the biomarker is not KRT24.

In particular embodiments, the predictive gene signature may include 2 or more of biomarkers ABI3, ANG, APBB2, CCL26, CDC20, CEP152, CFL1, CKLF, COL7A1, CYP4F3, DYSF, GNAT1, GRAMD4, HYAL2, IL10, ITFG3, JAM3, KLHL17, MAD2L1BP, MANSC1, MOBKL1B, NCBP1, NMU, PHOSPHO2, TYROBP, ZIC5,
15 ERGIC3, PDGFB, PSENEN, SATB1, SNX11, TMEM79, YTHDF1, EDIL3 and TUBB6, *e.g.*, ABI3 and ANG; GRAMD4 and HYAL2; NMU and PHOSPHO2; ZIC5 and PSENEN; or SNX11 and MOBKL1B. In other embodiments, the predictive gene signature includes at least 3 of the previously recited biomarkers, *e.g.*, APBB2, CDC20 and CKLF; COL7A1, DYSF and GNAT1; NCBP1, SATB1 and EDIL3; PSENEN,
20 DYSF and GNAT1; MANSC1, ZIC5 and CFL1; or CKLF, GRAMD4 and NMU. In other embodiments, the predictive gene signature includes at least 4 of the previously recited biomarkers, *e.g.*, ANG, CCL26, CEP152 and JAM3; APBB2, CYP4F3, ITFG3 and TYROBP; CYP4F3, MANSC1, PDGFB and YTHDF1; TUBB6, DYSF, PHOSPHO2 and CDC20; or CKLF, KLHL17, HYAL2 and ZIC5. In yet further
25 embodiments, the predictive gene signature includes at least 5 of the previously recited biomarkers, *e.g.*, IL10, CEP152, COL7A1, TYROBP and ERGIC3; TMEM79, SNX11, PSENEN, GNAT1 and GRAMD4; JAM3, SNX11, KLHL17, MOBKL1B and ERGIC3; or NMU, PHOSPHO2, PDGFB, CFL1 and ANG.

In various methods and or kits of the invention, the biomarker is not ABI3, is not
30 ANG, is not APBB2, is not CCL26, is not CDC20, is not CEP152, is not CFL1, is not CKLF, is not COL7A1, is not CYP4F3, is not DYSF, is not GNAT1, is not GRAMD4, is not HYAL2, is not IL10, is not ITFG3, is not JAM3, is not KLHL17, is not KRT24, is not MAD2L1BP, is not MANSC1, is not MOBKL1B, is not NCBP1, is not NMU, is not PCDH1, is not PHOSPHO2, is not SPTA1, is not TMIGD2, is not TYROBP, is not
35 ZIC5, is not ERGIC3, is not PDGFB, is not PSENEN, is not SATB1, is not SNX11, is not TMEM79, is not EDIL3, is not PAPLN, is not TUBB6 and/or is not YTHDF1.

In certain embodiments, the biomarker is not expressed at a detectable level. In another embodiment, the biomarker is expressed at a low level as compared to a control. Expression can be determined directly or indirectly by any suitable method. In certain embodiments, the level of expression of the biomarker is determined at the nucleic acid level using any suitable method. For example, the level of expression of the biomarker can be determined by detecting cDNA, mRNA or DNA. In particular embodiments, the level of expression of the biomarker is determined by using a technique selected from the group consisting of polymerase chain reaction (PCR) amplification reaction, reverse-transcriptase PCR analysis, quantitative reverse-transcriptase PCR analysis, Northern blot analysis, RNAase protection assay, digital RNA detection/ quantitation (*e.g.*, nanoString) and combinations or sub-combinations thereof.

In certain embodiments, the level of expression of the biomarker can be determined by detecting miRNA. Specifically, mRNA expression can be assessed indirectly by assessing levels of miRNA, wherein an elevated level of an miRNA which controls the expression of an mRNA is indicative of a low level of expression of the mRNA encoding the biomarker.

In other embodiments, the level of expression of the biomarker is determined at the protein level using any suitable method. For example, the presence or level of the protein can be detected using an antibody or antigen binding fragment thereof, which specifically binds to the protein. In particular embodiments, the antibody or antigen binding fragment thereof is selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab', F(ab')₂, ScFv, SMIP, affibody, avimer, versabody, nanobody, and a domain antibody, or an antigen binding fragment of any of the foregoing. In particular embodiments, the antibody or antigen binding portion thereof is labeled, for example, with a label selected from the group consisting of a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, and an enzyme-label. In certain embodiments, the level of expression of the biomarker is determined by using a technique selected from the group consisting of an immunoassay, a western blot analysis, a radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion, electrochemiluminescence immunoassay (ECLIA), ELISA assay, immunopolymerase chain reaction and combinations or sub-combinations thereof. In particular embodiments, the immunoassay is a solution-based immunoassay selected from the group consisting of electrochemiluminescence, chemiluminescence, fluorogenic chemiluminescence, fluorescence polarization, and time-resolved fluorescence. In other embodiments, the immunoassay is a sandwich immunoassay selected from the group consisting of electrochemiluminescence, chemiluminescence,

and fluorogenic chemiluminescence. Other assays which rely on agents capable of detecting the protein, such as those relying upon a suitable binding partner or enzymatic activity, can also be used (*e.g.*, use of a ligand to detect a receptor molecule).

Samples can be obtained from a subject by any suitable method, and may
5 optionally have undergone further processing step(s) (*e.g.*, freezing, fractionation, fixation, guanidine treatment, etc). Any suitable sample derived from a subject can be used, such as any tissue (*e.g.*, biopsy), cell, or fluid, as well as any component thereof, such as a fraction or extract. In various embodiments, the sample is a fluid obtained from the subject, or a component of such a fluid. For example, the fluid can be blood,
10 plasma, serum, sputum, lymph, cystic fluid, nipple aspirate, urine, or fluid collected from a biopsy (*e.g.*, lump biopsy). In other embodiments, the sample is a tissue or component thereof obtained from the subject. For example, the tissue can be tissue obtained from a biopsy (*e.g.*, lump biopsy), breast tissue, connective tissue, and/or lymphatic tissue. In a particular embodiment, the tissue is breast tissue, or a component thereof (*e.g.*, cells collected from the breast tissue). In a particular embodiment, the
15 component of the breast tissue are breast tissue cells. In another embodiment, the component of the breast tissue are circulating breast tumor cells.

In one embodiment, the subject is a human.

In another aspect, the present invention provides a kit for predicting whether
20 eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer, including reagents for determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1; and instructions for use of the kit to predict whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin
25 mesylate), may be used to treat a subject having breast cancer. For example, the reagent for determining the level of expression of the biomarker can be a probe for identifying a null mutation in the biomarker. The reagent for determining the level of expression of the biomarker can be a probe for amplifying and/or detecting the biomarker. In yet another embodiment, the reagent for determining the level of expression of the
30 biomarker can be an antibody, for example, an antibody specific for the product of the expression of the wild type or null mutant version of the biomarker.

In a particular embodiment, the kit further includes reagents for obtaining a biological sample from a subject. In another embodiment, the kit includes a control sample.

35 In another aspect, the present invention provides methods for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*,

eribulin mesylate), may be used to treat a subject having breast cancer by determining and/or identifying whether the subject carries at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a null mutation. In another aspect, the present invention provides methods for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer by assaying a sample derived from the subject to determine whether the subject carries at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a null mutation. In a further aspect, the present invention provides methods for determining the sensitivity of a breast tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof by determining and/or identifying whether said tumor is characterized by at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a null mutation. In yet another aspect, the present invention is directed to methods for treating a subject having breast cancer with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof by identifying whether at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a null mutation and administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate) to the subject.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts the high throughput siRNA screening methods in Breast Cancer Cell Lines performed as described in Example 1.

Figure 2 depicts the identification and selection of certain genes for further consideration as biomarkers of efficacy of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof.

Figure 3 depicts the confirmation assays performed as described in Example 1.

Figure 4 depicts the results of the QuantiTect SYBR Assays to determine the relative quantities of cDNAs after treatment with siRNA as set forth in Example 1.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides methods for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer, methods for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin

mesylate), may be used to treat a subject having breast cancer, methods for determining the sensitivity of a breast tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), and methods of treating a subject having breast cancer. Generally, the methods involve determining the level of expression of at least one biomarker as set forth in Table 1 in a sample derived from the subject, wherein a low level of expression of the biomarker is an indication that eribulin, or an analog thereof may be used to treat breast cancer and/or that the breast tumor is sensitive to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate).

The invention is based, at least in part, on the observation that a low level of expression, *e.g.*, the absence of expression, of the biomarkers identified herein is indicative of responsiveness to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate). As shown herein, siRNA techniques were employed to “knock down” expression of certain genes and assess the sensitivity of the resulting knock down cells to eribulin mesylate. Based on the findings from these studies, low levels of expression of each of the genes set forth in Table 1 was identified as being associated with the sensitivity of breast cancer cells to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate).

Unless otherwise defined herein, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. The meaning and scope of the terms should be clear, however, in the event of any latent ambiguity, definitions provided herein take precedent over any dictionary or extrinsic definition. Further, unless otherwise required by context, singular terms, for example, those characterized by “a” or “an”, shall include pluralities, *e.g.*, one or more biomarkers. In this application, the use of “or” means “and/or”, unless stated otherwise. Furthermore, the use of the term “including,” as well as other forms of the term, such as “includes” and “included”, is not limiting. Also, terms such as “element” or “component” encompass both elements and components comprising one unit and elements and components that comprise more than one unit unless specifically stated otherwise.

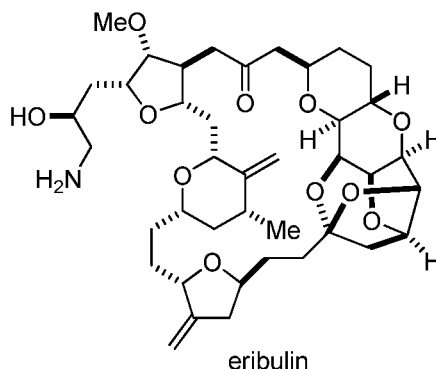
The phrase “determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer” refers to assessing the likelihood that treatment of a subject with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate) will be effective (*e.g.*, provide a therapeutic benefit to the subject) or will not be effective in the subject. Assessment of the likelihood that treatment will or will not be effective typically can be performed before treatment with

eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), has begun or before treatment is resumed. Alternatively or in combination, assessment of the likelihood of efficacious treatment can be performed during treatment, for example, to determine whether treatment should be continued or discontinued. For example, such an assessment can be performed (a) by determining the level of expression of a biomarker, for example, a biomarker selected from the group of biomarkers listed in Table 1, in a sample derived from said subject, wherein a low level of expression of the biomarker indicates that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat said subject having breast cancer, or (b) by assaying a sample derived from said subject to determine the level of expression in said sample of a biomarker, for example, a biomarker selected from the group of biomarkers listed in Table 1, wherein a low level of expression of the biomarker indicates that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat said subject having breast cancer.

The phrase “determining the sensitivity of a breast tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof”, as used herein, is intended to refer to assessing the susceptibility of a breast tumor, *e.g.*, breast cancer cells, to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate). Sensitivity of a tumor can include the ability of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), to kill tumor cells, to inhibit the spread and/or metastasis of tumor cells, and/or to inhibit the growth of tumor cells completely or partially (*e.g.*, slow down the growth of tumor cells by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%). The assessment can be performed (i) before treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), is begun; (ii) before treatment is resumed in the subject; and/or during treatment, for example, to determine whether treatment should be continued or discontinued. For example, such a determination can be performed (a) by determining the level of expression of a biomarker, *e.g.*, a biomarker selected from the group of biomarkers listed in Table 1, in said tumor, wherein a low level of expression of the biomarker in said tumor indicates that said tumor is sensitive to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, or (b) by determining the level of expression of a biomarker *e.g.*, a biomarker selected from the group of biomarkers listed in Table 1, in said tumor, and identifying said tumor as being sensitive to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, when said biomarker is expressed in said tumor at a low level.

The term “eribulin” as used herein refers to the art-recognized fully synthetic macrocyclic ketone analog of halichondrin B. As set forth in U.S. Patent No. 6,214,865, the entire contents of which are incorporated herein by reference, eribulin has the

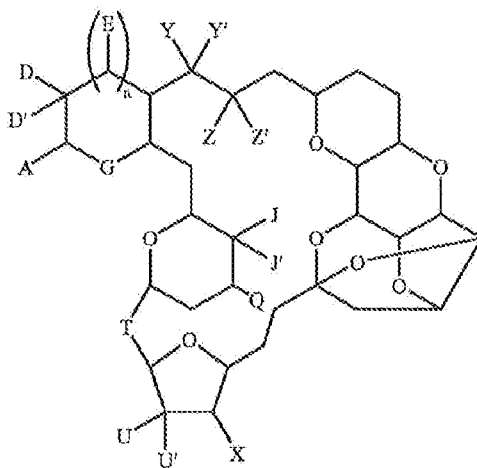
5 following structure



and can be generated using techniques as described therein or as described in Kim DS et al. (November 2009) *J. Am. Chem. Soc.* 131 (43): 15636–41, the entire contents of which are incorporated herein by reference. Eribulin is also known as ER-086526 and is

10 identified by CAS number 253128-41-5. Eribulin mesylate is also known as E7389.

As used herein, the term “eribulin analog” includes compounds in which one or more atoms or functional groups of eribulin have been replaced with different atoms or functional groups. For example, eribulin analogs include compounds having the following formula (I), which also encompasses eribulin:



(I)

15

In formula (I), A is a C₁₋₆ saturated or C₂₋₆ unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having between 1 and 13 substituents, preferably between 1 and 10 substituents, *e.g.*, at least one substituent selected from cyano, halo,

azido, Q₁, and oxo. Each Q₁ is independently selected from OR₁, SR₁, SO₂ R₁, OSO₂ R₁, NR₂ R₁, NR₂ (CO)R₁, NR₂ (CO)(CO)R₁, NR₄ (CO)NR₂ R₁, NR₂ (CO)OR₁, (CO)OR₁, O(CO)R₁, (CO)NR₂ R₁, and O(CO)NR₂ R₁. The number of substituents can be, for example, from 1 to 6, from 1 to 8, from 2 to 5, or from 1 to 4. Throughout the disclosure, numerical ranges are understood to be inclusive.

Each of R₁, R₂, R₄, R₅, and R₆ is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, C₆₋₁₀ aryl, C₆₋₁₀ haloaryl (*e.g.*, p-fluorophenyl or p-chlorophenyl), C₆₋₁₀ hydroxyaryl, C₁₋₄ alkoxy-C₆ aryl (*e.g.*, C₁₋₃ alkoxy-C₆ aryl, p-methoxyphenyl, 3,4,5-trimethoxyphenyl, p-ethoxyphenyl, or 3,5-diethoxyphenyl), C₆₋₁₀ aryl-C₁₋₆ alkyl (*e.g.*, benzyl or phenethyl), C₁₋₆ alkyl-C₆₋₁₀ aryl, C₆₋₁₀ haloaryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ haloaryl, (C₁₋₃ alkoxy-C₆ aryl)-C₁₋₃ alkyl, C₂₋₉ heterocyclic radical, C₂₋₉ heterocyclic radical-C₁₋₆ alkyl, C₂₋₉ heteroaryl, and C₂₋₉ heteroaryl-C₁₋₆ alkyl. There may be more than one R₁, for example, if A is substituted with two different alkoxy (OR₁) groups such as butoxy and 2-aminoethoxy.

Examples of A include 2,3-dihydroxypropyl, 2-hydroxyethyl, 3-hydroxy-4-perfluorobutyl, 2,4,5-trihydroxypentyl, 3-amino-2-hydroxypropyl, 1,2-dihydroxyethyl, 2,3-dihydroxy-4-perfluorobutyl, 3-cyano-2-hydroxypropyl, 2-amino-1-hydroxy ethyl, 3-azido-2-hydroxypropyl, 3,3-difluoro-2,4-dihydroxybutyl, 2,4-dihydroxybutyl, 2-hydroxy-2(p-fluorophenyl)-ethyl, -CH₂ (CO)(substituted or unsubstituted aryl), -CH₂ (CO)(alkyl or substituted alkyl, such as haloalkyl or hydroxyalkyl) and 3,3-difluoro-2-hydroxypent-4-enyl.

Examples of Q₁ include -NH(CO)(CO)-(heterocyclic radical or heteroaryl), -OSO₂ -(aryl or substituted aryl), -O(CO)NH-(aryl or substituted aryl), aminoalkyl, hydroxyalkyl, -NH(CO)(CO)-(aryl or substituted aryl), -NH(CO)(alkyl)(heteroaryl or heterocyclic radical), O(substituted or unsubstituted alkyl)(substituted or unsubstituted aryl), and -NH(CO)(alkyl)(aryl or substituted aryl).

Each of D and D' is independently selected from R₃ and OR₃, wherein R₃ is H, C₁₋₃ alkyl, or C₁₋₃ haloalkyl. Examples of D and D' are methoxy, methyl, ethoxy, and ethyl. In some embodiments, one of D and D' is H.

The value for n is 1 or preferably 0, thereby forming either a six-membered or five-membered ring. This ring can be unsubstituted or substituted, *e.g.*, where E is R₅ or OR₅, and can be a heterocyclic radical or a cycloalkyl, *e.g.* where G is S, CH₂, NR₆, or preferably O.

Each of J and J' is independently H, C₁₋₆ alkoxy, or C₁₋₆ alkyl; or J and J' taken together are =CH₂ or -O-(straight or branched C₁₋₅ alkylene)-O-, such as exocyclic methylenidene, isopropylidene, methylene, or ethylene.

Q is C₁₋₃ alkyl, and is preferably methyl.

T is ethylene or ethenylene, optionally substituted with (CO)OR₇, where R₇ is H or C₁₋₆ alkyl.

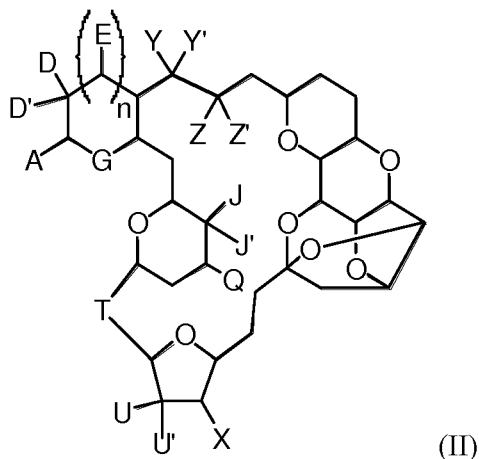
Each of U and U' is independently H, C₁₋₆ alkoxy, or C₁₋₆ alkyl; or U and U' taken together are =CH₂ or -O-(straight or branched C₁₋₅ alkylene)-O-.

5 X is H or C₁₋₆ alkoxy.

Each of Y and Y' is independently H or C₁₋₆ alkoxy; or Y and Y' taken together are =O, =CH₂, or -O-(straight or branched C₁₋₅ alkylene)-O-.

Each of Z and Z' is independently H or C₁₋₆ alkoxy; or Z and Z' taken together are =O, =CH₂, or -O-(straight or branched C₁₋₅ alkylene)-O-.

10 In certain embodiments, the eribulin analogs include compounds having the following formula (II):



In formula (II), the substitutions are defined as follows:

15 A is a C₁₋₆ saturated or C₂₋₆ unsaturated hydrocarbon skeleton, said skeleton being unsubstituted or having between 1 and 10 substituents, inclusive, independently selected from cyano, halo, azido, oxo, and Q₁.

Each Q₁ is independently selected from OR₁, SR₁, SO₂R₁, OSO₂R₁, NR₂R₁, NR₂(CO)R₁, NR₂(CO)(CO)R₁, NR₄(CO)NR₂R₁, NR₂(CO)OR₁, (CO)OR₁, O(CO)R₁,
20 (CO)NR₂R₁, and O(CO)NR₂R₁.

Each of R₁, R₂ and R₄ is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, C₆₋₁₀ aryl, C₆₋₁₀ haloaryl, C₆₋₁₀ hydroxyaryl, C₁₋₃ alkoxy-C₆ aryl, C₆₋₁₀ aryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ aryl, C₆₋₁₀ haloaryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ haloaryl, (C₁₋₃ alkoxy-C₆ aryl)-C₁₋₃ alkyl, C₂₋₉

heterocyclic radical, C₂₋₉ heterocyclic radical-C₁₋₆ alkyl, C₂₋₉ heteroaryl, and C₂₋₉ heteroaryl-C₁₋₆ alkyl.

Each of D and D' is independently selected from R₃ and OR₃, wherein R₃ is H, C₁₋₃ alkyl, or C₁₋₃ haloalkyl.

5 n is 0 or 1.

E is R₅ or OR₅, wherein R₅ is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl and C₁₋₆ aminoalkyl.

G is O.

10 Each of J and J' is independently H, C₁₋₆ alkoxy, or C₁₋₆ alkyl; or J and J' taken together are =CH₂.

Q is C₁₋₃ alkyl.

T is ethylene or ethenylene.

Each of U and U' is independently H, C₁₋₆ alkoxy, or C₁₋₆ alkyl; or U and U' taken together are =CH₂.

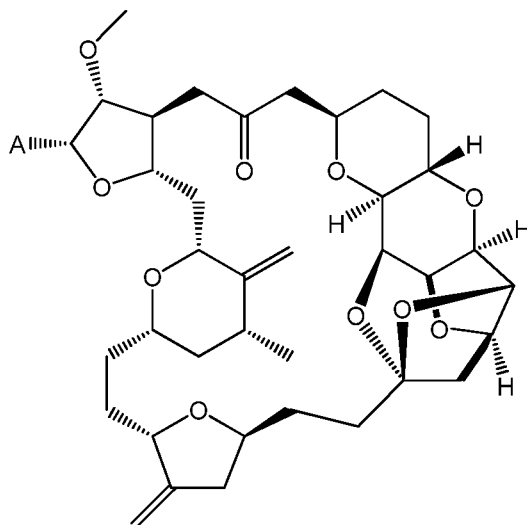
15 X is H or C₁₋₆ alkoxy.

Each of Y and Y' is independently H or C₁₋₆ alkoxy; or Y and Y' taken together are =O.

Each of Z and Z' is independently H or C₁₋₆ alkoxy; or Z and Z' taken together are =O.

20

In some embodiments, the eribulin analogs include compounds having the following formula (III):



(III)

wherein A is a C₁₋₆ saturated or C₂₋₆ unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having between 1 and 13 substituents, e.g., between 1 and 10 substituents selected from cyano, halo, azido, Q₁, and oxo;

- 5 each Q₁ is independently selected from OR₁, SR₁, SO₂R₁, OSO₂R₁, NR₂R₁, NR₂(CO)R₁, NR₂(CO)(CO)R₁, NR₄(CO)NR₂R₁, NR₂(CO)OR₁, (CO)OR₁, O(CO)R₁, (CO)NR₂R₁, and O(CO)NR₂R₁; and

- each of R₁, R₂, and R₄ is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, C₆₋₁₀ aryl, C₆₋₁₀ haloaryl, C₆₋₁₀ hydroxyaryl, C₁₋₄ alkoxy-C₆ aryl, C₆₋₁₀ aryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ aryl, C₆₋₁₀ haloaryl-C₁₋₆ alkyl, C₁₋₆ alkyl-C₆₋₁₀ haloaryl, (C₁₋₃ alkoxy-C₆ aryl)-C₁₋₃ alkyl, C₂₋₉ heterocyclic radical, C₂₋₉ heterocyclic radical-C₁₋₆ alkyl, C₂₋₉ heteroaryl, and C₂₋₉ heteroaryl-C₁₋₆ alkyl.

- Hydrocarbon skeletons contain carbon and hydrogen atoms and may be linear, branched, or cyclic. Unsaturated hydrocarbons include one, two, three or more C=C double bonds (sp²) or C≡C triple bonds (sp). Examples of unsaturated hydrocarbon radicals include ethynyl, 2-propynyl, 1-propenyl, 2-butenyl, 1,3-butadienyl, 2-pentenyl, vinyl (ethenyl), allyl, and isopropenyl. Examples of bivalent unsaturated hydrocarbon radicals include alkenylenes and alkylidenes such as methylidyne, ethylidene, ethylidyne, vinylidene, and isopropylidene. In general, compounds of the invention have hydrocarbon skeletons ("A" in formula (I)) that are substituted, e.g., with hydroxy, amino, cyano, azido, heteroaryl, aryl, and other moieties described herein. Hydrocarbon skeletons may have two geminal hydrogen atoms replaced with oxo, a bivalent carbonyl oxygen atom (=O), or a ring-forming substituent, such as --O--(straight or branched alkylene or alkylidene)-O-- to form an acetal or ketal.

C₁₋₆ alkyl includes linear, branched, and cyclic hydrocarbons, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, sec-pentyl, neo-pentyl, tert-pentyl, cyclopentyl, hexyl, isohexyl, sec-hexyl, cyclohexyl, 2-methylpentyl, tert-hexyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 1,3-dimethylbutyl, and
5 2,3-dimethyl but-2-yl. Alkoxy (--OR), alkylthio (--SR), and other alkyl-derived moieties (substituted, unsaturated, or bivalent) are analogous to alkyl groups (R). Alkyl groups, and alkyl-derived groups such as the representative alkoxy, haloalkyl, hydroxyalkyl, alkenyl, alkylidene, and alkylene groups, can be C₂₋₆, C₃₋₆, C₁₋₃, or C₂₋₄.

Alkyls substituted with halo, hydroxy, amino, cyano, azido, and so on can have
10 1, 2, 3, 4, 5 or more substituents, which are independently selected (may or may not be the same) and may or may not be on the same carbon atom. For example, haloalkyls are alkyl groups with at least one substituent selected from fluoro, chloro, bromo, and iodo. Haloalkyls may have two or more halo substituents which may or may not be the same halogen and may or may not be on the same carbon atom. Examples include
15 chloromethyl, periodomethyl, 3,3-dichloropropyl, 1,3-difluorobutyl, and 1-bromo-2-chloropropyl.

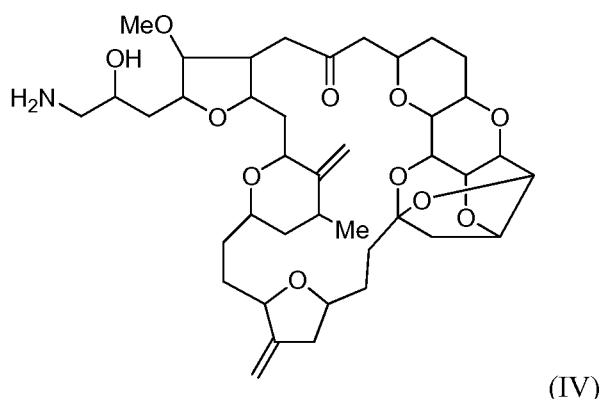
Heterocyclic radicals and heteroaryls include furyl, pyranyl, isobenzofuranyl, chromenyl, xanthenyl, phenoxathienyl, 2H-pyrrolyl, pyrrolyl, imidazolyl (e.g., 1-, 2- or 4-imidazolyl), pyrazolyl, isothiazolyl, isoxazolyl, pyridyl (e.g., 1-, 2-, or 3-pyridyl),
20 pyrazinyl, pyrimidinyl, pyridazinyl, indolizynyl, isoindolyl, 3H-indolyl, indolyl (e.g., 1-, 2-, or 3-indolyl), indazolyl, purinyl, 4H-quinolizynyl, isoquinolyl, quinolyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, pteridinyl, pyrrolinyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, indolinyl, isoindolinyl, and morpholinyl. Heterocyclic radicals and heteroaryls may be linked to
25 the rest of the molecule at any position along the ring. Heterocyclic radicals and heteroaryls can be C₂₋₉, or smaller, such as C₃₋₆, C₂₋₅, or C₃₋₇.

Aryl groups include phenyl, benzyl, naphthyl, tolyl, mesityl, xylyl, and cumenyl.

It is understood that "heterocyclic radical", "aryl", and "heteroaryl" include those having 1, 2, 3, 4, or more substituents independently selected from lower alkyl, lower
30 alkoxy, amino, halo, cyano, nitro, azido, and hydroxyl. Heterocyclic radicals, heteroaryls, and aryls may also be bivalent substituents of hydrocarbon skeleton "A" in formula (I).

The term "eribulin analog" includes eribulin prodrugs. The term "eribulin prodrugs" includes eribulin that has been chemically modified to be inactive or less
35 active until bioactivation (*e.g.*, metabolism *in vivo*) by an enzyme which cleaves the chemically modified portion of the eribulin prodrug, thereby providing the active form of eribulin.

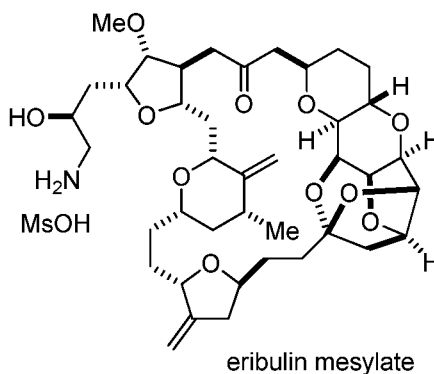
As used herein, the term "eribulin analog" includes all stereoisomers of eribulin and other compounds of formula (I), including diastereoisomers and enantiomers thereof. "Stereoisomers" refers to isomers that differ only in the arrangement of the atoms in space. "Diastereoisomers" refers to stereoisomers that are not mirror images of each other. "Enantiomers" refers to stereoisomers that are non-superimposable mirror images of one another. For example, Formula (IV) encompasses eribulin and such stereoisomers:



The phrase "pharmaceutically acceptable salt," as used herein, is a salt formed from an acid and a basic nitrogen group of Eribulin or an eribulin analog. Examples of such salts include acid addition salts and base addition salts, such as inorganic acid salts or organic acid salts (e.g., hydrochloric acid salt, sulfuric acid salt, citrate, hydrobromic acid salt, hydroiodic acid salt, nitric acid salt, bisulfate, phosphoric acid salt, super phosphoric acid salt, isonicotinic acid salt, acetic acid salt, lactic acid salt, salicylic acid salt, tartaric acid salt, pantothenic acid salt, ascorbic acid salt, succinic acid salt, maleic acid salt, fumaric acid salt, gluconic acid salt, saccharinic acid salt, formic acid salt, benzoic acid salt, glutaminic acid salt, methanesulfonic acid salt, ethanesulfonic acid salt, benzenesulfonic acid salt, p-toluenesulfonic acid salt, pamoic acid salt (pamoate)), as well as salts of aluminum, calcium, lithium, magnesium, calcium, sodium, zinc, and diethanolamine. It will be understood that reference to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, includes pharmaceutically acceptable salts of eribulin as well as pharmaceutically acceptable salts of an analog thereof. Examples of such pharmaceutically acceptable salts include, but are not limited to, a pharmaceutically acceptable salt of Formula I, a pharmaceutically acceptable salt of Formula II, a pharmaceutically acceptable salt of Formula III or a pharmaceutically acceptable salt of Formula IV.

In a particular embodiment, eribulin mesylate, a pharmaceutically acceptable salt form of eribulin is utilized in the methods of the present invention. Eribulin mesylate is

sold under the trade name HALAVEN[®]. The chemical name for eribulin mesylate is 11,15:18,21:24,28-Trieпоxy-7,9-ethano-12,15-methano-9H,15H-furo[3,2-i]furo[2',3':5,6]pyrano[4,3-b][1,4]dioxacyclopentacosin-5(4H)-one, 2-[(2S)-3-amino-2-hydroxypropyl]hexacosahydro-3-methoxy-26-methyl-20,27-bis(methylene)-, (2R,3R,3aS,7R,8aS,9S,10aR,11S,12R,13aR,13bS,15S,18S,21S,24S,26R,28R,29aS)-methanesulfonate (salt). Eribulin mesylate has the following structure



Eribulin mesylate is label indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease, including, for example, therapy with an anthracycline and a taxane in either the adjuvant or metastatic setting.

As used herein, the term “biomarker” is intended to encompass a substance that is used as an indicator of a biologic state and includes for example, genes (or portions thereof), mRNAs (or portions thereof), miRNAs (microRNAs), and proteins (or portions thereof). A “biomarker expression pattern” is intended to refer to a quantitative or qualitative summary of the expression of one or more biomarkers in a subject, such as in comparison to a standard or a control.

Various biomarkers which can be used in the methods described herein are summarized in Table 1. Table 1 provides gene abbreviations, Gene ID numbers and accession numbers for transcripts from which encoding nucleotide gene sequences can be identified. For example, gene ABI3 refers to a *Homo sapiens* ABI family, member 3. The nucleotide sequence for human ABI3 transcript variant 1 can be found at Accession Number NM_016428. Reference to a gene (e.g., ABI3) is intended to encompass naturally occurring or endogenous versions of the gene, including wild type, polymorphic or allelic variants or mutants (e.g., germline mutation, somatic mutation) of the gene, which can be found in a subject and/or tumor from a subject. In some embodiments, the sequence of the biomarker gene is at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at

least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% identical to a sequence identified in Table 1 by Accession Number or Gene_ID number. For example, sequence identity can be determined by comparing sequences using NCBI BLAST (e.g., Megablast with default parameters).

As used herein, the phrase “predictive gene signature” refers to expression levels of two or more biomarkers of the present invention in a subject that are indicative of responsiveness to treatment with eribulin, or an eribulin analog. For example, the low level expression of at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9 or at least 10 biomarkers from Table 1 in a subject may constitute a gene signature that indicates that the subject will respond positively to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (e.g., eribulin mesylate). Any sub-combination of 2 or more markers from Table 1 may constitute a predictive gene signature of the invention. In another example, the expression of at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9 or at least 10 biomarkers from Table 1 under particular threshold levels, or any sub-combination thereof, constitutes a gene signature that indicates that the subject will respond positively to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (e.g., eribulin mesylate).

A “low level of expression” of the biomarker, for example, a biomarker selected from the group of biomarkers listed in Table 1, refers to a level of expression of the biomarker in a test sample (e.g., a sample derived from a subject) that correlates with sensitivity to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (e.g., eribulin mesylate). This can be determined by comparing the level of expression of the biomarker in the test sample with that of a suitable control. A “low level of expression” also includes a lack of detectable expression of the biomarker.

In some embodiments, the level of expression of the biomarker is determined relative to a control sample, such as the level of expression of the biomarker in normal tissue (e.g., a range determined from the levels of expression of the biomarker observed in normal tissue samples). In these embodiments, a low level of expression will fall below or within the lower levels of this range. In some embodiments, the level of expression of the biomarker is determined relative to a control sample, such as the level of expression of the biomarker in samples (e.g., tumor samples, circulating tumor cells) from other subjects. For example, the level of expression of the biomarker in samples from other subjects can be determined to define levels of expression which correlate with sensitivity to treatment with eribulin, an analog thereof, or a pharmaceutically

acceptable salt thereof (*e.g.*, eribulin mesylate), and the level of expression of the biomarker in the sample from the subject of interest is compared to these levels of expression, wherein a comparable or lower level of expression in the sample from the subject is indicative of a “low level of expression” of the biomarker in the sample. In another example, the level of expression of the biomarker in samples (*e.g.*, tumor samples, circulating tumor cells) from other subjects can be determined to define levels of expression which correlate with resistance or non-responsiveness to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), and the level of expression of the biomarker in the sample from the subject of interest is compared to these levels of expression, wherein a lower level of expression in the sample from the subject is indicative of a “low level of expression” of the biomarker in the sample.

The term “known standard level” or “control level” can refer to an accepted or pre-determined expression level of the biomarker, for example, a biomarker selected from the group of biomarkers listed in Table 1 which is used to compare expression level of the biomarker in a sample derived from a subject. In one embodiment, the control expression level of the biomarker is the average expression level of the biomarker in samples derived from a population of subjects. For example, the control expression level can be the average expression level of the biomarker in breast cancer cells derived from a population of subjects with breast cancer. The population may be subjects who have not responded to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), or the population may be a group of subjects who express the respective biomarker at high or normal levels. In some embodiments, the control level may constitute a range of expression of the biomarker in normal tissue, as described above. For example, the control level may constitute a range of expression of the biomarker in tumor samples from a variety of subjects having breast cancer, as described above.

As further information becomes available as a result of routine performance of the methods described herein, population-average values for “control” level of expression of the biomarkers of the present invention may be used. In other embodiments, the “control” level of expression of the biomarkers may be determined by determining expression level of the respective biomarker in a subject sample obtained from a subject before the suspected onset of breast cancer in the subject, from archived subject samples, and the like.

Control levels of expression of biomarkers of the invention may be available from publicly available databases. In addition, Universal Reference Total RNA

(Clontech Laboratories) and Universal Human Reference RNA (Stratagene) and the like can be used as controls. For example, qPCR can be used to determine the level of expression of a biomarker, and an increase in the number of cycles needed to detect expression of a biomarker in a sample from a subject, relative to the number of cycles
5 needed for detection using such a control, is indicative of a low level of expression of the biomarker.

As used herein, the term "subject" or "patient" refers to human and non-human animals, *e.g.*, veterinary patients. The term "non-human animal" includes vertebrates, *e.g.*, mammals, such as non-human primates, mice, rabbits, sheep, dog, cat, horse, cow,
10 or other rodent, ovine, canine, feline, equine or bovine species. In one embodiment, the subject is a human.

The term "sample" as used herein refers to cells, tissues or fluids isolated from a subject, as well as cells, tissues or fluids present within a subject. The term "sample" includes any body fluid (*e.g.*, blood, lymph, cystic fluid, nipple aspirates, urine and
15 fluids collected from a biopsy (*e.g.*, lump biopsy)), tissue or a cell or collection of cells from a subject, as well as any component thereof, such as a fraction or extract. In one embodiment, the tissue or cell is removed from the subject. In another embodiment, the tissue or cell is present within the subject. Other samples include tears, plasma, serum, cerebrospinal fluid, feces, sputum and cell extracts. In one embodiment, the sample
20 contains protein (*e.g.*, proteins or peptides) from the subject. In another embodiment, the sample contains RNA (*e.g.*, mRNA molecules) from the subject or DNA (*e.g.*, genomic DNA molecules) from the subject.

As used herein, the term "breast cancer" refers generally to the uncontrolled growth of breast tissue and, more specifically, to a condition characterized by anomalous
25 rapid proliferation of abnormal cells in one or both breasts of a subject. The abnormal cells often are referred to as malignant or "neoplastic cells," which are transformed cells that can form a solid tumor. The term "tumor" refers to an abnormal mass or population of cells (*i.e.*, two or more cells) that result from excessive or abnormal cell division, whether malignant or benign, and pre-cancerous and cancerous cells. Malignant tumors
30 are distinguished from benign growths or tumors in that, in addition to uncontrolled cellular proliferation, they can invade surrounding tissues and can metastasize. In breast cancer, neoplastic cells may be identified in one or both breasts only and not in another tissue or organ, in one or both breasts and one or more adjacent tissues or organs (*e.g.* lymph node), or in a breast and one or more non-adjacent tissues or organs to which the
35 breast cancer cells have metastasized.

Eribulin, an analog thereof, or pharmaceutically acceptable salt thereof, can be used to treat breast cancer, and, accordingly, the methods of the present invention can be used in breast cancer and in subjects having breast cancer.

5 In one embodiment, the breast cancer is Estrogen Receptor (ER) negative breast cancer, Progesterone Receptor (PR) negative breast cancer and/or HER-2 negative breast cancer. For example, the breast cancer may be Estrogen Receptor (ER) negative and Progesterone Receptor (PR) negative breast cancer; Estrogen Receptor (ER) negative and HER-2 negative breast cancer; Progesterone Receptor (PR) negative and HER-2 negative breast cancer; or Estrogen Receptor (ER) negative breast cancer, Progesterone
10 Receptor (PR) negative breast cancer and HER-2 negative (triple negative) breast cancer. Assessment of ER, PR and HER-2 status can be done using any suitable method. For example, HER-2 status can be assessed by immunohistochemistry (IHC) and/or gene amplification by fluorescence *in situ* hybridization (FISH), for example, according to National Comprehensive Cancer Network [NCCN] guidelines.

15 The breast cancer can be for example, adenocarcinoma, inflammatory breast cancer, recurrent (*e.g.*, locally recurrent) and/or metastatic breast cancer. In some embodiments, the breast cancer is endocrine refractory or hormone refractory. The terms “endocrine refractory” and “hormone refractory” refer to a cancer that is resistant to treatment with hormone therapy for breast cancer, *e.g.*, aromatase inhibitors or
20 tamoxifen. Breast cancers arise most commonly in the lining of the milk ducts of the breast (ductal carcinoma), or in the lobules where breast milk is produced (lobular carcinoma). Accordingly, in various embodiments of the invention, the breast cancer can be ductal carcinoma or lobular carcinoma. Cancerous cells from the breast(s) may invade or metastasize to any other organ or tissue of the body. For example, cancer cells
25 often invade lymph node cells and/or metastasize to the liver, brain and/or bone.

In various embodiments of the present invention, the subject may be suffering from Stage I, Stage II, Stage III or Stage IV breast cancer. The stage of a breast cancer can be classified as a range of stages from Stage 0 to Stage IV based on its size and the extent to which it has spread. The following table summarizes the stages, which are well
30 known to clinicians:

STAGE	TUMOR SIZE	LYMPH NODE INVOLVEMENT	METASTASIS (SPREAD)
I	Less than 2 cm	No	No
II	Between 2-5 cm	No or in same side of breast	No
III	More than 5 cm	Yes, on same side of breast	No
IV	Not applicable	Not applicable	Yes

Various aspects of the invention are described in further detail in the following subsections.

5

I. Prediction of Responsiveness to Eribulin, an Analog thereof, or a Pharmaceutically Acceptable Salt thereof (*e.g.*, Eribulin Mesylate) in Subjects with Breast Cancer

In one aspect, the invention provides a method for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer and/or for determining the sensitivity of a breast tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate). The methods involve determining the expression level of at least one biomarker, for example, by assaying a sample derived from a subject having breast cancer. The identification of low levels of expression of at least one biomarker is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate) may be used for treatment of the breast cancer and/or that the breast tumor is sensitive to the treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate).

In the methods of the invention, the expression level of at least one biomarker selected from the group of biomarkers set forth in Table 1 is assessed, which, as explained herein, can comprise determining the level of expression of one or more of these genes (*e.g.*, ABI3, ANG) using various approaches, such as determining in a suitable sample the presence of certain DNA polymorphisms or null mutations, determining the level of RNA expressed from a gene, including an mRNA exemplified in Table 1 and/or other transcripts from the gene, or a protein product(s) of any of the foregoing.

TABLE 1: BIOMARKERS OF RESPONSIVENESS TO ERIBULIN, AN ANALOG THEREOF, OR A PHARMACEUTICALLY ACCEPTABLE SALT THEREOF (e.g., ERIBULIN MESYLATE)

GENE NAME	GENE_ID	ACCESSION NO.	SEQ ID NO:	NAME
ABI3	51225	NM_016428	1 & 2	Homo sapiens ABI family, member 3 (ABI3), transcript variant 1, mRNA
ANG	283	NM_001097577	3 & 4	Homo sapiens angiogenin, ribonuclease, RNase A family, 5 (ANG), transcript variant 2, mRNA
APBB2	323	NM_173075	5 & 6	Homo sapiens amyloid beta (A4) precursor protein-binding, family B, member 2 (APBB2), mRNA
CCL26	10344	NM_006072	7 & 8	Homo sapiens chemokine (C-C motif) ligand 26 (CCL26), mRNA
CDC20	991	NM_001255	9 & 10	Homo sapiens cell division cycle 20 homolog (S. cerevisiae) (CDC20), mRNA
CEP152	22995	NM_014985	11 & 12	Homo sapiens centrosomal protein 152kDa (CEP152), mRNA
CFL1	1072	NM_005507	13 & 14	Homo sapiens cofilin 1 (non-muscle) (CFL1), mRNA
CKLF	51192	NM_016326	15 & 16	Homo sapiens chemokine-like factor (CKLF), transcript variant 3, mRNA
COL7A1	1294	NM_000094	17 & 18	Homo sapiens collagen, type VII, alpha 1 (COL7A1), mRNA
CYP4F3	4051	NM_000896	19 & 20	Homo sapiens cytochrome P450, family 4, subfamily F, polypeptide 3 (CYP4F3), mRNA
DYSF	8291	NM_003494	21 & 22	Homo sapiens dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive) (DYSF), transcript variant 8, mRNA
EDIL3	10085	NM_005711	23 & 24	Homo sapiens EGF-like repeats and discoidin I-like domains 3 (EDIL3), mRNA
ERGIC3	51614	NM_015966	25 & 26	Homo sapiens ERGIC and golgi 3 (ERGIC3), transcript variant 2, mRNA
GNAT1	2779	NM_000172	27 & 28	Homo sapiens guanine nucleotide binding protein (G protein), alpha transducing activity polypeptide 1 (GNAT1), transcript variant 2, mRNA
GRAMD4	23151	NM_015124	29 & 30	Homo sapiens GRAM domain containing 4 (GRAMD4), mRNA
HYAL2	8692	NM_003773	31 & 32	Homo sapiens hyaluronoglucosaminidase 2 (HYAL2), transcript variant 1, mRNA
IL10	3586	NM_000572	33 & 34	Homo sapiens interleukin 10 (IL10), mRNA
ITFG3	83986	NM_032039	35 & 36	Homo sapiens integrin alpha FG-GAP repeat containing 3 (ITFG3), mRNA
JAM3	83700	NM_032801	37 & 38	Homo sapiens junctional adhesion molecule 3 (JAM3), mRNA
KLHL17	339451	NM_198317	39 & 40	Homo sapiens kelch-like 17 (Drosophila) (KLHL17), mRNA
KRT24	192666	NM_019016	41 & 42	Homo sapiens keratin 24 (KRT24), mRNA
MAD2L1BP	9587	NM_014628	43 & 44	Homo sapiens MAD2L1 binding protein (MAD2L1BP), transcript variant 2, mRNA
MANSC1	54682	NM_018050	45 & 46	Homo sapiens MANSC domain containing 1 (MANSC1), mRNA
MOBKL1B	55233	NM_018221	47 & 48	Homo sapiens MOB1, Mps One Binder kinase activator-like 1B (yeast) (MOBKL1B), mRNA
NCBP1	4686	NM_002486	49 & 50	Homo sapiens nuclear cap binding protein

				subunit 1, 80kDa (NCBP1), mRNA
NMU	10874	NM_006681	51 & 52	Homo sapiens neuromedin U (NMU), mRNA
PAPLN	89932	NM_173462	53 & 54	Homo sapiens papilin, proteoglycan-like sulfated glycoprotein (PAPLN), mRNA
PCDH1	5097	NM_002587	55 & 56	Homo sapiens protocadherin 1 (PCDH1), transcript variant 1, mRNA
PDGFB	5155	NM_002608	57 & 58	Homo sapiens platelet-derived growth factor beta polypeptide (simian sarcoma viral (v-sis) oncogene homolog) (PDGFB), transcript variant 1, mRNA
PHOSPHO2	493911	NM_001008489	59 & 60	Homo sapiens phosphatase, orphan 2 (PHOSPHO2), mRNA
PSENEN	55851	NM_172341	61 & 62	Homo sapiens presenilin enhancer 2 homolog (C. elegans) (PSENEN), mRNA
SATB1	6304	NM_002971	63 & 64	Homo sapiens SATB homeobox 1 (SATB1), transcript variant 1, mRNA
SNX11	29916	NM_013323	65 & 66	Homo sapiens sorting nexin 11 (SNX11), transcript variant 2, mRNA
SPTA1	6708	NM_003126	67 & 68	Homo sapiens spectrin, alpha, erythrocytic 1 (elliptocytosis 2) (SPTA1), mRNA
TMEM79	84283	NM_032323	69 & 70	Homo sapiens transmembrane protein 79 (TMEM79), transcript variant 1, mRNA
TMIGD2	126259	NM_144615	71 & 72	Homo sapiens transmembrane and immunoglobulin domain containing 2 (TMIGD2), mRNA
TUBB6	84617	NM_032525	73 & 74	Homo sapiens tubulin, beta 6 (TUBB6), mRNA
TYROBP	7305	NM_198125	75 & 76	Homo sapiens TYRO protein tyrosine kinase binding protein (TYROBP), transcript variant 2, mRNA
YTHDF1	54915	NM_017798	77 & 78	Homo sapiens YTH domain family, member 1 (YTHDF1), mRNA
ZIC5	85416	NM_033132	79 & 80	Homo sapiens Zic family member 5 (odd-paired homolog, Drosophila) (ZIC5), mRNA

Each of the accession numbers identified in Table 1, and their corresponding sequences, are hereby incorporated herein by reference.

In various embodiments, the level of expression of at least 2, 3, 4, 5, 6, 7, 8, 9 or 10 biomarkers selected from the group of biomarkers listed in Table 1 is determined.

In particular embodiments, a predictive gene signature comprising a sub-combination of 2 or more biomarkers selected from the group of biomarkers listed in Table 1 is used. In various embodiments, the level of expression of at least 2, at least 3, at least 4 or at least 5 biomarkers selected from the group of biomarkers listed in Table 1 is determined. For example, the predictive gene signature may include at least 2 biomarkers, *e.g.*, DYSF and EDIL3; GNAT1 and ERGIC3; KRT24 and PAPLN; MANSC1 and PDGFB; PCDH1 and PDGFB; or PHOSPHO2 and PSENEN. In another embodiment, the predictive gene signature may include at least 3 biomarkers, *e.g.*, COL7A1, YTHDF1 and ZIC5; CKLF, IL10 and TUBB6; CDC20, CFL1 and TMEM79; 15 HYAL2, NCBP1 and SNX11; or CEP152, NCBP1 and SATB1. In another embodiment, the predictive gene signature may include at least 4 biomarkers, *e.g.*,

APBB2, CCL26, PSENEN and SATB1; ANG, JAM3, KLHL17 and PAPLN; ITFG3, MAD2L1BP, NMU and PDGFB; SPTA1, TYROBP, SNX11 and PSENEN; GRAMD4, GNAT1, TMIGD2 and YTHDF1; or GRAMD4, HYAL2, PHOSPHO2 and TUBB6. In another embodiment, the predictive gene signature may include at least 5 biomarkers, *e.g.*, CCL26, CDC20, ERGIC3, EDIL3 and PCDH1; DYSF, NMU, PHOSPHO2, PSENEN and SNX11; APBB2, CKLF, CYP4F3, TUBB6 and YTHDF1; or CEP152, MAD2L1BP, SPTA1, TMEM79 and ZIC5.

In particular embodiments, the predictive gene signature may include 2 or more of biomarkers ABI3, ANG, APBB2, CCL26, CDC20, CEP152, CFL1, CKLF, COL7A1, CYP4F3, DYSF, GNAT1, GRAMD4, HYAL2, IL10, ITFG3, JAM3, KLHL17, KRT24, MAD2L1BP, MANSC1, MOBKL1B, NCBP1, NMU, PCDH1, PHOSPHO2, SPTA1, TMIGD2, TYROBP, ZIC5, ERGIC3, PDGFB, PSENEN, SATB1, SNX11, TMEM79 and YTHDF1, *e.g.*, ABI3 and ANG; APBB2 and CCL26; GNAT1 and GRAMD4; IL10 and ITFG3; MACSC1 and MOBKL1B; NMU and PCDH1; or TYROBP and ZIC5. In other embodiments, the predictive gene signature includes at least 3 of the previously recited biomarkers, *e.g.*, ABI3, ANG and APBB2; CCL26, CKLF and COL7A1; DYSF, GNAT1 and HYAL2; JAM3, KLHL17 and KRT24; NCBP1, NMU and PCDH1; SPTA1, TMIGD2 and TYROBP; or ZIC5, MAD2L1BP and CDC20. In other embodiments, the predictive gene signature includes at least 4 of the previously recited biomarkers, *e.g.*, ABI3, ANG, APBB2 and CCL26; CEP152, CFL1, CKLF and COL7A1; KRT24, MANSC1, MOBKL1B and SPTA1; TYROBP, TMIGD2, PHOSPHO2 and NMU; ABI3, GNAT1, KLHL17 and SPTA1; or CEP152, HYAL2, PCDH1 and TMIGD2. In yet further embodiments, the predictive gene signature includes at least 5 of the previously recited biomarkers, *e.g.*, CKLF, COL7A1, GRAMD4, JAM3 and PCDH1; APBB2, CEP152, DYSF, IL10 and TYROBP; CYP4F3, HYAL2, ITFG3, KLHL17 and KRT24; NCBP1, SPTA1, TMIGD2, IL10 and JAM3; or CCL26, PHOSPHO2, SPTA1, TMIGD2 and ZIC5.

In other embodiments, the predictive gene signature may include 2 or more of biomarkers ERGIC3, PDGFB, PSENEN, SATB1, SNX11, TMEM79 or YTHDF1, or any sub-combination thereof, *e.g.*, ERGIC3 and PDGFB; ERGIC3 and PSENEN; ERGIC3 and SATB1; ERGIC3 and SNX11; ERGIC3 and TMEM79; ERGIC3 and YTHDF1; PDGFB and PSENEN; PDGFB and SATB1; PDGFB and SNX11; PDGFB and TMEM79; PDGFB and YTHDF1; PSENEN and SATB1; PSENEN and SNX11; PSENEN and TMEM79; PSENEN and YTHDF1; SATB1 and SNX11; SATB1 and TMEM79; SATB1 and YTHDF1; SNX11 and TMEM79; SNX11 and YTHDF1; or TMEM79 and YTHDF1. In other embodiments, the predictive gene signature includes at least 3 biomarkers, for example, ERGIC3, PDGFB and PSENEN; SATB1, SNX11

and TMEM79; SNX11, TMEM79 and YTHDF1; or ERGIC3, PDGFB and SATB1. In further embodiments, the predictive gene signature includes at least 4 biomarkers, for example, ERGIC3, PDGFB, PSENEN and SATB1; SNX11, TMEM79, YTHDF1 and ERGIC3; or ERGIC3, PDGFB, PSENEN and YTHDF1. In further embodiments, the predictive gene signature includes at least 5 biomarkers, for example, ERGIC3, PDGFB, PSENEN, SATB1 and SNX11; ERGIC3, PDGFB, PSENEN, SATB1 and TMEM79; or PSENEN, SATB1, SNX11, TMEM79 and YTHDF1. In yet further embodiments, the predictive gene signature includes at least 6 biomarkers, for example, ERGIC3, PDGFB, PSENEN, SATB1, SNX11 and TMEM79; PDGFB, PSENEN, SATB1, SNX11, TMEM79 and YTHDF1; or ERGIC3, PSENEN, SATB1, SNX11, TMEM79 and YTHDF1. In yet another embodiment, the predictive gene signature includes 7 biomarkers, for example, ERGIC3, PDGFB, PSENEN, SATB1, SNX11, TMEM79 and YTHDF1.

In various embodiments, the biomarker is not one or more of SPTA1, PAPLN, PCDH1, TMIGD2 and/or KRT24. In a particular embodiment, the biomarker is not SPTA1, PAPLN, PCDH1, TMIGD2 and KRT24. In one embodiment, the biomarker is not SPTA1. In another embodiment, the biomarker is not PAPLN. In another embodiment, the biomarker is not PCDH1. In an alternative embodiment, the biomarker is not TMIGD2. In yet another embodiment, the biomarker is not KRT24.

In particular embodiments, the predictive gene signature may include 2 or more of biomarkers ABI3, ANG, APBB2, CCL26, CDC20, CEP152, CFL1, CKLF, COL7A1, CYP4F3, DYSF, GNAT1, GRAMD4, HYAL2, IL10, ITFG3, JAM3, KLHL17, MAD2L1BP, MANSC1, MOBKL1B, NCBP1, NMU, PHOSPHO2, TYROBP, ZIC5, ERGIC3, PDGFB, PSENEN, SATB1, SNX11, TMEM79, YTHDF1, EDIL3 and TUBB6, *e.g.*, ABI3 and ANG; GRAMD4 and HYAL2; NMU and PHOSPHO2; ZIC5 and PSENEN; or SNX11 and MOBKL1B. In other embodiments, the predictive gene signature includes at least 3 of the previously recited biomarkers, *e.g.*, APBB2, CDC20 and CKLF; COL7A1, DYSF and GNAT1; NCBP1, SATB1 and EDIL3; PSENEN, DYSF and GNAT1; MANSC1, ZIC5 and CFL1; or CKLF, GRAMD4 and NMU. In other embodiments, the predictive gene signature includes at least 4 of the previously recited biomarkers, *e.g.*, ANG, CCL26, CEP152 and JAM3; APBB2, CYP4F3, ITFG3 and TYROBP; CYP4F3, MANSC1, PDGFB and YTHDF1; TUBB6, DYSF, PHOSPHO2 and CDC20; or CKLF, KLHL17, HYAL2 and ZIC5. In yet further embodiments, the predictive gene signature includes at least 5 of the previously recited biomarkers, *e.g.*, IL10, CEP152, COL7A1, TYROBP and ERGIC3; TMEM79, SNX11, PSENEN, GNAT1 and GRAMD4; JAM3, SNX11, KLHL17, MOBKL1B and ERGIC3; or NMU, PHOSPHO2, PDGFB, CFL1 and ANG.

In various methods and or kits of the invention, the biomarker is not ABI3, is not ANG, is not APBB2, is not CCL26, is not CDC20, is not CEP152, is not CFL1, is not CKLF, is not COL7A1, is not CYP4F3, is not DYSE, is not GNAT1, is not GRAMD4, is not HYAL2, is not IL10, is not ITFG3, is not JAM3, is not KLHL17, is not KRT24, is not MAD2L1BP, is not MANSC1, is not MOBKL1B, is not NCBP1, is not NMU, is not PCDH1, is not PHOSPHO2, is not SPTA1, is not TMIGD2, is not TYROBP, is not ZIC5, is not ERGIC3, is not PDGFB, is not PSENEN, is not SATB1, is not SNX11, is not TMEM79, is not EDIL3, is not PAPLN, is not TUBB6 and/or is not YTHDF1.

Any suitable analytical method, can be utilized in the methods of the invention to assess (directly or indirectly) the level of expression of a biomarker in a sample. In some embodiments, a difference is observed between the level of expression of a biomarker, as compared to the control level of expression of the biomarker. In one embodiment, the difference is greater than the limit of detection of the method for determining the expression level of the biomarker. In further embodiments, the difference is greater than or equal to the standard error of the assessment method, and preferably the difference is at least about 2-, about 3-, about 4-, about 5-, about 6-, about 7-, about 8-, about 9-, about 10-, about 15-, about 20-, about 25-, about 100-, about 500- or about 1000-fold greater than the standard error of the assessment method. In some embodiments, the level of expression of the biomarker in a sample as compared to a control level of expression is assessed using parametric or nonparametric descriptive statistics, comparisons, regression analyses, and the like.

In some embodiments, a difference in the level of expression of the biomarker in the sample derived from the subject is detected relative to the control, and the difference is about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, or about 90% less than the expression level of the biomarker in the control sample.

The level of expression of a biomarker, for example, as set forth in Table 1, in a sample obtained from a subject may be assayed by any of a wide variety of techniques and methods, which transform the biomarker within the sample into a moiety that can be detected and/or quantified. Non-limiting examples of such methods include analyzing the sample using immunological methods for detection of proteins, protein purification methods, protein function or activity assays, nucleic acid hybridization methods, nucleic acid reverse transcription methods, and nucleic acid amplification methods, immunoblotting, Western blotting, Northern blotting, electron microscopy, mass spectrometry, *e.g.*, MALDI-TOF and SELDI-TOF, immunoprecipitations, immunofluorescence, immunohistochemistry, enzyme linked immunosorbent assays

(ELISAs), *e.g.*, amplified ELISA, quantitative blood based assays, *e.g.*, serum ELISA, quantitative urine based assays, flow cytometry, Southern hybridizations, array analysis, and the like, and combinations or sub-combinations thereof.

In one embodiment, the level of expression of the biomarker in a sample is
5 determined by detecting a transcribed polynucleotide, or portion thereof, *e.g.*, mRNA, or cDNA, of the biomarker gene. RNA may be extracted from cells using RNA extraction techniques including, for example, using acid phenol/guanidine isothiocyanate extraction (RNAzol B; Biogenesis), RNeasy RNA preparation kits (Qiagen) or PAXgene (PreAnalytix, Switzerland). Typical assay formats utilizing ribonucleic acid
10 hybridization include nuclear run-on assays, RT-PCR, quantitative PCR analysis, RNase protection assays (Melton *et al.*, *Nuc. Acids Res.* 12:7035), Northern blotting and *in situ* hybridization. Other suitable systems for mRNA sample analysis include microarray analysis (*e.g.*, using Affymetrix's microarray system or Illumina's BeadArray Technology).

15 In one embodiment, the level of expression of the biomarker is determined using a nucleic acid probe. The term "probe", as used herein, refers to any molecule that is capable of selectively binding to a specific biomarker. Probes can be synthesized by one of skill in the art, or derived from appropriate biological preparations. Probes can be specifically designed to be labeled, by addition or incorporation of a label. Examples of
20 molecules that can be utilized as probes include, but are not limited to, RNA, DNA, proteins, antibodies, and organic molecules.

As indicated above, isolated mRNA can be used in hybridization or amplification assays that include, but are not limited to, Southern or Northern analyses, polymerase chain reaction (PCR) analyses and probe arrays. One method for the determination of
25 mRNA levels involves contacting the isolated mRNA with a nucleic acid molecule (probe) that can hybridize to the biomarker mRNA. The nucleic acid probe can be, for example, a full-length cDNA, or a portion thereof, such as an oligonucleotide of at least about 7, 10, 15, 20, 25, 30, 35, 40, 45, 50, 100, 250 or about 500 nucleotides in length and sufficient to specifically hybridize under appropriate hybridization conditions to the
30 biomarker genomic DNA. In a particular embodiment the probe will bind the biomarker genomic DNA under stringent conditions. Such stringent conditions, for example, hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45° C., followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65° C., are known to those skilled in the art and can be found in Current Protocols in Molecular Biology, Ausubel *et al.*, eds.,
35 John Wiley & Sons, Inc. (1995), sections 2, 4, and 6, the teachings of which are hereby incorporated by reference herein. Additional stringent conditions can be found in

Molecular Cloning: A Laboratory Manual, Sambrook et al., Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (1989), chapters 7, 9, and 11, the teachings of which are hereby incorporated by reference herein.

In one embodiment, the mRNA is immobilized on a solid surface and contacted
5 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 probe(s) are immobilized on a solid surface, for example, in an Affymetrix gene chip array, and the probe(s) are contacted with mRNA. A skilled artisan can readily adapt mRNA detection methods for use in determining the level of
10 the biomarker mRNA.

The level of expression of the biomarker in a sample can also be determined using methods that involve the use of nucleic acid amplification and/or reverse transcriptase (to prepare cDNA) of for example mRNA in the sample, *e.g.*, by RT-PCR (the experimental embodiment set forth in Mullis, 1987, U.S. Pat. No. 4,683,202), ligase
15 chain reaction (Barany (1991) *Proc. Natl. Acad. Sci. USA* 88:189-193), self sustained sequence replication (Guatelli *et al.* (1990) *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh *et al.* (1989) *Proc. Natl. Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi *et al.* (1988) *Bio/Technology* 6:1197), rolling circle replication (Lizardi *et al.* , U.S. Pat. No. 5,854,033) or any other nucleic acid
20 amplification method, followed by the detection of the amplified molecules. These approaches are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers. In particular aspects of the invention, the level of expression of the biomarker is determined by quantitative fluorogenic RT-PCR (*e.g.*, the TaqManTM System). Such methods typically utilize pairs of oligonucleotide
25 primers that are specific for the biomarker. Methods for designing oligonucleotide primers specific for a known sequence are well known in the art.

The expression levels of biomarker mRNA can be monitored using a membrane blot (such as used in hybridization analysis such as Northern, Southern, dot, and the like), or microwells, sample tubes, gels, beads or fibers (or any solid support comprising
30 bound nucleic acids). See, for example, U.S. Pat. Nos. 5,770,722, 5,874,219, 5,744,305, 5,677,195 and 5,445,934, the contents of which as they relate to these assays are incorporated herein by reference. The determination of biomarker expression level may also comprise using nucleic acid probes in solution.

In one embodiment of the invention, microarrays are used to detect the level of
35 expression of a biomarker. 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, *e.g.*, U.S. Pat. Nos. 6,040,138, 5,800,992 and 6,020,135, 6,033,860, and 6,344,316, the contents of which as they relate to these assays are incorporated herein by reference. High-density oligonucleotide arrays are particularly useful for determining the gene expression profile for a large number of RNA's in a sample.

Expression of a biomarker can also be assessed at the protein level, using a detection reagent that detects the protein product encoded by the mRNA of the biomarker, directly or indirectly. For example, if an antibody reagent is available that binds specifically to a biomarker protein product to be detected, then such an antibody reagent can be used to detect the expression of the biomarker in a sample from the subject, using techniques, such as immunohistochemistry, ELISA, FACS analysis, and the like.

Other known methods for detecting the biomarker at the protein level include methods such as electrophoresis, capillary electrophoresis, high performance liquid chromatography (HPLC), thin layer chromatography (TLC), hyperdiffusion chromatography, and the like, or various immunological methods such as fluid or gel precipitation reactions, immunodiffusion (single or double), immunoelectrophoresis, radioimmunoassay (RIA), enzyme-linked immunosorbent assays (ELISAs), immunofluorescent assays, and Western blotting.

Proteins from samples can be isolated using a variety of techniques, including those well known to those of skill in the art. The protein isolation methods employed can, for example, be those described in Harlow and Lane (Harlow and Lane, 1988, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

In one embodiment, antibodies, or antibody fragments, are used in methods such as Western blots or immunofluorescence techniques to detect the expressed proteins. Antibodies for determining the expression of the biomarkers of the invention are commercially available. For example, ERGIC-3 specific antibodies are commercially available from Santa Cruz Biotechnology, Inc. (ERGIC-3 (P-16) Antibody and ERGIC-3 (Y-23) Antibody) and Sigma Aldrich (HPA015968, AV47209, HPA015242, SAB4502151). PDGFB specific antibodies are commercially available from Santa Cruz

Biotechnology, Inc. (*e.g.*, PDGF-B (C-5) Antibody and PDGF-B (H-55) Antibody) and Sigma Aldrich (*e.g.*, HPA011972, SAB2101755 and SAB2900226). PSENEN specific antibodies are commercially available from Origene (*e.g.*, Catalog No. TA306367) and Sigma Aldrich (*e.g.*, PRS3981, WH0055851M1, PRS3979 and P5622). Further by way of example, SATB1 antibodies are commercially available from, for example, Abcam (Catalog No. ab49061, ab92307 and ab70004), Abnova Corporation (Catalog No. PAB13379), and Aviva Systems Biology (Catalog No. ARP33362_P050). SNX11 antibodies are commercially available from Abcam (Catalog Nos. ab4128, ab67578, ab76816 and ab76762) and Abnova Corporation (Catalog Nos. PAB6362 and H00029916-B01). TMEM79 Antibodies are commercially available from, for example, Abcam (Catalog No. ab81539) and Sigma Aldrich (Catalog No. SAB2102475). Finally, YTHDF1 antibodies are commercially available from, for example, Abnova Corporation (Catalog No. PAB17446), Aviva Systems Biology (Catalog No. ARP57032_P050) and Santa Cruz Biotechnology (Catalog No. sc-86026).

It is generally preferable to immobilize either the antibody or proteins on a solid support for Western blots and immunofluorescence techniques. Suitable solid phase supports or carriers include any support capable of binding an antigen or an antibody. Well-known supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite.

One skilled in the art will know many other suitable carriers for binding antibody or antigen, and will be able to adapt such support for use with the present invention. For example, protein isolated from cells can be run on a polyacrylamide gel electrophoresis and immobilized onto a solid phase support such as nitrocellulose. The support can then be washed with suitable buffers followed by treatment with the detectably labeled antibody. The solid phase support can then be washed with the buffer a second time to remove unbound antibody. The amount of bound label on the solid support can then be detected by conventional means. Means of detecting proteins using electrophoretic techniques are well known to those of skill in the art (see generally, R. Scopes (1982) *Protein Purification*, Springer-Verlag, N.Y.; Deutscher, (1990) *Methods in Enzymology* Vol. 182: *Guide to Protein Purification*, Academic Press, Inc., N.Y.).

Other standard methods include immunoassay techniques which are well known to one of ordinary skill in the art and may be found in Principles And Practice Of Immunoassay, 2nd Edition, Price and Newman, eds., MacMillan (1997) and Antibodies, A Laboratory Manual, Harlow and Lane, eds., Cold Spring Harbor Laboratory, Ch. 9 (1988), each of which is incorporated herein by reference in its entirety.

Antibodies used in immunoassays to determine the level of expression of the biomarker, may be labeled with a detectable label. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by incorporation of a label (e.g., a radioactive atom), coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin.

In one embodiment, the antibody is labeled, *e.g.* a radio-labeled, chromophore-labeled, fluorophore-labeled, or enzyme-labeled antibody. In another embodiment, an antibody derivative (*e.g.*, an antibody conjugated with a substrate or with the protein or ligand of a protein-ligand pair (*e.g.*, biotin-streptavidin), or an antibody fragment (*e.g.* a single-chain antibody, or an isolated antibody hypervariable domain) which binds specifically with the biomarker is used.

In one embodiment of the invention, proteomic methods, *e.g.*, mass spectrometry, are used. Mass spectrometry is an analytical technique that consists of ionizing chemical compounds to generate charged molecules (or fragments thereof) and measuring their mass-to-charge ratios. In a typical mass spectrometry procedure, a sample is obtained from a subject, loaded onto the mass spectrometry, and its components (*e.g.*, the biomarker) are ionized by different methods (*e.g.*, by impacting them with an electron beam), resulting in the formation of charged particles (ions). The mass-to-charge ratio of the particles is then calculated from the motion of the ions as they transit through electromagnetic fields.

For example, matrix-associated laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) or surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF MS) which involves the application of a biological sample, such as serum, to a protein-binding chip (Wright, G.L., Jr., *et al.* (2002) *Expert Rev Mol Diagn* 2:549; Li, J., *et al.* (2002) *Clin Chem* 48:1296; Laronga, C., *et al.* (2003) *Dis biomarkers* 19:229; Petricoin, E.F., *et al.* (2002) 359:572; Adam, B.L., *et al.* (2002) *Cancer Res* 62:3609; Tolson, J., *et al.* (2004) *Lab Invest* 84:845; Xiao, Z., *et al.* (2001) *Cancer Res* 61:6029) can be used to determine the expression level of a biomarker at the protein level.

Furthermore, *in vivo* techniques for determination of the expression level of the biomarker include introducing into a subject a labeled antibody directed against the biomarker, which binds to and transforms the biomarker into a detectable molecule. As

discussed above, the presence, level, or even location of the detectable biomarker in a subject may be detected by standard imaging techniques.

In general, where a difference in the level of expression of a biomarker and the control is to be detected, it is preferable that the difference between the level of expression of the biomarker in a sample from a subject having breast cancer and being treated with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), or being considered for treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), and the amount of the biomarker in a control sample, is as great as possible. Although this difference can be as small as the limit of detection of the method for determining the level of expression, it is preferred that the difference be greater than the limit of detection of the method or greater than the standard error of the assessment method, and preferably a difference of at least about 2-, about 3-, about 4-, about 5-, about 6-, about 7-, about 8-, about 9-, about 10-, about 15-, about 20-, about 25-, about 100-, about 500-, 1000-fold greater than the standard error of the assessment method.

In another aspect, the present invention provides methods for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer by determining and/or identifying whether the subject carries at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a polymorphism, for example, a mutation, that results in decreased expression and/or reduced function of the encoded protein, wherein the presence of a polymorphism in at least one gene is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, will be effective in treating a subject. In another aspect, the present invention provides methods for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), will be effective in treating a subject having breast cancer by assaying a sample derived from the subject to determine whether the subject carries at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a polymorphism, for example, a mutation, that results in decreased expression and/or reduced function of the encoded protein, wherein the presence of the polymorphism in at least one gene in said sample is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat said subject. In a further aspect, a method is provided for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, will be effective in treating a subject having breast cancer, the method comprising determining the presence of a polymorphism that results in reduced expression and/or function in a gene encoding a biomarker selected from the group of biomarkers listed in Table 1 in a sample derived

from said subject, and predicting that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat said subject based on the presence of the polymorphism.

5 In a further aspect, the present invention provides methods for determining the sensitivity of a breast tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof by determining and/or identifying whether said tumor contains a polymorphism in at least one gene resulting in reduced expression and/or function of the encoded protein, wherein the gene is selected from the group of biomarkers set forth in Table 1. Identification and/or determination that the tumor
10 contains such a polymorphism is indicative of sensitivity of said tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof. In yet another aspect, the present invention is directed to methods for treating a subject having breast cancer with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof by identifying whether a sample derived from said subject has at least one gene, selected
15 from the group of biomarkers set forth in Table 1, which contains a polymorphism resulting in reduced expression and/or function of the encoded protein and administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate) to the subject when the polymorphism is identified.

20 In another aspect, the present invention provides methods for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer by determining and/or identifying whether the subject carries at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a null mutation, wherein the presence
25 of a null mutation in at least one gene is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt there, will be effective in treating the subject. In another aspect, the present invention provides methods for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer by assaying a sample derived from
30 the subject to determine whether the subject carries at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a null mutation, wherein the presence of a null mutation in at least one gene in said sample is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt there, will be effective in treating the subject. In a further aspect, a method is provided for predicting whether
35 eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat a subject having breast cancer, the method comprising determining the presence of a null mutation in a biomarker selected from the group of biomarkers listed in Table 1 in

a sample derived from said subject, and predicting that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat said subject based on the presence of said null mutation.

5 In a further aspect, the present invention provides methods for determining the sensitivity of a breast tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof by determining and/or identifying whether said tumor contains a null mutation in at least one gene, selected from the group of biomarkers set forth in Table 1. Identification and/or determination that the tumor contains a null mutation is indicative of sensitivity of said tumor to treatment with
10 eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof. In yet another aspect, the present invention is directed to methods for treating a subject having breast cancer with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof by identifying whether a sample derived from said subject has at least one gene, selected from the group of biomarkers set forth in Table 1, which contains a null mutation and
15 administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate) to the subject when a null mutation is identified.

As used herein, the term “null mutation” refers to a mutation in a genomic DNA sequence that causes the product of the gene to be non-functional or largely absent. Such
20 mutations may occur in the coding and/or regulatory regions of the gene, and may be changes of individual residues, or insertions or deletions of regions of nucleic acids. These mutations may also occur in the coding and/or regulatory regions of other genes which may regulate or control the gene and/or the product of the gene so as to cause the gene product to be non-functional or largely absent. The null mutation may be a
25 deletion of the native gene or a portion thereof. These sequence disruptions or modifications may include insertions, missense, frameshift, deletion, or substitutions, or replacements of DNA sequence, or any combination thereof. For example, the null mutation may result in the insertion of a premature stop codon. The null mutation results in functional inactivation of the gene product by, for example, inhibiting its
30 production partially or completely; disrupting, inhibiting or curtailing the translation of the protein product, or resulting in a nonfunctional protein. The null mutation may be a pre-existing mutation in the subject or a mutation which arose in a tumor. The presence of a null mutation in a biomarker can be indicated by a lack of detectable expression of the biomarker. However, the presence of a null mutation can be determined by other
35 methods. For example, in such embodiments, a sample of the subject’s DNA may be sequenced in order to identify the presence of a null mutation. Any of the well-known methods for sequencing the biomarkers may be used in the methods of the invention,

such as the methods described in, for example, U.S. Patent No. 5,075,216, Engelke *et al.* (1988) *Proc. Natl. Acad. Sci. U.S.A.* 85, 544-548 and Wong *et al.* (1987) *Nature* 330, 384-386; Maxim and Gilbert (1977) *Proc. Natl. Acad. Sci. U.S.A.* 74:560; or Sanger (1977) *Proc. Natl. Acad. Sci. U.S.A.* 74:5463. In addition, any of a variety of automated
5 sequencing procedures can be utilized see, *e.g.*, Naeve, C.W *et al.* (1995) *Biotechniques* 19:448, including sequencing by mass spectrometry (see, *e.g.*, PCT International Publication No. WO 94/16101; Cohen *et al.* (1996) *Adv. Chromatogr.* 36:127-162; and Griffin *et al.* (1993) *Appl. Biochem. Biotechnol.* 38:147-159.

Determining the presence or absence of a null mutation in the sample may also
10 be accomplished using various techniques such as polymerase chain reaction (PCR) amplification reaction, reverse-transcriptase PCR analysis, single-strand conformation polymorphism analysis (SSCP), mismatch cleavage detection, heteroduplex analysis, Southern blot analysis, Western blot analysis, deoxyribonucleic acid sequencing, restriction fragment length polymorphism analysis, haplotype analysis, serotyping, and
15 combinations or sub-combinations thereof.

Any suitable sample obtained from a subject having breast cancer can be used to assess the level of expression, including a lack of expression, of the biomarker, for example, a biomarker provided in Table 1. For example, the sample may be any fluid or component thereof, such as a fraction or extract, *e.g.*, blood, plasma, lymph, cystic fluid,
20 urine, nipple aspirates, or fluids collected from a biopsy (*e.g.*, lump biopsy), obtained from the subject. In a typical situation, the fluid may be blood, or a component thereof, obtained from the subject, including whole blood or components thereof, including, plasma, serum, and blood cells, such as red blood cells, white blood cells and platelets. The sample may also be any tissue or fragment or component thereof, *e.g.*, breast tissue,
25 connective tissue, lymph tissue or muscle tissue obtained from the subject.

Techniques or methods for obtaining samples from a subject are well known in the art and include, for example, obtaining samples by a mouth swab or a mouth wash; drawing blood; or obtaining a biopsy. Isolating components of fluid or tissue samples (*e.g.*, cells or RNA or DNA) may be accomplished using a variety of techniques.

30 The sample from the cancer may be obtained by biopsy of the patient's cancer. In certain embodiments, more than one sample from the patient's tumor is obtained in order to acquire a representative sample of cells for further study. For example, a patient with breast cancer may have a needle biopsy to obtain a sample of cancer cells. Several biopsies of the tumor may be used to obtain a sample of cancer cells. In other
35 embodiments, the sample may be obtained from surgical excision of the tumor. In this

case, one or more samples may be taken from the excised tumor for analysis using the methods of the invention.

After the sample is obtained, it may be further processed. The cancer cells may be cultured, washed, or otherwise selected to remove normal tissue. The cells may be
5 trypsinized to remove the cells from the tumor sample. The cells may be sorted by fluorescence activated cell sorting (FACS) or other cell sorting technique. The cells may be cultured to obtain a greater number of cells for study. In certain instances the cells may be immortalized. For some applications, the cells may be frozen or the cells may be embedded in paraffin.

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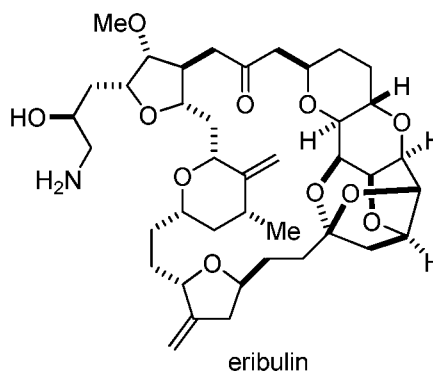
II. Treatment with Eribulin, Analogs Thereof, or Pharmaceutically Acceptable Salts Thereof (e.g., Eribulin Mesylate)

Given the observation that the expression levels of certain biomarkers, for example, those set forth in Table 1, in a subject having breast cancer influences the
15 responsiveness of the subject to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (e.g., eribulin mesylate), a skilled artisan can select an appropriate treatment regimen for the subject based on the expression levels of the biomarkers in the subject. Accordingly, the present invention provides methods for treating a subject having breast cancer by (i) identifying a subject having breast cancer
20 in which at least one biomarker selected from the group of biomarkers listed in Table 1 has a low level of expression and (ii) administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (e.g., eribulin mesylate), to the subject. In another aspect, the present invention provides methods for treating a subject having breast cancer by (i) assaying a sample derived from the subject
25 to determine the level of expression of at least one biomarker selected from the group of biomarkers listed in Table 1 and (ii) administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (e.g., eribulin mesylate) to the subject when a low level of expression of the at least one biomarker is detected in the sample.

30 In various embodiments, the subject may have been previously treated with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (e.g., eribulin mesylate). In other embodiments, the subject may be under consideration for treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (e.g., eribulin mesylate), for the first time. The level of expression of one or more, e.g., at
35 least 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10, biomarkers identified in Table 1 is determined. If level of expression of at least one biomarker (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10

biomarkers) is determined to be a low level of expression, treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), is likely to be efficacious. However, it is not necessary that all of the biomarkers assayed have a low level of expression as compared to the respective control. For example, while certain biomarkers may be present at normal or high levels of expression, treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be indicated when, for example, a low level of expression is present for at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9 or at least 10 biomarkers.

When a low level of expression of one or more of the biomarkers of the invention is found (*e.g.*, due to the presence of a null mutation in the biomarker gene) in a sample derived from a subject having breast cancer, the subject may be treated with eribulin, having the following the structure, with a pharmaceutically acceptable salt of eribulin, or with an eribulin analog or pharmaceutically acceptable thereof.



15

In some embodiments, a pharmaceutically acceptable salt of eribulin is administered to the subject, such as eribulin mesylate.

The treatment regimen for eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), that is selected typically includes at least one of the following parameters and more typically includes many or all of the following parameters: the dosage, the formulation, the route of administration and/or the frequency of administration. Selection of the particular parameters of the treatment regimen can be based on known treatment parameters for eribulin previously established in the art such as those described in the Dosage and Administration protocols set forth in the FDA Approved Label for HALAVEN[®], the entire contents of which are incorporated herein by reference. For example, eribulin mesylate can be administered intravenously

on Days 1 and 8 of a 21 day cycle, for example at a dose of 1.4 mg/m^2 , or if a dose reduction is indicated (*e.g.*, for hepatic or renal impairment), at a dose of 0.7 mg/m^2 or 1.1 mg/m^2 . Various modifications to dosage, formulation, route of administration and/or frequency of administration can be made based on various factors including, for
5 example, the disease, age, sex, and weight of the patient, as well as the severity or stage of cancer (see, for example, U.S. Patent No. 6,653,341 and U.S. Patent No. 6,469,182, the entire contents of each of which are hereby incorporated herein by reference).

As used herein, the term "therapeutically effective amount" means an amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin
10 mesylate) as described herein, that is capable of treating breast cancer. The dose of a compound to be administered according to this invention will, of course, be determined in light of the particular circumstances surrounding the case including, for example, the compound administered, the route of administration, condition of the patient, and the pathological condition being treated, for example, the stage of breast cancer.

For administration to a subject, eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), typically is formulated into a pharmaceutical composition comprising eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier. Therapeutic compositions typically should be sterile and adequately stable under the
15 conditions of manufacture and storage. Pharmaceutical compositions also can be administered in a combination therapy, *i.e.*, combined with other agents, such as those agents set forth below (see, for example, U.S. Patent No. 6,214,865 and U.S. Patent No. 6,653,341, the entire contents of each of which are hereby incorporated herein by reference).

As used herein, "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible. Preferably, the carrier is suitable for parenteral (*e.g.*, intravenous, intramuscular, subcutaneous, intrathecal) administration (*e.g.*, by injection or infusion). Depending on the route of
20 administration, the active compound may be coated in a material to protect the compound from the action of acids and other natural conditions that may inactivate the compound.

The pharmaceutical compositions may include one or more pharmaceutically acceptable salts, as defined above.

There are numerous types of anti-cancer approaches that can be used in
35 conjunction with eribulin, an analog thereof, or a pharmaceutically acceptable salt

thereof (*e.g.*, eribulin mesylate) treatment, according to the invention. These include, for example, treatment with chemotherapeutic agents, biological agents (*e.g.*, hormonal agents, cytokines (such as interleukins, interferons, granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), and granulocyte
5 macrophage colony stimulating factor (GM-CSF)), chemokines, vaccine antigens, and antibodies), anti-angiogenic agents (*e.g.*, angiostatin and endostatin), radiation, and surgery, as described in more detail in U.S. Pat. No. 6,653,341 B1 and U.S. Publ. No. 2006/0104984 A1, the teachings of which are incorporated herein by reference in their entirety.

10 The methods of the invention can employ these approaches to treat the same types of cancers as those for which they are known in the art to be used, as well as others, as can be determined by those of skill in this art. Also, these approaches can be carried out according to parameters (*e.g.*, regimens and doses) that are similar to those that are known in the art for their use. However, as is understood in the art, it may be
15 desirable to adjust some of these parameters, due to the additional use of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), with these approaches. For example, if a drug is normally administered as a sole therapeutic agent, when combined with eribulin, according to the invention, it may be desirable to decrease the dosage of the drug, as can be determined by those of skill in
20 this art. Examples of the methods of the invention, as well as compositions that can be used in these methods, are provided below.

Chemotherapeutic drugs of several different types including, for example, antimetabolites, antibiotics, alkylating agents, plant alkaloids, hormonal agents, anticoagulants, antithrombotics, and other natural products, among others, can be used in
25 conjunction with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, according to the invention. Specific, non-limiting examples of these classes of drugs, as well as cancers that can be treated by their use, are as follows.

Numerous approaches for administering anti-cancer drugs are known in the art, and can readily be adapted for use in the present invention. In the case that one or more
30 drugs are to be administered in conjunction with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), for example, the drugs can be administered together, in a single composition, or separately, as part of a comprehensive treatment regimen. For systemic administration, the drugs can be administered by, for example, intravenous infusion (continuous or bolus). Appropriate
35 scheduling and dosing of such administration can readily be determined by those of skill

in this art based on, for example, preclinical studies in animals and clinical studies (*e.g.*, phase I studies) in humans.

Many regimens used to administer chemotherapeutic drugs involve, for example, intravenous administration of a drug (or drugs) followed by repetition of this treatment after a period (*e.g.*, 1-4 weeks) during which the patient recovers from any adverse side effects of the treatment. It may be desirable to use both drugs at each administration or, alternatively, to have some (or all) of the treatments include only one drug (or a subset of drugs).

10 Kits of the Invention

The invention also provides compositions and kits for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer. These kits include reagents for determining the level of expression of at least one, for example, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10, biomarker(s) selected from the group of biomarkers listed in Table 1 and instructions for use of the kit to predict whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), may be used to treat a subject having breast cancer.

The kits of the invention may optionally comprise additional components useful for performing the methods of the invention. By way of example, the kits may comprise reagents for obtaining a biological sample from a subject, a control sample, and/or eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate).

In one embodiment, the reagents for determining the expression level of at least one biomarker in a biological sample from the subject comprises a nucleic acid preparation sufficient to detect expression of a nucleic acid, *e.g.*, mRNA, encoding the biomarker. This nucleic acid preparation includes at least one, and may include more than one, nucleic acid probe or primer, the sequence(s) of which is designed such that the nucleic acid preparation can detect the expression of nucleic acid, *e.g.*, mRNA, encoding the biomarker in the sample from the subject. A preferred nucleic acid preparation includes two or more PCR primers that allow for PCR amplification of a segment of the mRNA encoding the biomarker of interest. In other embodiments, the kit includes a nucleic acid preparation for each of at least 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 biomarkers provided in Table 1.

Alternatively, the reagents for detecting expression levels in the subject of one or more biomarkers predictive of responsiveness to eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), can comprise a reagent that detects the gene product of the nucleic acid encoding the biomarker(s) of interest
5 sufficient to distinguish it from other gene products in a sample from the subject. A non-limiting example of such a reagent is a monoclonal antibody preparation (comprising one or more monoclonal antibodies) sufficient to detect protein expression of at least one biomarker in a sample from the subject, such as a peripheral blood mononuclear cell sample.

10 The means for determining the expression level of the biomarkers of Table 1 can also include, for example, buffers or other reagents for use in an assay for evaluating expression (*e.g.*, at either the nucleic acid or protein level).

In another embodiment, the kit can further comprise eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof (*e.g.*, eribulin mesylate), for treating breast
15 cancer or another cancer, as described herein in the subject.

Preferably, the kit is designed for use with a human subject.

The present invention is further illustrated by the following examples which should not be construed as further limiting. The contents of all references, patents and
20 published patent applications cited throughout this application, as well as the Figures and the Appendix of sequences provided herein, are expressly incorporated herein by reference in their entirety.

EXAMPLES

25 **EXAMPLE 1: IDENTIFICATION OF RESISTANCE BIOMARKERS FOR TREATMENT WITH ERIBULIN**

siRNA techniques were employed to “knock down” expression of certain genes and assess the sensitivity of the resulting knock down cells to eribulin. Based on these studies, the expression of those genes set forth in Table 1 were identified as being
30 associated with the sensitivity of breast cancer cells to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof.

siRNA Transfection Optimization and Assay Development

Transfection conditions for human breast cancer cell lines MDA-MB-231 (ATCC Catalog No. HTB26TM) and BT-549 (ATCC Catalog No. HTB122TM) were optimized using transfection reagent DharmaFect 1 from Dharmacon. The MDA-MB-231 and BT-549 cell lines have been reported to be Estrogen Receptor (ER) negative, Progesterone Receptor (PR) negative and HER-2 negative (triple negative). As a non-targeting negative control we used Silencer Negative Control #1 siRNA from Applied Biosystems. The siGENOME TOX (siTOX) Transfection Control (Dharmacon), an RNA duplex designed to induce cell death, was used as a positive control for cell proliferation assays. A reverse transfection procedure in which siRNA was first mixed with transfection reagent and then cells were added to the well, was used in all experiments. Cell viability was compared in cells treated with medium, negative control siRNA and siTOX reagent combined with different amount of DharmaFect 1. Final selected transfection conditions were as follows: MDA-MB-231 cells at 0.035 μ l of DharmaFect 1 per well, while BT-549 cells at 0.05 μ l of DharmaFect 1 per well. Assays and library screening were performed at 50 nM final concentration of siRNAs. Efficacy of transfection was further confirmed by qPCR with control SMARTpool siRNA reagents targeting PPIA and GAPDH genes (Dharmacon).

High-throughput siRNA Screening

The whole human genome siRNA library was purchased from Dharmacon. The library was diluted to 5 μ M. Each well contained 4 SMARTpool siRNA reagents, each directed against a particular gene (four siRNAs targeting the same gene in a single well). More than 18,500 human genes were targeted with this library. 4 μ l of each set of siRNAs from the library plates were transferred to 384-well master plates containing 36 μ l OPTI-MEM medium per well. 40 μ l of diluted DharmaFect 1 reagent were added to each well of the master plate and mixed. 10 μ l of siRNA and transfection reagent mixture per well were distributed into five screening plates. After 10 min incubation, cells in 40 μ l of growth medium were added to each well. Each screening plate included several replicates of negative control siRNA, positive control siTOX as well as medium plus transfection reagent (no siRNA) containing wells. After a 24 hour incubation, 3 screening plates received 10 μ l of DMSO diluted in cell growth medium, while 2 repeats were treated with 10 μ l of eribulin mesylate (E7389) in growth medium, yielding a final concentration corresponding to the IC₂₀ for E7389 for the cell line tested (0.75 nM E7389 for MDA-MB-231; eribulin was provided in a stock solution of DMSO and diluted in growth medium) (see Figure 1). Cell viability was determined at 96 hours after

transfection by CellTiter-Glo luminescent assay from Promega. 10 µl of CellTiter-Glo solution per well were used. Plates were mixed for 2 minutes on a horizontal shaker, incubated for 10 minutes and read on an EnVision® multilabel plate reader from PerkinElmer.

5

Identification of Primary Hits

Identification of genes with a significant effect on cell sensitivity to E7389 was performed by a method that was similar to the method described for a paclitaxel siRNA screen (Whitehurst *et al.* (2007) *Nature* 446:815-819). Briefly, measurement of each
10 well was normalized by average of medium plus transfection reagent containing reference wells on a plate (32 wells/plate). The biological replicates were averaged for DMSO and E7389-treated plates. For each gene, a two sample t-test was performed to identify significantly different values for wells treated with two different conditions. To
15 narrow down the hit list, the magnitude of response was taken into account by arranging all data according to fold change ratio (average E7389/average DMSO) in ascending order. 364 genes with a fold change among the lowest 5 percentile of the distribution passed the cut-off level. Then, hypothetical open reading frames and genes encoding hypothetical proteins were excluded and the analysis was focused on the 240 remaining genes (see Figure 2).

20

Confirmation Assays

siRNA SMARTpools for the 240 selected genes were ordered in ON-TARGET^{plus} format from Dharmacon. These reagents contain a modified sense strand to prevent interaction with RISC and favor antisense strand uptake. The antisense strand
25 seed region is modified to decrease off-target activity and enhance target specificity. These reagents were used for confirmation secondary screening. To identify common genes influencing sensitivity of cancer cells to E7389, BT-549 breast cancer cells were screened with the 240 selected siRNA pools. The screening was performed using the same protocol as the primary screen with MDA-MB-231 cells, with the final
30 concentration of eribulin mesylate (E7389) in each well corresponding to the IC₂₀ for BT-549 cells (0.25 nM E7389).

Data analysis showed that the treatment with 40 out of 240 siRNA pools caused significant differences when comparing E7389-treated wells to carrier-treated wells in both cell lines (Table 2).

To confirm specific down-regulation of 40 genes with siRNA pools, quantitative PCR analysis of targeted mRNAs was performed. MDA-MB-231 and BT-549 cells were transfected with 40 ON-TARGET^{plus} siRNAs or non-targeting negative control siRNA according to the above protocol. 48 hours later cells were lysed and cDNAs were

5 synthesized according to the manufacturer's instructions for use of the TaqMan® Gene Expression Cells-to-CT™ Kit (Applied Biosystems). Relative quantities of remaining cDNAs after the treatment with siRNAs were evaluated using QuantiTect SYBR Green PCR Kit with the gene-specific QuantiTect Primer Assays (Qiagen). Results of the analysis are shown in Figure 4. The following 18 genes were down-regulated more than

10 50 percent in both tested cell lines: CFL1, NMU, MOBKL1B, HYAL2, PSENEN, CYP4F3, ITFG3, EDIL3, YTHDF1, CDC20, CCL26, TMEM79, MANSC1, DYSF, ERGIC3, GRAMD4, NCBP1, SNX11. 14 genes were down-regulated more than 50 percent in at least one cell line (PDGFB, APBB2, SATB1, MAD2L1BP, TUBB6, CEP152, KLH17, COL7A1, CKLF, PHOSPHO2, GNAT1, ABI3, TYROBP, IL10),

15 while other 3 genes were down-regulated more than 35 percent in at least one cell line (ANG, ZIC5, JAM3). Expression of SPTA1, PAPLN, PCDH1, TMIGD2, and KRT24 was either not detectable by this method in MDA-MB-231 cells or didn't change after siRNA treatment in BT-549 cells. The foregoing results indicate that down-regulation of the 40 genes can lead to increased sensitivity to eribulin, an analog thereof, or

20 pharmaceutically acceptable salt thereof.

Table 2. List of 40 overlapping genes from the screening of MDA-MB-231 and BT-549 cells. Fold changes (FC) compared to control and associated p-values are depicted.

gene	Gene ID	MDA-MB-231		BT-549	
		FC	t-test	FC	t-test
PSENEN	55851	0.70	0.03	0.39	0.00
PHOSPHO2	493911	0.56	0.04	0.44	0.02
CCL26	10344	0.71	0.02	0.45	0.03
CDC20	991	0.47	0.03	0.47	0.03
MAD2L1BP	9587	0.47	0.00	0.48	0.01
JAM3	83700	0.63	0.04	0.55	0.00
KLHL17	339451	0.65	0.04	0.57	0.00
PCDH1	5097	0.71	0.02	0.61	0.06
ABI3	51225	0.66	0.04	0.62	0.04
TMIGD2	126259	0.66	0.05	0.62	0.04
NCBP1	4686	0.72	0.04	0.63	0.02
IL10	3586	0.72	0.02	0.64	0.05
ANG	283	0.74	0.02	0.64	0.00
KRT24	192666	0.69	0.01	0.65	0.00
TMEM79	84283	0.66	0.01	0.67	0.02
PDGFB	5155	0.65	0.00	0.68	0.03
SNX11	29916	0.68	0.05	0.68	0.05
CFL1	1072	0.69	0.02	0.68	0.05
CKLF	51192	0.62	0.03	0.70	0.01
TUBB6	84617	0.73	0.01	0.71	0.01
HYAL2	8692	0.67	0.02	0.71	0.05
TYROBP	7305	0.73	0.04	0.71	0.01
APBB2	323	0.70	0.00	0.71	0.02
YTHDF1	54915	0.61	0.02	0.73	0.01
CEP152	22995	0.46	0.03	0.74	0.05
COL7A1	1294	0.73	0.03	0.75	0.05
NMU	10874	0.67	0.00	0.76	0.05
SPTA1	6708	0.38	0.03	0.76	0.02
ERGIC3	51614	0.70	0.05	0.76	0.05
SATB1	6304	0.67	0.02	0.77	0.04
MOBKL1B	55233	0.74	0.03	0.77	0.01
GNAT1	2779	0.66	0.04	0.78	0.03
ITFG3	83986	0.73	0.05	0.78	0.05
DYSF	8291	0.26	0.01	0.78	0.05
MANSC1	54682	0.65	0.03	0.78	0.05
EDIL3	10085	0.65	0.01	0.79	0.05
GRAMD4	23151	0.72	0.00	0.79	0.01
ZIC5	85416	0.69	0.03	0.80	0.05
PAPLN	89932	0.71	0.03	0.80	0.01
CYP4F3	4051	0.74	0.02	0.81	0.01

APPENDIX

NUCLEIC ACID AND AMINO ACID SEQUENCES OF BIOMARKERS

Gener Name	Gene ID	Accession NO.	Name
ABI3	51225	NM_016428	Homo sapiens ABI family, member 3 (ABI3), transcript variant 1, mRNA
mRNA Sequence			
TCCTATCCACCTCCACTCCCCTGTCCCTTGGTGACTCATCCCTGAGCTTCCCAAGGAAGCCCCACCCCT CTGCCCTTTCCTCCCGCCTTCCATGAGTGGAAAAATCCACCTCCGCCCCCTATAGCAGGCCAGCCCCCTTC CTCCCCAGTCTCCGACCCCATCCCCAGCCGACCAGTTTCTCTCCAGGACCAGGGAGCAATCAGAGCTG CCCCGACCTTGGCTTTCCTCTGCTGGGTGGGATTGGGGGCTGGGCCCCAAATGGGCCCCCTGGCTTCCCCC TTCTCTGGGCGAGGGACAGAGAGACACAGGCTCGGGGAGCAGGACTGACTTCTCTTGTCCCGGAATGA GCATGCCTGCCCTTTGCAAGCAGGTTTGGGTCTCAGCAGAGGAAACCAAAAGCAATAAGAGGGAGGGAA GGCAGAGCAACCAATCAAGGGCAGGGTGAGACTCAAAACGAGCGGGCTCCCTGGGGAGCCAGACAGAGGC TGGGGGTGATGGCGGAGCTACAGCAGCTGCAGGAGTTTGAGATCCCCACTGGCCGGGAGGCTCTGAGGGG CAACCACAGTGCCCTGCTGCGGGTCGCTGACTACTGCGAGGACAACATATGTGCAGGCCACAGACAAGCGG AAGGCGCTGGAGGAGACCATGGCCTTCACTACCCAGGCACTGGCCAGCGTGGCCTACCAGGTGGGCAACC TGGCCGGGCACACTCTGCGCATGTTGGACCTGCAGGGGGCCGCCCTGCGGCAGGTGGAAGCCCGTGTAAG CACGCTGGGCCAGATGGTGAACATGCATATGGAGAAGGTGGCCCCGAAGGGAGATCGGCACCTTAGCCACT GTCCAGCGGCTGCCCCCGGCCAGAAGGTCATCGCCCCAGAGAACCTACCCCTCTCACGCCCTACTGCA GGAGACCCCTCAACTTTGGCTGCCTGGACGACATTGGCCATGGGATCAAGGACCTCAGCACGCAGCTGTC AAGAACAGGCACCCCTGTCTCGAAAGAGCATCAAGGCCCTGCCACACCCGCCTCCGCCACCTTGGGGAGA CCACCCCGGATTCCCGAGCCAGTGCACCTGCCGTGGTGCCCGACGGCAGACTCTCCGCCGCCTCCTCTG CGTCTTCCCTGGCCTCGGCCGGCAGCGCCGAAGGTGTGGTGGGGGCCCCACGCCCAAGGGGCAGGCAGC ACCTCCAGCCCCACCTCTCCCCAGCTCCTTGGACCCACCTCCTCCACCAGCAGCGCTGAGGTGTTCCAG CGGCCCTCCACGCTGGAGGAGTTGTCCCCACCCACCAGGACGAAGAGCTGCCCTGCCACTGGACCTGC CTCCTCTCCACCCCTGGATGGAGATGAATTGGGCTGCCTCCACCCACCAGGATTTGGGCTGATGA GCCCAGCTGGGTGCCTGCCTCATACTTGGAGAAAGTGGTGACACTGTACCCATACACCAGCCAGAAGGAC AATGAGCTCTCCTTCTCTGAGGGCACTGTCTGTGTACTCGCCGCTACTCCGATGGCTGGTGCGAGG GCGTCAGCTCAGAGGGGACTGGATTCTTCCCTGGGAACATGTGGAGCCAGCTGCTGACAGCCAGGGC TCTCTGGGCAGCTGATGTCTGCACTGAGTGGGTTTCATGAGCCCCAAGCCAAAACAGCTCCAGTCACAG CTGGACTGGGTCTGCCCACCTCTTGGGCTGTGAGCTGTGTTCTGTCTCTCTCCATCGGAGGGAGAAGG GGTCTTGGGAGAGAGAATTTATCCAGAGGCTGTGTCAGATGGGGAAGAGCTGGAAACCAAGAAGTTTG TCAACAGAGGACCCCTACTCCATGCAGGACAGGGTCTCCTGCTGCAAGTCCCAACTTTGAATAAAACAGA TGATGTCTGTGACTGCCCCACAGAGATAAGGGGCCAGGAGGGATTGAAAGGCATCCCACTTCTAAGGCT GCTGCTAATTACAGCCCCAACCTCCAACCCACCAGCTGACCTAGAAGCAGCATCTTCCCATTTCTCAG TACCCACAAAAGTGACGCCACATTGGACCCACAGACCCCTCTGCAGCCATTGACTGCAACTTGTTCTTT TGCCCATTTGAAAAAAAAAAAAAAAAAAAA (SEQ ID NO: 1)			
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ANG	283	NM_001097577	Homo sapiens angiogenin, ribonuclease, RNase A family, 5 (ANG), transcript variant 2, mRNA
mRNA Sequence			
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<p>TTTGTGTTGGTCTTCGTGCTGGGTCTGGGTCTGACCCACCGACCCTGGCTCAGGATAACTCCAGGTAC ACACACTTCCTGACCCAGCACTATGATGCCAAACACAGGGCCGGGATGACAGATACTGTGAAAGCATCA TGAGGAGACGGGGCCTGACCTCACCTGCAAAGACATCAACACATTTATTCATGGCAACAAGCGCAGCAT CAAGGCCATCTGTGAAAACAAGAATGGAACCCTCACAGAGAAAACCTAAGAATAAGCAAGTCTTCTTTC CAGGTACCACTTGCAAGCTACATGGAGGTTCCCCCTGGCCTCCATGCCAGTACCGAGCCACAGCGGGT TCAGAAACGTTGTTGTTGCTTGTAATGGCTTACCTGTCCACTTGGATCAGTCAATTTTCCGTGCTCC GTAACCAGCGGGCCCTGGTCAAGTGCTGGCTCTGCTGTCTTGCCTTCCATTTCCCTCTGCACCCAGA ACAGTGGTGGCAACATTCATTGCCAAGGGCCCAAAGAAAGAGCTACCTGGACCTTTTGTCTTCTGTTTGA CAACATGTTTAATAATAAAAAATGCTCTTGATAICAGTAAGAA (SEQ ID NO: 3)</p>			
Translated protein sequence			
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APBB2	323	NM_173075	Homo sapiens amyloid beta (A4) precursor protein-binding, family B, member 2 (APBB2), mRNA
mRNA Sequence			
<p>GCCAAAGCCTGGAGAAGTGAATCTCGTCAGCGCCGCTCCCTGCGCGGGACTCGCGGAACGGCACTGAGC ATGCTCAGTTGCCGAGCCCGTTCTGGTCTCAAGTAGGAAGCTAGTGCCTGTAACCGCATCTGATCTGG GCGCTCCGGGAAGGGCGAGACTGGAGCAGAGCCGCTGGGCGCCGGAGCCGAGGCGAGCGCCGCGCACC ACTGGTTGGAGTTGCTGTGGGTGAGCTGCTGTGGTCTGTAGCCAAGCATGCTGTGGTCGGATCTGCCAG CCGTGGAACAGAAACATTTGCTGGATGGAATTCATAAAAGAAAGCTCCTGTGAAAAGCTGAGGCTGAC AATAATTTAAGCAAAATCAGATCGATCTCTTTGGGCTGCCTGACCTCCTTGGGTGCTTGCTATTAATTAA CAGACTTTGTGGGGAAGGAGCTTGCCCTTCTGAGCTTTGTACCAAAGACCTGGGAAAACCTAACCAT CTCAGCTTTCTCTGAGGACTTGGGAACCTGCCGAGGCTCTGCCAATGTGTTGACTGTCTGCTATGGGCTCA CTGTTGTCCAGGCAGCTCATATTTCAAATTATAACCTATTTTCTGCACCATTGCTGACGCTGGTGATCC ATGTCAGAAGTACTTCCAGCTGACTCAGGTGTTGACACCTTGGCAGTGTTTATGGCCAGCAGCGGAACCTA CAGACGTCACAAATCGGAACAGCCAGCCACACCACAAACACCCCTTAACCTCCGATCTCCCACAATGA ACTGTTGAACGCTGAAATAAAACACACAGAAACCAAGAACAGCACACCTCCCAATGCAGGAAAAAATAT GCCTAACTAACATCCAGGCGCCATGGGCTCTCGGATCCAGCTGCACAGCCCTGCTGGGAAATGGCT CTGCCAATCAAGCTGGTGAATAATGGGAGAACAGCTCCGTAAGGCTGCAGAGCAAGGCGAGCAGGA CCCCAACAAAACCTGAGCCCACTGCAGTCATCAACATAACTTCTGAGAAGTTAGAGGGTAAAGAGCCC CACCCACAGGATTCCTCGAGCTGTGAGATTTTACCTCCAGCCAGGAGAACTAAGAGCTTCTTAAATT ACTATGCAGATCTGAAACCTCAGCCAGAGAAGTAGAGCAGAACCAGGCAATCACCATGGGACTGCGGA AGAGAAATCCAGCCAGTCCAGGGCCAGGCCTCCACCATCATTGGGAATGGCGATTTGCTGCTGCAGAAA CCAAACAGACCCAGTCCAGCCCTGAAGACGGCCAAGTAGCCACAGTGTCATCCAGCCAGAAACCAAGA AGGATCATCCGAAAACAGGGGCCAAACCGACTGTGCACTGCACCGGATCCAGAACCTGGCACCGAGCGA TGAGGAGTCCAGCTGGACAACGTTGTCCCAAGACAGTGCCTCACCCAGCTCCCGGATGAAACAGATATA TGGAGTGATCACTCATTTTCACTGATCCAGATTTGCCGCTGGCTGGAAAAGAGTCAGTGACATTGCCG GGACCTATTATTGGCACATCCCAACAGGAACGACTCAGTGGGAACGGCCGCTCTCCATCCCAAGCAGATCT CCAGGTTCTAGGAAAGGTCATCTAGTTCTGTAAACGCTATCTCCACCCAGAGAACGAGGATTTGCAT GCAGCCACTGTAAACCGGACCCAGTTTAAAGAGGTTTGAAGGAGCAACCTACAGCTATGCATCTTTGA AACTCAGAAATGCCACACCCCTGATGATGATGATTCTTGTAGTATCAACAGTGACCCAGAAGCCAAGTG TTTTGCTGTGCTTCTCTGGGATGGGTAGAGATGGCAGAAGAGGACCTCGCCCCCGGTAAAGTAGTGTT GCGGTCAACAACTGCATCAGGCAACTTTCTACTGCAAAAATGACATCCGAGACACAGTCGGGATTGGG GAGAGGGGAAAGACATGTACCTGATCTGGAGAATGACATGCTCAGCCTGGTGGACCCCATGGACCGCAG CGTGCTGCACTCGCAGCCCATCGTCAGCATCCGCGTGTGGGGCTGGGCCGCGACAATGGCCGGGATTTT GCTTATGTAGCAAGAGATAAAGATACAAGAATTTTGAAATGTCATGTATTTTCATGTGACACACCAGCAA AAGCCATTGCCACAAGTCTCCAGGATCTGCTCCAAGATTATGGCTGAACGGAAGAATGCCAAGCGCT GGCCTGCAGCTCCTTACAGGAAAGGGCCAATGTGAACCTCGATGTCCCTTTGCAAGATTTTCCAACACCA AAGACTGAGCTGGTCCAGAAGTTCACGTCAGTACTTGGGCATGTTACCTGTAGACAAACAGTCGGAA TGGATATTTTGAACAGTGCCATAGAAAATCTTATGACCTCATCCAACAAGGAGGACTGGCTGTCAGTGAA CATGAACGTGGCTGATGCCACTGTGACTGTATCAGTGAAAAGAATGAAGAGGAAGTCTTAGTGGAATGT CGTGTGCGATTCTGTCTTTCATGGGTGTTGGGAAGGACGTCCACACATTTGCCTTCATCATGGACACGG GGAACCAGCGCTTTGAGTGCCACGTTTTCTGGTGGCAGCCTAATGCTGGTAACGTGCTGAGGCGGTGCA GGCCGCTGCATGTTACGATATCAGAAGTGCTTGGTAGCCAGGCGCCTTCTCAGAAAGTTGACACCT CCACCGCCAGCAGATTAGTAACAGAGAGTCAACAACCAATGTAAACGAGGGGTCTTATCCCTCATTG ACATTTGAAACAGAAACGCCCTGTACCGAAATGCCATAGCTGCACATGCAAAAGGACTCGGCTATTTA</p>			

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CCL26	10344	NM_006072	Homo sapiens chemokine (C-C motif) ligand 26 (CCL26), mRNA
mRNA Sequence			
CTGGAATTGAGGCTGAGCCAAAGACCCAGGGCCGTCTCAGTCTCATAAAAGGGGATCAGGCAGGAGGAG TTTGGGAGAAACCTGAGAAGGGCCTGATTTGCAGCATCATGATGGGCCTCTCCTTGGCCTCTGCTGTGCT CCTGGCCTCCCTCCTGAGTCTCCACCTTGGAAGTCCACACAGTGGGAGTGACATATCCAAGACCTGCTGC TTCCAATACAGCCACAAGCCCTTCCCTGGACCTGGGTGCGAAGCTATGAATTCACCAAGTAAACAGCTGCT CCCAGCGGGCTGTGATATTTACTACCAAAAGAGGCAAGAAAGTCTGTACCCATCCAAGGAAAAAATGGGT GCAAAAAATACATTTCTTTACTGAAAACCTCCGAAACAATTGTGACTCAGCTGAATTTTCATCCGAGGACGC TTGGACCCCGCTCTTGGCTCTGCAGCCCTCTGGGGAGCCTGCGGAATCTTTTCTGAAGGTACATGGACC CGCTGGGAGGAGAGGGTGTTCCTCCAGAGTTACTTTAATAAAGGTGTTCATAGAGTTGACTTGTTT AT (SEQ ID NO: 7)			
Translated protein sequence			
MMGLSLASAVLLASLLSLHLGTATRGSDISKTCFQYSHKPLPW TWVRSYEFTSNCSQRAVIFTTKRGKKVCTHPRKKWQKYISLLKTPKQL (SEQ ID NO: 8)			
CDC20	991	NM_001255	Homo sapiens cell division cycle 20 homolog

			(<i>S. cerevisiae</i>) (CDC20), mRNA
mRNA Sequence			
GAGGCGTAAGCCAGGCGTGTTAAAGCCGGTCGGAAGTCTCCGGAGGGCACGGGCTCCGTAGGCACCAAC TGCAAGGACCCCTCCCCCTGCGGGCGCTCCCATGGCACAGTTCGCGTTCGAGAGTGACCTGCACTCGCTG CTTCAGCTGGATGCACCCATCCCCAATGCACCCCTGCGCGCTGGCAGCGCAAAGCCAAGGAAGCCGAG GCCCCGCCCCCTCACCCATGCGGGCCGCCAACCGATCCACAGCGCCGGCAGGACTCCGGGCCGAACTCC TGGCAAATCCAGTTCCAAGGTTAGACCCTCTAGCAAACCTGGCGGTGACCGCTATATCCCCCATCGC AGTGCTGCCCAGATGGAGGTGGCCAGCTTCTCTGAGCAAGGAGAACCAGCCTGAAAACAGCCAGACGC CCACCAAGAAGGAACATCAGAAAGCCTGGGCTTTGAACCTGAACGGTTTGTATGTAGAGGAAGCCAAGAT CCTTCGGCTCAGTGGAAAACCAAAATGCGCCAGAGGGTTATCAGAACAGACTGAAAGTACTCTACAGC CAAAAGGCCACTCTGGCTCCAGCCGGAAGACCTGCCGTTACATTCTCTCCCTGCCAGACCGTATCCTGG ATGCGCCTGAAATCCGAAATGACTATTACCTGAACCTTGTGGATTGGAGTTCTGGGAATGTACTGGCCGT GGCACTGGACAACAGTGTGTACCTGTGGAGTGAAGCTCTGGTGACATCCTGCAGCTTTTCAAATGGAG CAGCCTGGGGAATATATATCTCTGTGGCTGGATCAAAGAGGGCAACTACTTGGCTGTGGGCACCAGCA GTGCTGAGGTGCAGCTATGGGATGTGCAGCAGCAGAAACGGCTTCGAAATATGACCAGTCACTCTGCCCCG AGTGGGCTCCCTAAGCTGGAACAGCTATATCTGTCCAGTGGTTCACGTCTTGGCCACATCCACCACCAT GATGTTCCGGTAGCAGAACACCATGTGGCCACACTGAGTGGCCACAGCCAGGAAGTGTGTGGGCTGCGCT GGGCCCCAGATGGACGACATTGGCCAGTGGTGGTAATGATAACTTGGTCAATGTGTGGCCTAGTGTCTC TGGAGAGGGTGGCTGGGTTCTCTGCAGACATTCACCCAGCATCAAGGGGCTGTCAAGGCCGTAGCATGG TGTCCCTGGCAGTCCAATGTCTGGCAACAGGAGGGGGCACCAGTGATCGACACATTGCATCTGGAATG TGTGCTCTGGGGCTGTCTGAGTGCCGTGGATGCCATTCCAGGTGTGCTCCATCTCTGTTCTCCCCA TTACAAGGAGCTCATCTCAGGCCATGGCTTTGCACAGAACCAGCTAGTTATTTGGAAGTACCAACCATG GCCAAGGTGGCTGAACTCAAAGGTACACATCCCGGGTCTGAGTCTGACCATGAGCCAGATGGGGCCA CAGTGGCATCCGCAGCAGCAGATGAGACCTGAGGCTATGGCGCTGTTTTGAGTTGGACCCTGCGCGGCG GCGGGAGCGGGAGAAGGCCAGTGCAGCCAAAAGCAGCCTCATCCCAAGGCATCCGTGAAGACCAACC CATCACCTCAGTTGTTTTTATTTTCTAATAAAGTCATGTCTCCCTTCATGTTTTTTTTTAAAAAAA AAAAAAAAAAAAAAAA (SEQ ID NO: 9)			
Translated protein sequence			
MAQFAFESDLHSLQLDAPIPNAPPARWQRKAKEAAGPAPSPMR AANRSHSAGRTPGRTPGKSSSKVQTTPSKPGGDRIIPHRSAQMEVASFLLSKENQPE NSQTPTKKEHQKAWALNLNGFDVEEAKILRLSGKPQNAPEGYQNRLKVLYSQKATPGS SRKTCRYIPSLPDRIIDAPEIRNDYYLNLVDWSSGNVLAVALDNSVYLWSASSGDILQ LLQMEQGEYISSVAWIKEGNYLAVGTSSAEVQLWDVQQKRLRNMTSHSARVGSLSW NSYILSSGSRSGHIHHHDVRAEHHVATLSGHSQEVCGLRWAPDGRHLASGGNDNLVN VWPSAPGEGGWVPLQFTFQHGAVKAWCPWQSNVLATGGGTSRHIRIWNVCSGAC LSAVDAHSQVCSILWSPHYKELISGHGFAQNQLVIWKYPTMAKVAELKGHTSRVLSLT MSPDGTAVASAADETLRLWRCFELDPARRREREKASAAKSSLIHQGIR (SEQ ID NO: 10)			
			Homo sapiens centrosomal protein 152kDa (CEP152), mRNA
CEP152	22995	NM_014985	
mRNA Sequence			
GCCACCGGGCGAGCTTCTAGTCGGCGATTGAAGGATGCGAGTGCTCCTTAAGGGCTCCGCCCCGTGAG TTCGGTTGTGACTAGGAAGGAGCTAGTGGACTAGAGCCAGGGTAAGGGGATCTGCTAGAAGTTGGTCTTC CGCCAGGACTAGAGTTTCTCGCGGTAAACAGCTCCGTGGCCTCCGGAGGACCATGTCATTAGACTTTGG CAGTGTGGCACTACCAGTGCAAAATGAAGATGAAGAGTATGACGAAGAGGACTATGAAAGAGAGAAAGAG TTGCAGCAGTTACTCACAGACCTTCCCCATGACATGCTGGATGACGACCTCTCCTCTCCAGAGCTCCAGT ATTCCGACTGCAGCGAGGATGGCACAGACGGACAACCACATCATCTGAGCAATTGGAGATGAGCTGGAA TGAGCAAATGCTGCCCAAATCTCAAAGTGTAATGGCTATAATGAAATTCAGAGTTTATATGCTGGAGAA AAATGTGGTAATGTCTGGGAAGAAAATAGAAGTAAACTGAAGACCGACATCCTGTGTACCATCCTGAAG AAGGTGGAGATGAAGGTGGAAGTGGTTATAGTCTCCAAGTAAATGTGAACAGACTGATTATATCACCT TCCTGAAAACCTTAGGCCATATACCAATGGTCAGAAGCAGGAATTTAATAACCAAGCAACCAATGTAATT AAATTTTCAGATCCTCAATGGAACATTTTCAGGCTCCAGTTGTCAAGGTTTGAACCGTATAATAAAG TGACATATAAACCTTATCAGTCTTCTGCCAGAATAATGGCTCACCAGCCCAGGAGATAACAGGAAGTGA CACATTGGAAGGCCTGCAACAACAATTTTTAGGAGCTAATGAGAACTCTGCAGAAAATATGCAGATTATT CAACTTCAGGTTCTTAACAAAGCAAAAGAGAGACAACTGGAGAACCTAATTGAAAAGTTAAATGAAAGTG AACGTCAAATTCGATATCTGAATCACCAGCTTGTAAATAATAAAGATGAAAAGGATGGTTTGACTCTCAG			

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GCCTTAATATTCCAAAGGCCTGATGGTGTATGTATAATCTGCTTTTGTGTGGTGCTTATTTTGGTTTCT AAACCATCTATTTTATACTTATAAATTGACTCACTCTGCAGTGTAACTTATTTAAATAAACTTGCATA TGGTCTGTAAAAA (SEQ ID NO: 11)			
Translated protein sequence			
MSLDFGSVALPVQNEDEEYDEEDYEREKELQQLLTDLPHDMLDD DLSSPELQYSDCEDGTDGQPHHPEQLEMSWNEQMLPKSQSVNGYNEIQSLYAGEKCG NVWEENRSKTEDRHPVYHPEEGGDEGGSGYSPPSKCEQTDLYHLPENFRPYTNGQKQE FNNQATNVIKFSDPQWNHFQGPSCQGLEPYNKVTYKPYQSSAQNNGSPAQIEITGSDTF EGLQQQFLGANENSAENMQIIQLQVLNKAKEQLENLIEKLNESERQIRYLNHQLVII KDEKDGLTSLRESQKLFQNGKEREIQLEAQIKALETQIQALKVNEEQMIKKSRTEM ALESKQQLVDLHHSSELQRAREQHEISVMGLTKKYEEQVLSLQKNLDATVTALKEQE DICSRLKDHVKQLERNQEAIKLEKTEIINKLTRSLEESQKQCAHLLQSGSVQEVQQLQ FQLQQAQKAHAMSANMNKALQEELTELKDEISLYESAACKLGIHPSDSEGELNIELTES YVDLGIIKVNWKKSKVTSIVQEEDPNEELSKDEFILKLKAEVQRLLGNSMKRHLVSQ LQNDLKDCHKKIEDLHQVKKDEKSIEVETKTDTSEKPKNQLWPESSTSDVVRDDILL KNEIQVLQQQNQELKETEGKLRNTNQDLNQMQRQVQDFDHDKQEAVDRCERTYQQHH EAMKTQIRESLLAKHALEKQQLFEAYERTHLQLRSELDKLNKEVTAVQECYLEVCREK DNLELTLRKTTEKEQQTQEKIKEKLIQQLEKEWQSKLDQTIKAMKKKTLDCGSQTDQV TTSDVISKKEMAIMIEEQKCTIQONLEQEKDIAIKGAMKKLEIELELKHENITKQVE IAVQNAHQRWLGELPELAEYQALVKAQKQWEEQHEVSVNKRISFAVSEAKEKWKSEL ENMRKNILPGKELEEKIHSQKELELKNEEVPVIRAEALAKARSEWNKEKQEEIHRIQ EQNEQDYRQFLDDHRNKINEVLAAAKEDFMKQKTELLQKETELQTCLDQSRREWMTQ EAKRIQLEIYQYEEDILTVLGVLLSDTQKEHISDSEDKQLLEIMSTCSSKWSVQYFE KLKGCIIQAFQDTLPLLVENADPEWKKRNMAELSKDSASQGTGQGDGPAAGHHAQPL ALQATEAEAEENNKVVEELIEENNDMNKLEELQTLCKTPPRSLSAGAIENACLPCSG GALEELRGQYIKAVKKIKCDMLRYIQESKERAEMVKAEVLRRERQETARKMRKYLYIC LQQILQDDGKEGAEEKIMNAASKLATMAKLLLETPISSKSQSKTTQSALPLTSEMLIAV KKSkrndvNQKIPCCIESKNSVNTITRTLCEQAPKRAACNLQRLLENSEHQSIKHV GSKETHLEFQFGDGSCKHLNSLPRNVSPFVPCGEGGGFGLHKKKDLLSDNGSESLPH SAAYPFLGTLGNKPSPRCTPGPSESGCMHITFRDSNERLGLKVYKCNPLMESENAASE KSQGLDVQEPVVKDGGDLSDCLGWPSSSATLSFDSREASFVHGRPQGTLEIPSES VKS KQFSPSGYLSDTESNMICQTMKCQRYQTPYLSEETTYLEPGKISVNCGHPSRHKADR LKSDFKKLSSTLPSSVCQQPSRKLIVPLSSQQDSGDFSPFVNLD (SEQ ID NO: 12)			
CFL1	1072	NM_005507	Homo sapiens cofilin 1 (non-muscle) (CFL1), mRNA
mRNA Sequence			
GGCCGGCGGGAAGACTCCGTTACCCAGCGAGCGAGGCGGCGGCGCAGGGCCAGCGGACTCCATTTCCCGT CGGCTCGCGGTGGGAGCGCCGGAAGCCCGCCCCACCCCTCATTGTGCGGCTCCTACTAAACGGAAGGGC CGGGAGAGGCCGCGTTTCAGTCGGGTCCCGGCAGCGGCTGCAGCGCTCTCGTCTTTCGCGGCTCTCGGTGC CCTCTCCTTTTCGTTTCCGGAAACATGGCCTCCGGTGTGGCTGTCTCTGATGGTGTATCAAGGTGTTCA ACGACATGAAGGTGCGTAAGTCTTCAACGCCAGAGGAGGTGAAGAAGCGCAAGAAGGCGGTGCTCTTCTG CCTGAGTGAGGACAAGAAGAACATCATCTGGAGGAGGGCAAGGAGATCCTGGTGGGCGATGTGGGCCAG ACTGTCGACGACCCCTACGCCACCTTTGTCAAGATGCTGCCAGATAAGGACTGCCGCTATGCCCTCTATG ATGCAACCTATGAGACCAAGGAGAGCAAGAAGGAGGATCTGGTGTATTATCTTCTGGGCCCCCGAGTCTGC GCCCCTTAAGAGCAAAATGATTTATGCCAGCTCCAAGGACGCCATCAAGAAGAAGCTGACAGGGATCAAG CATGAATTGCAAGCAAACCTGCTACGAGGAGGTCAAGGACCGCTGCACCCCTGGCAGAGAAGCTGGGGGGCA GTGCCGTCATCTCCCTGGAGGGCAAGCCTTTTGAGAGCCCTTCTGGCCCCCTGCCTGGAGCATCTGGCAG CCCCACACCTGCCCTTGGGGGTGTCAGGCTGCCCCCTTCTGCCAGACCGGAGGGGCTGGGGGGATCCCA GCAGGGGGAGGGCAATCCCTTACCCCCAGTTGCCAAACAGACCCCCCACCCTGGATTTTCTTCTCCC TCCATCCCTTGACGGTTCTGGCCTTCCCAAACIGCTTTTGATCTTTTGATTCTTCTGGGCTGAAGCAGA CCAAGTTCACCCCGAGGACCCCGAGTTGTGGGGGAGCCTGTATTTTTTTAACAACATCCCCATTCCCCAC CTGGTCTCTCCCCCTTCCCATGCTGCCAACTTCTAACCGCAATAGTGACTCTGTGCTTGTCTGTTTAGTTC TGTGTATAAATGGAATGTTGTGGAGATGACCCCTCCCTGTGCCGGCTGGTTCCTCTCCCTTTTCCCCTGG TCACGGCTACTCATGAAGCAGGACAGTAAGGGACCTTCGATTAAAAAAGACAATAATAAAAA (SEQ ID NO: 13)			
Translated protein sequence			

MASGVAVSDGVIKVFNDMKVRKSSSTPEEVKKRKKAVLFCLSEDK KNIILEEGKEILVGDVGQTVDDPYATFVKMLPDKDCRYALYDATYETKESKKEDLVFI FWAPESAPLKSKMIYASSKDAIKKKLTGIKHELQANCYEEVKDRCTLAEKLGGSAVIS LEGKPL (SEQ ID NO: 14)			
CKLF	51192	NM_016326	Homo sapiens chemokine-like factor (CKLF), transcript variant 3, mRNA
mRNA Sequence			
ATGCGCGCAAGAGAGCGGGAAGCCGAGCTGGGCGAGAAGTAGGGGAGGGCGGTGCTCCGCCGCGGTGGCG GTTGCTATCGCTTCGCAGAACCTACTCAGGCAGCCAGCTGAGAAGAGTTGAGGGAAAGTGCTGCTGCTGG GTCTGCAGACGCGATGGATAACGTGCAGCCGAAAAATAAACATCGCCCCCTTCTGCTTCAGTGTGAAAGGC CACGTGAAGATGCTGCGGCTGGTGTGTTGCACTTGTGACAGCAGTATGCTGTCTTCCGACGGGGCCCTTA TTTACCGGAAGCTTCTGTTCAATCCAGCGGTCTTACCAGAAAAAGCCTGTGCATGAAAAAAGAAGT TTTGTAATTTTATATTACTTTTAGTTTGATACTAAGTATTAAACATATTTCTGTATTCTCCACATATT TTCTGCAGTTATTTAACTCAGTATAGGAGCTAGAGGAAGAGATTTCCGAAGTCTGCACCCCGCGCAGAG CACTACTGTAACCTCCAAGGAGCGCTGGGAGCAGCGGGATCGGGTTTCCGGCACCCGGGCTGGGTGG CAGGGAAGAATGTGCCGGGATCCGCCTCAGGGATCTTTGAATCTCTTTACTGCCTGGCTGGCCGGCAGCT CCG (SEQ ID NO: 15)			
Translated protein sequence			
MDNVQPKIKHRPFCFSVKGHVKMLRLVFALVTAVCCCLADGALIY RKLLFNPSGPYQKKPVHEKKEVL (SEQ ID NO: 16)			
COL7A1	1294	NM_000094	Homo sapiens collagen, type VII, alpha 1 (COL7A1), mRNA
mRNA Sequence			
GATGACGCTGCGGCTTCTGGTGGCCGCGCTCTGCGCCGGGATCCTGGCAGAGGCGCCCCGAGTGCGAGCC CAGCACAGGGAGAGAGTGACCTGCACGCGCCTTTACGCCGCTGACATTGTGTTCTTACTGGATGGCTCCT CATCCATTGGCCGCGAGCAATTCCGCGAGGTCCGACGCTTTCTCGAAGGGCTGGTGTGCTTCTCTG AGCAGCCAGTGACAGGGTGTGCGCTTTGCCACAGTGCAGTACAGCGATGACCCACGGACAGAGTTCGGC CTGGATGCACTTGGCTCTGGGGGTGATGTGATCCGCGCCATCCGTGAGCTTAGCTACAAGGGGGCAACA CTCGCACAGGGGCTGCAATTCTCCATGTGGCTGACCATGTCTTCTGCCCCAGCTGGCCCGACCTGGTGT CCCCAGGTCTGCATCCTGATCACAGACGGGAAGTCCAGGACCTGGTGGACACAGCTGCCCAAAGGCTG AAGGGGACAGGGGTCAAGCTATTTGCTGTGGGGATCAAGAATGCTGACCCTGAGGAGCTGAAGCGAGTTG CCTCACAGCCACCAGTGACTTCTTCTTCTTCGTCATGACTTCAGCATCTTGAGGACACTACTGCCCT CGTTTCCCGGAGAGTGTGCAGACTGCTGGTGGCGTGCTGTGACCCGACCTCCGGATGACTCGACCTCT GCTCCACGAGACCTGGTGTGCTGAGCCAAGCAGCCAATCCTTGAGAGTACAGTGGACAGCGGCCAGTG GCCCTGTGACTGGCTACAAGGTCCAGTACACTCCTCTGACGGGGCTGGGACAGCCACTGCCGAGTGAGCG GCAGGAGGTGAACGTCCCAGCTGGTGAGACCAGTGTGCGGCTGCGGGGTCTCCGGCCACTGACCGAGTAC CAAGTGACTGTGATTGCCCTCTACGCCAACAGCATCGGGGAGGCTGTGAGCGGGACAGCTCGGACCACTG CCCTAGAAGGGCCGGAAGTACCATCCAGAATACCACAGCCACAGCCTCCTGGTGGCCTGGCGGAGTGT GCCAGGTGCCACTGGCTACCGTGTGACATGGCGGGTCTCAGTGGTGGGCCCACACAGCAGCAGGAGCTG GGCCCTGGGCAGGGTTTCAAGTGTGCTGCGTGACTTGGAGCCTGGCACGGACTATGAGGTGACCGTGAGCA CCCTATTTGGCCGAGTGTGGGGCCCGCACTTCCCTGATGGCTCGCACTGACGCTTCTGTTGAGCAGAC CCTGCGCCCGGTATCTTGGGCCCCACATCCAATCTCTTCTGGAAGTGGTGGCTGAGGCCCCGTGGC TACCGGTTGGAATGGCGGCTGAGACTGGCTTGAGCCACCGCAGAAGGTGGTACTGCCCTCTGATGTGA CCCGCTACCAAGTTGGATGGGTGACAGCCGGGCACTGAGTACCGCCTCACACTCTACACTCTGCTGGAGGG CCACGAGGTGGCCACCCCTGCAACCGTGGTTCCCACTGGACAGAGCTGCCTGTGAGCCCTGTAACAGAC CTGCAAGCCACCGAGCTGCCCGGCGAGCGGTGCGAGTGTCTGGAGCCAGTCCCTGGTGCCACCCAGT ACCGCATCATTGTGCGCAGCACCCAGGGGTTGAGCGGACCCTGGTGTCTTCTGGGAGTCAGACAGCATT CGACTTGGATGACGTTTCAAGCTGGGCTTAGCTACACTGTGCGGGTGTCTGCTCGAGTGGGTCCCCGTGAG GGCAGTGCCAGTGTCTCACTGTCCGCGGGAGCCGAACTCCACTTGCTGTTCCAGGGCTGCGGGTTG TGGTGTGAGATGCAACGCGAGTGAGGGTGGCCIGGGGACCCGTCCTGGAGCCAGTGGATTTCGGATTAG CTGGAGCACAGGCAGTGGTCCGAGTCCAGCCAGACACTGCCCCAGACTCTACTGCCACAGACATCACA GGGCTGCAGCCTGGAACCACTACCAGGTGGCTGTGTCGGTACTGCGAGGCAGAGAGGAGGGCCCTGCTG CAGTCATCGTGGCTCGAACGAGCCACTGGGCCCAGTGAGGACGGTCCATGTGACTCAGGCCAGCAGCTC ATCTGTACCAATTACCTGGACCAGGGTTTCTGGCGCCACAGGATACAGGGTTTCTGGCACTCAGCCCAC GGCCAGAGAAATCCAGTTGGTTTCTGGGGAGGCCACGGTGGCTGAGCTGGATGGACTGGAGCCAGATA			

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ID NO: 17)

Translated protein sequence

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CYP4F3	4051	NM_000896	Homo sapiens cytochrome P450, family 4, subfamily F, polypeptide 3 (CYP4F3), mRNA
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mRNA Sequence

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Translated protein sequence			
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DYSF	8291	NM_003494	Homo sapiens dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive) (DYSF), transcript variant 8, mRNA
mRNA Sequence			
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TCCCCACAGGGTGGCCAGACGATGTGAGCCTACTCAGTCTTGGGGAAGACGTGCTCATCGACATTGATG
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CTGATTGCTCTGCCAGGTGGGCGAGACAGACAGATGGACCGGCCACACTCCAGAGTTGCTAACATGGA
GCTCTGAGATCACCCCACTTCCATCATTTCTTCTCCCCAACCCACGCTTTTTTGGATCAGCTCAGAC
ATATTTCAGTATAAAACAGTTGGAACCACAAAAA (SEQ ID NO: 21)

Translated protein sequence

MLRVFILYAENVHTPDDISDAYCSAVFAGVKKRTKVIKNSVNP
VWNEGFEDWLKGIPLDQGSSELHVVDHETMGRNRLGEAKVPLREVLATPSLSASFN
APLLDTKKQPTGASLVLVQVSYPPLPGAVPLFPPTPLEPSPTLPDLVDVADTGGEDT
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DFQIRVQVIEGRQLPGVNIKPVVKVTAAGQTKRTRIHKGNSPLFNETLFFNLFDSPGE
LFDEPIFITVVDSSRLRDTALLGEFRMDVGTIYREPRHAYLRKWL LLSDDDFDSAGAR
GYLKTSLCVLGPDEAPLERKDPSEDKEDIESNLLRPTGVALRGAHFCLKVFRADLP
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MFPSMCEKMRIRI IDWDR LTHNDIVATTYLSMSKISAPGGEIEEEPAGAVKPSKASDL
DDYLGLFPTFGPCYINLYGSPREFTGFPDPYTELNTGKGEVAYRGRLLSLETKLVE
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DRLEAGLEQVHLALKAQCSTEDVDSLVAQLTDELIAGCSQPLGDIHETPSATHLDQYL
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GSQPSGELLASFE LIQREKPAIHHIPGFVEVQETSRILDESED TDLPPPPQREANIYM
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DPRRPDTSFLWFTSPYKTMKFILWRRFRWAIILFI ILLFLAIFYAFPNYAAMK
LVKPF (SEQ ID NO: 22)

EDIL3	10085	NM_005711	Homo sapiens EGF-like repeats and discoidin I-like domains 3 (EDIL3), mRNA
mRNA Sequence			

AGAAGCCCCGACGCCGCCGCGCGGAGAACAGCGACAGCCGAGCGCCCGGTCCGCTGTCTGCCGGTGGGT
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 GCAGGCAAAAGGGGAGGAAAGGCTCCTCTCTTTAGTCACTCTCGCCCTCTCCAAGAAATTGTTTAAAC
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 GGTGGTAGTTTCCCAGGAAGGCACAGGTGGAGTT (SEQ ID NO: 23)

Translated protein sequence

MKRSVAVWLLVGLSLGVPQFGKGDICDPNPCENGIGICLPGLADG
 SFSCECPDGFDPNCSSVVEVASDEEPTTSAGPCTPNPCHNGGTCEISEAYRGDTFIG
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 PLGIEGGIISNQQITASSTHRALFGLQKWYPYARLNKKGLINAWTAAENDRWPWQI
 NLQRKMRVTGVITQGAKRIGSPEYIKSYKIAYSNDGKTWAMYKVKGTTNEDMVFRGNID
 NNTPYANSFTPIKAQYVRLYPQVCRRHCTLRMELLGCELSGCSEPLGMKSGHIQDYQ
 ITASSIFRTLNMDFTWEPKARLDKQKVNAWTSGHNDQSQWLQVDLLVPTKVTGII
 TQGAQDFGHVQFVGSYKLAYSNDGEHWTVYQDEKQRKDKVFQGNFNDTHRKNVIDPP
 IYARHIRILPWSWYGRITLRSELLGCTEEE (SEQ ID NO: 24)

ERGIC3	51614	NM_015966	Homo sapiens ERGIC and golgi 3 (ERGIC3), transcript variant 2, mRNA
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mRNA Sequence

GTGGCTCCAGGCCGGAAGAGGGAGTCTGTAGGGGCGGGCCGGCTGGCGTCCCTTTCCGGCCGGTCCCCA

<p>TGGAGGCGCTGGGGAAGCTGAAGCAGTTTCATGCGCTACCCCAAGACTTTGGAGGACTTCCGGGTCAAGAC CTGCGGGGGCGCCACCGTGACCATTTGTCAGTGGCCTTCTCATGCTGCTACTGTTTCTGTCCGAGCTGCAG TATTACCTCACCACGGAGGTGCATCCTGAGCTCTACGTGGACAAGTCGCGGGGAGATAAACTGAAGATCA ACATCGATGTACTTTTTCCGCACATGCCTTGTGCTATCTGAGTATTGATGCCATGGATGTGGCCGGAGA ACAGCAGCTGGATGTGGAACACAACCTGTTCAAGCAACGACTAGATAAAGATGGCATCCCCGTGAGCTCA GAGGCTGAGCGGCATGAGCTTGGGAAAGTCGAGGTGACGGTGTGTTGACCCTGACTCCCTGGACCCTGATC GCTGTGAGAGCTGCTATGGTGTGAGGCAGAAGATATCAAGTGTGTAACACCTGTGAAGATGTGCGGGA GGCATATCGCCGTAGAGGCTGGGCCTTCAAGAACCCAGATACTATTGAGCAGTGCCGGCGAGAGGGCTTC AGCCAGAAGATGCAGGAGCAGAAGAATGAAGGCTGCCAGGTGTATGGCTTCTTGAAGTCAATAAGGTGG CCGGAAACTTCCACTTTGCCCTGGGAAGAGCTTCCAGCAGTCCCATGTGCACGTCCATGACTTGCAGAG CTTTGGCCTTGACAACATCAACATGACCCACTACATCCAGCACCTGTCAATTTGGGGAGGACTATCCAGGC ATTGTGAACCCCTGGACCACACCAATGTACATGCGCCCAAGCCTCCATGATGTTCCAGTACTTTGTGA AGGTGGTGGCCACTGTGTACATGAAGGTGGACGGAGAGGTACTGAGGACAAATCAGTTCTCTGTGACCAG ACATGAGAAGGTTGCCAATGGGCTGTGGGCGACCAAGGCCTTCCCGGAGTCTTCGTCTCTATGAGCTC TCGCCCATGATGGTGAAGCTGACGGAGAAGCACAGGTCTTACCCACTTCCTGACAGGTGTGTGCGCCA TCATTGGGGGCATGTTACAGTGGCTGGACTCATCGATTGCTCATCTACCACTCAGCACGAGCCATCCA GAAGAAAATTGATCTAGGGAAGACAACGTAGTCACCCCTCGGTGCTTCCTCTGTCTCTCTTTCTCCCTGG CCTGTGTTGTCCCCAGCCTCTGCCACCTCCACCTCCTCGGTGAGCCCCAGCCCCAGGTTGATAAATC TATTGATTGATTGTGATAGTAAAAAAAAAAAAAAAA (SEQ ID NO: 25)</p>			
Translated protein sequence			
<p>MEALGKLGKQFDAYPKTLEDFRVKTCGGATVTIVSGLLMLLLFLS ELQYYLTTEVHPELYVDKSRGDKLKINIDVLFPHMPCAYLSIDAMDVAGEQQLDVEHN LFFKQRLDKDGIPVSSEAERHELKGVEVTVFDPDSLDPDRCESCYGAEAEEDIKCCNTCE DVREAYRRRGWAFKNPDTIEQCRREGFSQKMQEKNNEGCQVYGFLEVNVKVGAFNFHAP GKSFQQSHVHVHDLQSFGLDNINMTHYIQHLSFGEDYPGIVNPLDHTNVTAPQASMMF QYFVKVVPVYMKVDGEVLRNQFSVTRHEKVANGLLGQGLPGVFVLYELSPMMVKL TEKHRSFTHFLTGVCAIIGGMFTVAGLIDSLIYHSARAIQKKIDLGKTT (SEQ ID NO: 26)</p>			
GNAT1	2779	NM_000172	Homo sapiens guanine nucleotide binding protein (G protein), alpha transducing activity polypeptide 1 (GNAT1), transcript variant 2, mRNA
mRNA Sequence			
<p>AGTTGATTGCAGGTCCTCCTGGGGCCAGAAGGTTGCTGGGAGGCCAGGTTCTGGGGATCCCCCTCCATCC AGAAGAACCACCTGCTCACTCTGTCCCTTCGCCCTGCTGCTGGGACCATGGGGGCTGGGGCCAGTGCTGAG GAGAAGCACTCCAGGGAGCTGGAAAAGAAGCTGAAAGAGGACGCTGAGAAGGATGCTCGAACCGTGAAGC TGCTGCTTCTGGGTGCGGTGAGTCCGGGAAGAGCACCATCGTCAAGCAGATGAAGATTATCCACCAGGA CGGGTACTCGCTGGAAGAGTGCTCGAGTTTATCGCCATCATCTACGGCAACACGTTGCAGTCCATCCTG GCCATCGTACGCGCCATGACCACACTCAACATCCAGTACGGAGACTCTGCACGCCAGGACGACGCCCCGA AGCTGATGCACATGGCAGACACTATCGAGGAGGGCAGATGCCAAGGAGATGTGGACATCATCCAGCG GCTGTGGAAGGACTCCGGTATCCAGGCCCTGTTTGTAGCGCGCCTCGGAGTACCAGCTCAACGACTCGGCG GGCTACTACCTCTCCGACCTGGAGCGCCTGGTAACCCCGGGCTACGTGCCACCCAGCAGGACGTGCTGC GCTCGCGAGTCAAGACCACTGGCATCATCGAGACGCAAGTCTCCTTCAAGGATCTCAACTCCCGGAIGTT CGATGTGGGCGGGCAGCGCTCGGAGCGCAAGAAGTGGATCCACTGCTTCGAGGGCGTGACCTGCATCATC TTCATCGCGGCGCTGAGCGCTACGACATGGTGTAGTGGAGGACGACGAAGTGAACCGCATGCACGAGA GCCTGCACCTGTTCAACAGCATCTGCAACCACCGCTACTTCGCCACGACGTCCATCGTCTCTTCTTAA CAAGAAGGACGTCTTCTTCGAGAAGATCAAGAAGGCGCACCTCAGCATCTGTTTCCCGGACTACGATGGA CCCAACACCTACGAGGACGCCGGCAACTACATCAAGGTGCAGTTCTCGAGCTCAACATGCGGCGCGACG TGAAGGAGATCTATTCCACATGACGTGCGCCACCGACACGCAGAACGTCAAATTTGTCTTCGACGCTGT CACCGACATCATCAAGGAGAACCCTCAAAGACTGTGGCCTCTTCTGAGGCCAGGGCCTGTGCTGCAGT CGGGGACAAGGAGCTTCCGTCTGGCAAGGCCGGGGCACAATTTGCATCCCCCTCAGCTAGACGCACAGAC TCAGCAATAAACCTTTGCATCAGGCTCCAGCTGTCTTCTTGGTGGAGGACTTAATTATCACAAGTCAT GGGCATTTATTAAGTGCCCAAGTGCTGGGTTGGGCATGAAGTGGGAAGATGGCCCCCTCCAGGAAGAAGTA CCTGGCCTGACAAGGTGGGGCACTCTTGGGGGTATGGGACCAACTCATGGCTTTTTCACGGGAGTTGAGGA GAGAGGAGCTGTGGAATAATTTACTGGGACAGTCTTGATCAAGAGGGAGTTTGTAGGTGGAGGCTCAT TCTGGCAGGGACCGTAGTGTCTACCAGCCCCAGAAACATGGGCTTATGGCCACAGGAGTTCAGTGGAGCA AGAGCAGGGGAGGAGAGACGTGGACAGGTGCCAAAGCCAGTCGGAGGGCCTGGGCTTTCTCAGAAGGTG ATGGAGAGTCTTGAAGCCCTCGAGGCAGGAACATAATTGCAGGGCTGGGATTAGGTTGAGGGAAGTGAG</p>			

GCACACTCACCTTGGGTGCAACATTTAAGGCGATGCCAAAAAATTTAGTAACCAAGGTAAATAATATTAG GATAATATTTTTAAAAATCAAAATGAATGCAAAACCCACAATGAATGAAATATCAAAATCCAACAGAGGA TCAAACAGAGGCATGCTAAGATATATTGGGGCTTGAAGCAAAGGGAAAACATTTTGTGCTATATGTTTG TAGGGATTTTTTGCCAGTTTTAAAAATACATGTAATCAAAAGTTTACTATCTCAGCCACTTGCCGGIGTA TAGTTTGGTGGTGTTAAGTACATTCTAATGTTGTACAACCACCGCAACTGTTTCATCTCCAGAACTCCTT TCCTCTTGTAACACTGTAACCTCTGTACCCATGAAAAATAACCCCCATTCCTGCCTTCCCCCGGCTCCT GGCATCCACCATTCTACTTTCCATCTCTATGAATGTGACTGCTCTAAGTGCCTCAGATGTGTGGGTCCAT GAAGTCTTTGTCTTTTTGCAACTGGCTTATTTCACTTAGCATCATGTCTTCAAGGTTTATTCATGTGTAG CATATGGCAGAATCTCCTTCTTTTAAAGGTTGAATAATATTCATTGTATATATTCACACTTTGTTTA TTTATTCATCTATTGATGAATGGTTACATCTGCCTTTTGGCTATTGTGAATAATGCTGCTATGAACATGG GTGTACAAATCTCTCAAAAAAAAAAAAAAAAAA (SEQ ID NO: 27)			
Translated protein sequence			
MGAGASAEKHSRELEKKLKEDAEDARTVKLLLLLGAGESGKST IVKQMKIIHQDGYSLEECLEFIAIIYGNLQSLAIVRAMTTLNIQYGDSARQDDARK LMHMADTIEEGTMPKEMSDIIQRLWKDSGIQACFERASEYQLNDSAGYYLSDLERLVT PGYVPTQDVLRSRVKTTGIIETQFSFKDLNFRMFDVGGQRSEKRWIHCFEQVTCII FIAALSAYDMVLVEDDEVNRMHESLHLFNSICNHRFYFATTSIVLFLNKKDVFFEKIKK AHLSCIFPDYDGPNTYEDAGNYIKVQFLELNMRDVKIYSHMTCATDTQNVKFVFDA VTDIIEKENLKDCLF (SEQ ID NO: 28)			
GRAMD4	23151	NM_015124	Homo sapiens GRAM domain containing 4 (GRAMD4), mRNA
mRNA Sequence			
CGTCATGTTAGGGTGAAGCAGAGGACCTCAGTGTCTGAACATGCTAAGGAGGTTGGACAAAAATCAGGTTCA GAGGTCACAAGAGAGATGACTTCCTCGATCTAGCGGAGTCTCCAAATGCCTCGGACACCGAATGCAGCGA CGAAATCCCCCTGAAGGTACCGCGGACCTCGCCCCGGGACAGCGAGGAGCTGAGGGACCTGCTGGTCCA GGGACCCTCATCATGGCCACAGGAGTCCAGGACTTTAACCGGACAGAGTTTGATCGACTGAATGAGATCA AAGGTCACCTGGAATTTGCCTTATTGGAACAACTTTCTTACAGGAGGAGCTCCGGAAGCTGCGAGAAGA AACCAACGCGGAGATGCTGCGGCAGGAGCTGGACCGCGAGCGGCAGCGGCGGATGGAGCTGGAGCAGAAG GTGCAGGAGGTGCTGAAGGCCAGAACCGAGGAGCAGATGGCTCAGCAGCCCCAAAAGGGCAGGCCCAGG CCAGCAATGGAGCAGAGCGCCGAGCCAGGGGCTGTCTCGCGCTGCAGAAGTGTTCTACGAGCGGTT CGGGGAGTACGTGGAGGACTTCCGGTTCAGCCCGAGGAGAACACTGTGGAGACAGAGGAACCCCTGAGC GCCCCAGGTTAACTGAAAAATGAGACGGCTCAAGCGCGGTGCCAAGCCGGTCACTAATTTGTGAAGA ACCTCTCTGCCTTATCCGACTGGTACTCCGCTACACGCTCGCCATTGCCTTACCCGTGTACATGAATGC CGTGTGGCATGGCTGGGCCATCCCATTTGTTCTTATTCTAGCAATTTCTGAGGTTATCCCTCAATTACCTC ATCGCCAGGGGGTGGCGGATACAGTGGAGCATCGTGCCCAAGTGTCTGAGCCCGTGGAACCTCCAAAGG AAGACCTGACTGTGTCTGAGAAGTTCAGCTGGTGTGAGCGTCGCCAGAAAGCCCAGAACCTTTTCGG GAAGATGGCTGACATCTTGAGAAGATCAAGAACTTGTTTCATGTGGGTCCAGCCGGAGATCACACAGAAG CTGTATGTGGCGCTCTGGGCTGCCTTCTGGCTCTCTGCTTCTTCCCTACCGCTTGGTGGGGCTTGCCG TGGGACTCTATGCTGGTATCAAGTTCTTCTCATTGATTTTCATCTTTAAACGCTGCCCCGAGGCTGCGCGC CAAGTACGACACGCCCTATATCATCTGGAGGAGTCTCCCCACCGACCCGAGCTCAAGGAGCGCTCCAGC GCCGAGTCTACGCAGGCTGCAGACGACCTCGTACCGGAGCTACGTACCCAGCGCACCGGCCCGGCTGG GTAAAGAGGAGGACGCCGGTCTGCTTCCACAGCACCAAGAAGGGCAATTCCACGAGATCTTCAATCTGAC AGAAAACGAGCGTCCGCTGGCGGTGTGCGAGAATGGCTGGCGCTGTGCCTCATCAACAGGGACCGGAAG ATGCCACGGACTACATCAGGAACGGGGTGCTCTACGTCACGGAGAATTACTTGTGCTTCGAAAAGCTCCA AATCTGGGTCTCAGAGAGGAACAAAGTCATCAAGCTAGTGGACATCACGGACATCCAGAAGTACAAGGT CCTGTCTGTCTCCAGGCTCAGGCATGGGGATTGCCGTGTGACGCCATCCACCCAGAAACCGCTCGTG TTTGGTGCCATGGTGCACAGGGATGAGGCCTTCGAGACCATTTCTAGCCAGTACATCAAGATCACTCAG CGGCAGCGTCTGGCGGGGACAGCTAGTATTGACTTGCCAGGACGTTGCTGGAATTTTCTTTTCTTTT CTTTTCTTTTCTTTTACGATTTGGTAGTGAAACAATTGGACATCTCATGAGCTTTTGCAATAA TTCTCCTGGACCTGTGGTTCTATTGTGTGACCTCTGCGTTTTATCGACCAAGAAGGGGCCAGGGCTCAC AGGGACGGGGGTGCCCCCTCTCCACAGGGCACGTCAAGTGCCTCTGAGGGCCACCCGAGACTGGGGGAG GGGGCAGAGGCCCTCGGGGGCCCCGTGGAGAAGACACACAGGACCCCTGGCCCTGCCCTTCTCCGTTCCAG CCTGGACAGAGAAACCTCTCCAGCCACCCCAAGAGGTTCTCGCAACCTTGTGTCCCGCTCTCCAGAGGCC AGAAGCTCGTCCACCACCAAGCCATAGCTGAAGAGTGCAGGGGCCCTTCTCTCTGGGGACAGAAAGATGT CGTCAAGGAGGGACATGGGGGCTTTCACCAACCACCGAGAAACGGGCTGGCGGCCCTCCTTCTCTTA CATGAGACCCTCCTGTGGCATTGCCCCTTGGTGCAGGGCTGGGGCCGGGCGAGTGACCTGCTGCGCT CCACACTCGCTCCACGGGAACAGAGAGGGTGAGAAGGGCCACCCCTCGCTGCTCTCAGTGTCTTTGGT			

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 TGAACCCACCTTGGCGCTGAGGCAACACAGGTGGGCACTGACCCACCCCGAGGGCGGCTGCAGAGG
 CAGTCCCCGACACAATGGCCACACCTCTCTCCCCAGGGCCCGGCAGTGCCCAAGGATGGGTCCGGGGCC
 TCGGGGCAATGAGCGCTCTCTCCTAGGTGCTGGGATTGAGTCCCCAAACACAGCGGGAGGGGTCCCTGG
 GGCAGATGGGGCTTTACCAGCGTCGGGTGGTTTGTTCGAGTCCCTTTGTGGAGAAAGGAGATGAAAA
 CTGACCACGTGCCAGGTGTGGCCGAAGCCCCAGGGAGGGCCACATTGCGGGGAGCGGGGGTCTGGGGGAG
 GGCCACCGACTGGCTCTGCTGCCAGCACAGGCCCTCCCTGGAAGTCTCGGGAGCGGAGCGCGGATCGG
 CACGGGCTCTGGGCTCCCCGTGGAGAGAAGCTGTAGTTTTTACCAAATTGTGTACATCTGGGCAGATGTT
 TAATTTCTGTGACTAATCACTGAAGTAGACGAATGTAAATTTTTTATGTCTGAAGCCTGAGTCTATTTT
 GGATCTGTAAATAATCATTGCCAGTGTGACTTTTGTTCACAAAAGGATGTACTGTATTAAGAACCGAT
 GAAAAAATCTCCTGTAAACATTTTTTAAGAAAACCTTTGTTTGTAAAGAAAAAGTATTGTATAAATT
 ATAATTTTTATTAAATAAACCTAAATGCTTTGTGCTAAGGCTCAAAAAAAAAAAAAAAAAAAAAA (SEQ ID

NO: 29)

Translated protein sequence

MLRRLDKIRFRGHKRDDFLDLAESPNASDTECSDEIPLKVPRTS
 PRDSEELRDPAGPGTILIMATGVQDFNRTEFDRLNEIKGHLEIALLEKHFLQEELRKLK
 EETNAEMLRQELDRERQRMELEQKVQEVVKARTEEQMAQQPPKGQAQASNGAERSQ
 GLSSRLQKWFYERFGEYVEDFRFQPEENTVETEEPLSARRLTENMRRLKRGAKPVTNF
 VKNLSALSDWYSVYTSIAIAFTVYMNNAVHGWAIPLFLFLAILRLSLNYLIARGWRIQW
 SIVPEVSEPEPPKEDLTVEKFLVLVDVAQKAQNLFKGMADILEKIKNLFMWVQPEI
 TQKLYVALWAAFLASCFFPYRLVGLAVGLYAGIKFFLIDFIFKRCPRLRKYDTPYII
 WRSPLTDPQLKERSAAVSRRLQTTSSRSYVPSAPAGLGKEEDAGRFHSTKKGNFHEI
 FNLTENERPLAVCENGWRCCLINRDRKMPTDYIRNGVLYVTENYLCFESSKSGSSKRN
 KVIKLVDTIDIQYKVLVSLPGSGMGIIVSTPSTQKPLVFGAMVHRDEAFETILSQYI
 KITSAAASGGDS (SEQ ID NO: 30)

HYAL2	8692	NM_003773	Homo sapiens hyaluronoglucosaminidase 2 (HYAL2), transcript variant 1, mRNA
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mRNA Sequence

TTTCTCTCAGGGGCGAGCAGGAAGTGAGGAGAAAGGGCTGGGATGGGAGGCGGGAGCGGATGGGAGGGA
 ATGGGGTTTATCAAGTCTCGGCGAGCTGCCCCACGGGCGAGCAGCTGGCGCAAGTAGCTAGCTGGAGAG
 GCTACCCCGAGGAAGGAGGGAGGCCACCGACCTACTGGGCGGACGGACTCCACACAGTTCTGAGCTGG
 TGCCAGGCAGGTGACACCTCTGCAGCCCCAGCATGCGGGCAGGCCCAGGCCCCACCGTTACATTGGCC
 CTGGTGTCTGGCGGTGTCTATGGGCCATGGAGCTCAAGCCACAGCACCACCCATCTTCACTGGCCGGCCCT
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 CTTTGATGTGCAGGCCTCACCTAATGAGGGTTTTGTGAACCAGAATATTACCATCTTCTACCGCGACCGT
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 TTTGGGCACACCGGAAGATGCTGCAGAAACGTGTGGAGCACTACATTCGGACACAGGAGTCTGCGGGGCT
 GGCGGTATCGACTGGGAGGACTGGCGACCTGTGTGGGTGCGCAACTGGCAGGACAAAGATGTGTATCGC
 CGGTTATCACGCCAGCTAGTGGCCAGTCGTACCCCTGACTGGCCTCCAGACCGCATAGTCAAACAGGCAC
 AATATGAGTTTGTAGTTCGCAGCACAGCAGTTTCATGCTGGAGACACTGCGTTATGTCAAGGCAGTGGCGCC
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 TACACAGGCCGCTGCCCTGATGTTGAGGTGGCCCGCAATGACCAGCTGGCTGGCTGTGGGCTGAGAGCA

CGGCCCTCTTCCCGTCTGTCTACCTGGACGAGACACTTGCTTCCCTCCCGCCATGGCCGCAACTTTGTGAG CTTCCGTGTTTCAGGAGGCCCTTCGTGTGGCTCGCACCCACCATGCCAACCATGCACTCCCAGTCTACGTC TTCACACGACCCACCTACAGCCGAGGCTCACGGGGCTTAGTGAGATGGACCTCATCTCTACCATTTGGCG AGAGTGCAGGCCCTGGGCGCAGCTGGTGTATCCTCTGGGGTGACGCGGGGTACACCACAAGCACGGAGAC CTGCCAGTACCTCAAAGATTACCTGACACGGCTGCTGGTCCCCCTACGTGGTCAATGTGTCTGGGCCACC CAATATTGCAGCCGGGCCCCAGTGCCATGGCCAATGGGCGCTGTGTGCGCCGCAACCCCCAGTGCCAGTACCT TCCTGCATCTCAGCACCAACAGTTTCCGCCTAGTGCCTGGCCATGCACCTGGTGAACCCAGCTGCGACC TGTGGGGGAGCTCAGTTGGGCGGACATTGACCACCTGCAGACACACTTCCGCTGCCAGTGCTACTTGGGC TGGAGTGGTGAGCAATGCCAGTGGGACCATAGGCAGGCAGCTGGAGGTGCCAGCGAGGCCCTGGGCTGGGT CCCACCTACCAGTCTGCTGGCTCTGGCAGCCCTGGCCTTTACCTGGACCTGTAGGGGTCTCTGCCTA GCTGCCTAGCAAGCTGGCCTCTACCACAAGGGCTCTCTTAGGCATGTAGGACCCTGCAGGGGTGGACAA ACTGGAGTCTGGAGTGGGCAGAGCCCCAGGAAGCCAGGAGGGCATCCATACCAGCTCGCACCCCCCTG TTCTAAGGGGGAGGGGAAGTCCCTGGGAGGCCCTTCTCTCCCTGCCAGAGGGGAAGGAGGTACAGCTG GGCTGGGAGGACCTGACCCTACTCCCTTGCCCTAGATAGTTTATTATTATTATTATTTGGGGTCTCTT TTGTAAATTAACATAAAACAATTGCTTCTCTGCTTGGATTTGT (SEQ ID NO: 31)			
Translated protein sequence			
MRAGPGPTVTLALVLAVSWAMELKPTAPPIFTGRPFVVAWDVPT QDCGPRLKVPLDLNADFVQASPNEGFVNQNIIFYRDLRLGLYPRFDSAGRSVHGGVPQ NVSLWAHRKMLQKRVEHYIRTQESAGLAVIDWEDWRPVWVRNWQDKDVYRRLSRQLVA SRHPDWPPDRIVKQAQYEFEEFAAQFMLETIRYKAVRPRHLWGFYLPDCYNHDYVQ NWESYTGRCPDVEVARNDQLAWLWAEALFSPVYLDETLASSRHGRNFSFRVQEAL RVARTHHANHALPVYVFTRPYSRRLTGLSEMDLISTIGESAALGAAGVILWGDAGYT TSTETCQYLKDYLTRLLVPYVNVSWATQYCSRAQCHGHGRCVRRNPSASTFLHLSTN SFRLVPGHAPGEPQLRPVGELSWADIDHLQTHFRQCQYLGWSGEQCQWDHRQAAGGAS EAWAGSHLTSLLALAALAFWTWL (SEQ ID NO: 32)			
IL10	3586	NM_000572	Homo sapiens interleukin 10 (IL10), mRNA
mRNA Sequence			
ACACATCAGGGGCTTGCTCTTGCAAAACCAAAACCACAAGACAGACTTGCAAAAGAAGGCATGCACAGCTC AGCACTGCTCTGTTGCCTGGTCTCTGACTGGGGTGAGGGCCAGCCAGGCCAGGGCACCCAGTCTGAG AACAGCTGCACCCACTTCCCAGGCAACCTGCCAACATGCTTCGAGATCTCCGAGATGCCCTCAGCAGAG TGAAGACTTTCTTTCAAATGAAGGATCAGCTGGACAACCTGTTGTTAAAGGAGTCCTTGCTGGAGGACTT TAAGGGTTACCTGGGTTGCCAAGCCTTGCTGAGATGATCCAGTTTTACCTGGAGGAGGTGATGCCCCAA GCTGAGAACCAAGACCCAGACATCAAGGCGCATGTGAACCTCCCTGGGGGAGAACCTGAAGACCCTCAGGC TGAGGCTACGGCGCTGTCATCGATTTCTTCCCTGTGAAAACAAGAGCAAGGCCGTGGAGCAGGTGAAGAA TGCCTTTAATAAGCTCCAAGAGAAAGGCATCTACAAAGCCATGAGTGAGTTTGACATCTTCATCAACTAC ATAGAAGCTACATGACAAATGAAGATACGAACTGAGACATCAGGCTGGCGACTCTATAGACTCTAGGAC ATAAATTAGAGGTCTCCAAAATCGGATCTGGGGCTCTGGGATAGCTGACCCAGCCCCCTTGAGAAACCTTA TTGTACCTCTCTTATAGAATATTTATTACCTCIGATACCTCAACCCCATTTCTATTTATTTACTGAGCT TCTCTGTGAACGATTTAGAAAAGAGCCCAATATTATAATTTTTTTCAATATTTATTTTACCTGTTT TTAAGCTGTTTCCATAGGGTGACACACTATGGTATTTGAGTGTTTTAAGATAAATTATAAGTTACATAAG GGAGGAAAAAAATGTTCTTTGGGGAGCCAACAGAAGCTTCCATTCCAAGCCTGACCACGCTTTCTAGCT GTTGAGCTGTTTTCCCTGACCTCCCTCTAATTTATCTTGCTCTGCGGCTTGGGGCTTCCTAAGTCTACA AATACTCTTAGGAAGAGAAACCAGGGAGCCCCCTTTGATGATTAATTCACCTTCCAGTGTCTCGGAGGGAT TCCCCTAACCTCATTCCCCAACCACTTCATTCTTGAAAAGCTGTGGCCAGCTTGTTATTTATAACAACCTA AATTTGGTTCTAGGCCGGGCGCGGTGGCTCACGCTGTAATCCCAGCACTTTGGGAGGCTGAGGCGGGTG GATCACTTGAGGTGAGGAGTTCCTAACCCAGCTGGTCAACATGGTGAAACCCCGTCTCTACTAAAAATAC AAAAATTAGCCGGGCATGGTGGCGCGCACCTGTAAATCCAGCTACTTGGGAGGCTGAGGCAAGAGAATTG CTTGAACCCAGGAGATGGAAGTTGCAGTGAGCIGATATCATGCCCTGTACTCCAGCTGGGTGACAGAG CAAGACTCTGTCTCAAAAAATAAAAAATAAAATTTGGTTCTAATAGAAGTCAAGTTTAACTAGAAT TTATTCATCTCTCTGGGAATGTTACATTGTTTGTCTGTCTTCATAGCAGATTTTAATTTGAATAAATA AATGTATCTTATTCACATC (SEQ ID NO: 33)			
Translated protein sequence			
MHSSALLCCLVLLTGVRASPGQGTQSENSCTHFPGNLNPMLRDL RDAFSRVKTFQMKDQLDNLKESLLEDFKGYLGCAQALSEMIQFYLEEVMPOAENQD PDIKAHVNSLGENLKLRLRLRRCHRFLPCENKSKAVEQVKNFNLQEKGIYKAMSE FDIFINYIEAYMTMKIRN (SEQ ID NO: 34)			

ITFG3	83986	NM_032039	Homo sapiens integrin alpha FG-GAP repeat containing 3 (ITFG3), mRNA
mRNA Sequence			
AGTGACGCCAGGGGGCGGGGCCAGCGGCGCGGTTCGGGTGAGAGGCCGCGGCGGCAGGTCCACCTGGGCTT GCGAAGGCACAGATTCCCCGTCCACAGCTCACGACCAGATGCACCAGCAGGAGTCCACATCGAGGACGTC CTCCGGGCACTCCCACGACCAGTGACCAGGAGTTAAACTTTGGGATGTGCCCGTGATGTTGGACCACAAG GACTTAGAGGCCGAAATCCACCCCTTGAAAAATGAAGAAAGAAAATCGCAGGAAAATCTGGGAAATCCAT CAAAAAATGAGGATAACGTGAAAAGCGCGCCTCCACAGTCCCGGCTCTCCCGGTGCCGAGCGGCGGCGTT TTTTCTTTTCATTGTTTCTCTGCCTTTTTGTGGTGTTCGTCTCATTCGTCTATCCCGTGTCCAGACCGG CCGGCGTCACAGCGAATGTGGAGGATAGACTACAGTGCCGCTGTTATCTATGACTTTCTGGCTGTGGATG ATATAAACGGGGACAGGATCCAAGATGTTCTTTTCTTTATAAAAAACCAACAGCAGCAACAATTTTCAG CCGATCCTGTGTGGACGAAGGCTTTTCTCTCCCTGCACCTTTGCAGCTGCTGTGTGCGGGGCCAACGGC AGCACGCTCTGGGAGAGACCTGTGGCCCAAGACGTGGCCCTCGTGGAGTGTGCTGTGCCCCAGCCAAGAG GCAGTGAGGCACCTTCTGCCTGCATCCTGGTGGGCAGACCCAGTTCTTTCATTGCAGTCACTTGTTCAC AGGGGAAACCCTGTGGAACCACAGCAGCAGCTTCAGCGGGAATGCGTCCATCCTGAGCCCTCTGCTGCAG GTGCCTGATGTGGACGGCGATGGGGCCCCAGACCTGCTGGTTCTCAGCCAGGAGCGGGAGGAGGTTAGTG GCCACCTCTACTCCGGCAGCACCGGGCACCAGATTGGCCTCAGAGGCAGCCTTGGTGTGGACGGGAAAG TGGCTTCTCTTTCACGTCACCAGGACAGGTGCCCACTACATCCTCTTTCCCTGCGCAAGCTCCCTCTGC GGCTGCTCTGTGAAGGCTCTTACGAGAAGGTGACCGGGAGCGGCGGCCGTTCAAGAGTGACCCGCACT GGGAGAGCATGCTCAATGCCACCACCCGCAGGATGCTTTCCACAGCTCTGGAGCAGTGCCTACCTGAT GCATGTCCCAGGGAACGCCGGTGCAGATGTGCTTCTGTGGGCTCAGAGCCCTTCGTGCTGCTGGACGGG CAGGAGCTGACGCTCGCTGGACACCCAGGCAGCCATGTCTTGAGAAAACCCATCTTCGCGCCGTACA AACCAGACACCTTGGCTGTAGCCGTTGAAAACGGAACCTGGCACCGACAGACAGATCCTGTTTCTGGACCT TGGCACTGGAGCCGTCCTGTGTAGCCTAGCCCTCCCGAGCCTCCCTGGGGGTCCACTGTCCGCCAGCCTG CCGACCGCAGACCACCGCTCAGCCTTCTTCTTCTGGGGCTCCACGAGCTGGGGAGCACCAGCGAGACGG AGACCGGGGAGGCCCCGGCACAGCCTGTACATGTTCCACCCACCCGCGCGCTGCTGCTGGAGCTGGC CAATGTCTCTACCCACATTGTCGCTTTGACGCCGCTCTGTTTGGCCAAGCCGCCACGCCGCTACATC CTTCTGACAGGCCCGGCAGACTCAGAGGCACCCGGCCTGGTCTCTGTGATCAAGCACAGGTGCGGGACC TTGTCCCAAGCAGCAGGGTGGTCCGCTGGGTGAGGTGGGCCAGACAGTGACCAAGCCATCAGGGACCG GTTCTCCCGCTGCGGTACCAGAGTGAGGCGTAGAGGCACGCCAGCCAGAGCCTGTGGAGAGACTCCGCC TGCTGACACTAAACGTCCTGGGAAGTGGGCCCTTCCCTGGGTCTCTGCACTGACTCCCCACTCCTGACC CTGGTGATGGTGCCTACTGGGCAGCAGCAGCCTTACCAGTCTCCATGATCACACCCAGGGACCTGCATG GGTGAGGGGACACCCGCGCTCTCTCCCGCCAGCATCCTCCCTGAGTCCCCACACAGGGCCTCACTCT GCACCCACACAGGGTCCCGCTCACACCAGGCAGCCTTCATAGTGGTCTCCCTGGCCACCTTGGGCAGAGC TGGGTGATGCAGCACCCATCCTTACCCGGTGCCCTCTCCTTGCCAGCTCTCTCCCGAGCCAGAGCGGCC ATCGCGTAGAAAGAACCAGGGTGTCCCGGGACAGGCCGCTCCCCACCCATCCTGTAGAAGTCCATTCC CCTTTTCCCTCTGTGCTCTGTCCCCAAGGAGTCATGGAACCTCAGGGTACTGGGCCCAACGGGAACCT GAGACAGCTCCAGCTTCGAGCCCTTCCCGGAGCTACAGGGGATCCTCTAGCATGGGGGTGTGACTTG GTTCTTTGACCAGGTCTGTGAGGAAGCCTGGAGCAAGGCTCTCCCCAGCAGGATGGGTGGGGCCTGC TCTGGAGCTGAGCCCGTGGCCGCTCAGAGGTGCTCTAGTGGTGTGTCAGCTGTCTACTGGCTGCAITG CTGTGAATATCCCAAGGAACCTGGCTGTGGAATGCGTGTGTTGGGTGAGTCTGTGCCCTCTCAGTAGACACT GGAGCTGCTCTGTCCCTGAAGAGGCCCGTGGCCAGGCATGGCAAGCGCTGCCTCTCCCTTCCGGTG CTCACACGCCCCAGCGGTGCCACCCGATGCAGGACTCACTCTGTGCCTTGCTGCTCCTGAGGCCCAAGG GCAGCCATGGTGTCTGTACTGCTCGGGCCGCCAGGTACAGAGCCTGAGCTTCTGTAGCCAAAGCAGCC TGATGACCCACCCACCAAGGAAGAAAGCAGAATAAACATTTTTGCACTGCCTGAAAAACCCCGGTGGTCA GGCGTGAGCCTAAAAA (SEQ ID NO: 35)			
Translated protein sequence			
MLDHKDLEAEIHPLKNEERKSQENLGNPSKNEENVKSAPPQSRL SRCRAAAFFLSLFLCLFVVFVSVFVPCPDRPASQRMWRIDYSAAVIYDFLAVDDING DRIQDVLFLYKNTNSSNFSRSCVDEGFSSPCTFAAAVSGANGSTLWERPVAQDVALV ECAVPQPRGSEAPSACILVGRPSSFIQVNLFTGFTLWNHSSFSGNASILSPLLQVPD VDGDGAPDLLVLTQEREVSGHLYSGSTGHQIGLRGSLGVDGESGFLHVTRTGAHYI LFPCASSLCGCSVKGLYEKVTGSGGPFKSDPHWESMLNATTRMLSHSSGAVRYLMHV PGNAGADVLLVGSEAFVLLDGQELTPRWTPKAAHVLRKPIFGRYKPDTLAVAVENG TG TDRQILFLDLGTGAVLCSLALPSLPGGPLSASLPTADHRSAFFFWGLHELGSTSETET GEARHSLYMFHTLPRVLELANVSTHIVAFDAVLFEPSRHAAYILLTGFPADSEAPGL VSVIKHKVRDLVPSSRVVRLGEGGPDSDQAIRDFRSRLRYQSEA (SEQ ID NO: 36)			

JAM3	83700	NM_032801	Homo sapiens junctional adhesion molecule 3 (JAM3), mRNA
mRNA Sequence			
<p> TAGACCTCAGCTTCCTCTGTCACCATGGTGCCGGCTCGGCTGGGCCCCGGCGGTCGCCATGGTAACTGGGG CGGGTCGCAGGGTCCTGGCAGGCTGGGCGCATGCGCGCGGGGACTACAAGCCGCGCCGCGCTGCCGCTGG CCCCCTCAGCAACCCTCGACATGGCGCTGAGGCGGCCACCGCGACTCCGGCTCTGCGCTCGGCTGCCTGAC TTCTTCTGCTGCTGCTTTTCAGGGGCTGCCTGATAGGGGCTGTAAATCTCAAATCCAGCAATCGAACCC CAGTGGTACAGGAATTTGAAAGTGTGGAACGTCTTGCATCATTACGGATTTCGAGACAAGTGACCCAG GATCGAGTGAAGAAAATTCAAGATGAACAAACCACATATGTGTTTTTTGACAACAAAATTCAGGGAGAC TTGGCGGGTTCGTGCAGAAATACTGGGAAGACATCCCTGAAGATCTGGAATGTGACACGGAGAGACTCAG CCCTTTATCGCTGTGAGGTCGTGCTCGAAATGACCGCAAGGAAATTGATGAGATTGTGATCGAGTTAAC TGTGCAAGTGAAGCCAGTGACCCCTGTCTGTAGAGTGCCGAAGGCTGTACCAGTAGGCAAGATGGCAACA CTGCACTGCCAGGAGAGTGAGGGCCACCCCGGCCCTCACTACAGCTGGTATCGCAATGATGTACCACTGC CCACGGATTCCAGAGCCAATCCAGATTTCGCAATTCTTCTTTCCACTTAAACTCTGAAAACAGGCACTTT GGTGTTCACTGCTGTTTACAAGGACGACTCTGGGCACTACTCTGCATTGCTTCCAATGACGCAGGCTCA GCCAGGTGTGAGGAGCAGGAGATGGAAGTCTATGACCTGAACATTGGCGGAATTATTGGGGGGTTCTGG TTGTCTTGCTGTACTGGCCCTGATCAGTTGGGCATCTGCTGTGCATACAGACGTGGCTACTTCATCAA CAATAAACAGGATGGAGAAAGTTACAAGAACCAGGGAAACCAGATGGAGTTAACTACATCCGCACTGAC GAGGAGGGCGACTTCAGACACAAGTCATCGTTTGTGATCTGAGACCCGCGGTGTGGCTGAGAGCGCACAG AGCGCACGTGCACATACCTCTGCTAGAAATCCTGTCAAGGCAGCGAGAGCTGATGCACTCGGACAGAGC TAGACATCATTGAGAAGCTTTTCGTTTTGGCCAAAGTTGACCACTACTCTTCTTACTTAAACAGCCAC ATGAATAGAAGAAATTTTCTCAAGATGGACCCGTTAAATATAACCAAGGAAGCAAACTGGGTGCGTT CACTGAGTTGGGTTCTTAATCTGTTTTCTGGCCTGATTCGCCCATGAGTATTAGGGTGATCTTAAAGAGTT TGCTCAGCTAAACGCCCCTGCTGGGCCCTGTGAAGCCAGCATGTTCACTGCTGTTTCAAGCAGCCACG ACAGCACCATGTGAGATGGCGAGGTGGCTGGACAGCACCAGCAGCGCATCCCGCGGGAAACCAGAAAAG GCTTCTTACACAGCAGCCTTACTTCATCGGCCACAGACACCACCGCAGTTTCTTCTTAAAGGCTCTGCT GATCGGTGTGTCAGTGTCCATTGTGGAGAAGCTTTTGGATCAGCATTGTGTAACCAACAAAATCAG GAAGGTAAATTGGTTGCTGGAAGAGGGATCTTGCTGAGGAACCCGCTGTGTTCAACAGGGTGTGAGGAT TTAAGGAAAACCTTCGTCTTAGGCTAAGTCTGAAATGGTACTGAAATATGCTTTTCTATGGGTCTTGT ATTTTATAAAATTTTACATCTAAATTTTGTCTAAGGATGTATTTTGATTATTGAAAAGAAAATTTCTATT TAACTGTAAATATATTGTATACAATGTTAAATAACCTATTTTTTTAAAAAAGTTCAACTTAAGGTAGA AGTTCCAGCTACTAGTGTTAAATTGGAATATCAATAATTAAGAGTATTTTACCCAAGGAATCCCTCTC ATGGAAGTTTACTGTGATGTTCCTTTTCTCACACAAGTTTTAGCCTTTTTCACAAGGGAACCTCATACTGT CTACACATCAGACCATAGTTGCTTAGGAAACCTTTAAAAATTCAGTTAAGCAATGTTGAAATCAGTTTG CATCTCTTCAAAAGAAACCTCTCAGGTTAGCTTTGAACTGCCTCTTCTGAGATGACTAGGACAGTCTGT ACCCAGAGGCCACCCAGAAGCCCTCAGATGTACATACAGATGCCAGTCAGCTCCTGGGGTTGCGCCAG GCGCCCCGCTCTAGCTCACTGTGCTCGCTGCTGTCAGGAGGCGCCTGCCATCCTTGGGCCCTGGCAG TGGCTGTGTCAGTGAAGCTTTACTCAGTGGCCCTTGCTTTCATCCAGCAGAGCTCTCAGGTGGGCACTG CAGGGACACTGGTGTCTTCCATGTAGCTGCCAGCTTTGGGCTCCTGTAACAGACCTCTTTTGGTTATG GATGGCTCACAAAATAGGGCCCCCAATGCTATTTTTTTTTTAAAGTTGTTTAAATTATTGTTAAGATT GTCTAAGGCCAAAGCAATTGCGAAATCAAGTCTGTCAAGTACAATAACATTTTTTAAAGAAAATGGATC CCCTGTTCTCTTTGCCACAGAGAAAGCACCCAGACGCCACAGGCTCTGTGCGATTTCAAAACAAACCA TGATGGAGTGGCGGCCAGTCCAGCCTTTTAAAGAACGTGAGGTGGAGCAGCCAGGTGAAAGGCTGGCGG GGAGGAAAGTGAACGCCTGAATCAAAGCAGTTTTCTAATTTTGACTTTAAATTTTTCATCCGCCGGAG ACCTGCTCCCATTTGTGGGGGACATTAGCAACATCACTCAGAAGCCTGTGTTCTTCAAGAGCAGGTGT TCTCAGCTCACATGCCCTGCCGTGCTGGACTCAGGACTGAAGTGTGTAAAGCAAGGAGCTGCTGAGAA GGAGCACTCCACTGTGTGCTGGAGAATGGCTCTCACTACTCACCTTGTCTTTCAGCTTCCAGTGTCTTG GGTTTTTTTACTTTTACAGCTTTTTTTTTAATGTCATACATGAGACTGTGTTGACTTTTTTTAGTTATGT GAAACACTTTGCGCGAGGCCGCTGGCAGAGGCAAGAAATGCTCCAGCAGTGGCTCAGTGTCCCTGGTG TCTGCTGCATGGCATCCTGGATGCTTAGCATGCAAGTTCCTTCCATCATTGCCACCTTGGTAGAGAGGGA TGGCTCCCCACCTCAGCGTTGGGGATTACGCTCCAGCCTCCTTCTTGGTTGTGATAGTATAGGGTAG CCTTATTGCCCTCTTCTTATACCTTAAACCTTCTACACTAGTGCCATGGGAACCAAGGTCTGAAAAAG TAGAGAGAAGTGAAGTAGAGTCTGGGAAGTAGCTGCCTATAACTGAGACTAGACGGAAAAGGAATACTC GTGATTTTAAAGATATGAATGTGACTCAAGACICGAGGCCGATACGAGGCTGTGATTCTGCCTTTGGATG GATGTTGCTGTACACAGATGTACAGACTGTACTAACACACCGTAATTGGCATTGTTTAACCTCATT TATAAAGCTTCAAAAAACCCAAAAACCCAAA (SEQ ID NO: 37) </p>			
Translated protein sequence			

MVPARLGPVAMVTGAGRRVLGAWAHARGDYKPRRAAAGPSATL DMALRRPPRLRLCARLPDFFLLLLFRGCLIGAVNLKSSNRTPVVQEFESVELSCIITD SQTSDPRIEWKKIQDEQTTYVFFDNKIQGDLAGRAEILGKTSLKIWNVTRRDSALYRC EVVARNDRKEIDEIVIELTVQVKPVTVCVRPKAVPVGKMATLHCQSEGHPRPHYSW YRNDVPLPTDSRANPRFRNSSFHLNSETGTLVFTAVHKDDSGQYYCIASNDAGSARCE EQEMEYVDLNIIGGIIGVVLVLAVALITLGICCAYYRRGYFINNKQDGESYKNPGKPD GVNYIRTDEEGDFRHKSSFVI (SEQ ID NO: 38)			
KLHL17	339451	NM_198317	Homo sapiens kelch-like 17 (Drosophila) (KLHL17), mRNA
mRNA Sequence			
AGTGAGCGACACAGAGCGGGCCGCCACCGCCGAGCAGCCCTCCGGCAGTCTCCGCGTCCGTTAAGCCCGC GGGTCTCCGCGAATCGGCGGTGGGTCCGGCAGCCGAATGCAGCCCCGAGCGAGCGCCCGGGCCGAGG ACGCAGAGCCCGGAGCACGGCAGCCCGGGGCCCGGGCCGAGGCGCCCGCCTCCACCGCCGAGCCGC CGGCCCCGAGGCGAGAGCGCACGCGGCCCGGCGAGGCTCGGCCCGCAGCCCCCATGGAGGGAGCCGTGCA GCTGCTGAGCCGCGAGGGCCACAGCGTGGCCCAACTCCAAGCGGCACTACCACGATGCCTTCGTGGCC ATGAGCCGCATGCGCCAGCGCGGCTCCTGTGCGACATCGTCCTGCACGTGGGTGCCAAGGAGATCCGTG CGCACAAAGTGGTGTGGCTCCTGCAGCCCCTACTTCCACGCCATGTTCAAAATGAGATGAGCGAGAG CCGCCAGACCCACGTGACGCTGCACGACATCGACCCTCAGGCCTTGACCAGCTGGTGCAGTTTGCCTAC ACGGCTGAGATTGTGGTGGGCGAGGGCAATGTGCAGACTCTGCTCCCAGCCGCCAGTCTCCTGCAGCTGA ATGGCGTCCGAGACGCTTGCTGCAAGTTTCTACTGAGTCAGCTCGACCCCTCCAAC TGCTGGGTATCCG GGGCTTTGCCGATGCGCACTCCTGCAGCGACCTGCTCAAGGCCGCCACAGGTACGTGCTGCAGCACTTC GTGGACGTGGCCAAGACCGAGGAGTTTATGCTGTGCCCCCTGAAACAGGTTCTGGAAC TGTTCTCTAGCG ACAGCCTGAACGTGCCTTCAGAGGAGGAGGTCTACCGAGCCGTCTGAGCTGGGTGAAACACGACGTGGA CGCCCCGAGGCGAGCATGTCCACGGCTCATGAAGTGTGTGCGGCTGCCCTTGCTGAGCCGCGACTTCCTG CTGGGCCACGTGGATGCCGAGAGCCTGGTGAGGCACCACTGACTGCAAGGACCTCCTCATCGAGGCC TGAAGTTCCACCTGCTGCCTGAGCAGAGGGGCGTCTAGGCACCGCCGACACGTCCCCGGCGCTGCGA GGGGGCCGGGCTGTGCTTTTGTGCTGTGGGCGCGGGAGCCTGTTTGCCATCCACGGAGACTGTGAGGCC TACGACACGCGCACCGACCGCTGGCACGTGGTGGCTCCATGTCCACGCGCCGGGCCCGGTGGGAGTGG CTGCGGTGGGGAACCGGCTCTATGCTGTGGGCGGCTATGATGGGACCTCAGACCTGGCTACCGTGGAGTC CTACGACCCCGTGACTAACACGTGGCAGCCGAGGTGTCCATGGGCACAAGGCGAAGCTGCCTGGGTGTG GCCGCTTGCACTGGAATCCTGTACTCGGCCGCGGCTATGACGGGGCCTCCTGCCTGAACAGTGCTGAAC GCTACGACCCCTGACCGGAACGTGGACGTCCGTGCTGCCATGAGCACC CGAGGCGCTATGTGCGAGT GGCCACGCTTGATGGGAACCTGTATGCTGTGGGCGGCTACGACAGCTCCTCACACCTGGCCACTGTGGAG AAGTATGAGCCCCAGGTGAACGTGTGGTGCCTGCGGCTGGCGTCCATGCTGAGCCGACGCAGCTCAGCGGGCG TGGCCGTGCTGGAGGGTGCCCTGTACGTGGCAGGGGGAACGACGGCACCGAGCTGCCTCAACTCGGTAGA GAGATACAGTCCAAAGGCTGGAGCCTGGGAAAGCGTGGCGCCCATGAATATCCGCAGGAGCACGCATGAC CTGGTGCCATGGACGGATGGTTGTACGCCGTGGGGGTAACGACGGTAGCTCCAGCCTCAACTCCATCG AGAAGTACAACCCGAGGACCAACAAGTGGGTGGCCGCATCTGCAITTCACCCGGCGCAGCAGTGTGGG TGTGGCGGTGCTGGAGCTGCTCAATTTCCCGCCGCACTCCTCCCGACGCTGTCCGTGCTCTCCACAGC CTCTGACCCACCTACCACAGAGGCGCTGCAGCTCCACATGCCCTTAAGGGGACCGTGGCCCCCACCAGG GACGTCTCGCCATCCGTTACGCTCTGTCATCCATTCTTATGCTTTATTTAGTTGTTTATTATTATT TAGTTATTATCTTATTATTATTGAGGGGTGAGGAGTGCCACGGCTGCCCGTTTACACCTTTAGCGTCTGGT CCTCCTGCGTGTCTCCCTCCACTGCCTGCATGGGGGGCGCGGGGAGTGACAGGCGGGGGCTCACC CCCCAGGGCGGTGCTGCTCAGACCTTGACGGCTGTGGAGCAAGAGGCCCTGGGTCTCTCAAGCAGCT GCAGACCCAGCTCGAATTTTGCACATGGCGGGGTCCCGGAAGGGTGGGGAGCAGTTGCTCTCTGTC GTCGTCTGCCGTGTGCCATCTTCTGATCTGTAGTGGGTGCACACGCGTGCCTGGGACCCACACA GCAATACGAGTCCAACCTAATAAACACATTTCTGGGTTCTCAAAAAAAAAAAAAAAAAA (SEQ ID NO:			
39)			
Translated protein sequence			
MQPRSERPAGRTQSPHEGSPGPGPEAPPPPPQPPAPEAERTP RQARPAAPMEGAVQLLSREHGSVAHNSKRHYHDAFVAMSRMRQRLLCDIVLHVAAKE IRAHKVVLASCSPIYFHAMFTNEMSESRTHTVTLHDIDPQALDQLVQFAYTAEIVVGE NVQTLPLPAASLLQLNGVRDACCKFLLSQLDPSNCLGIRGFADAHSCDLLKAAHRYVL QHFDVDAKTEEFMLPLKQVLELVSSDSLNPSEEEVYRAVLSWVKHDVDARRQHVP LMKCVRLPLLSRDFLLGHVDAESLVRHHPDCKDLLIEALKFHLLPEQRGVLTSTRTP RRCEGAGPVLFAVGGGSLFAIHGDCEAYDTRTDVHVVASMSTRRARVGAAGVGNRLY AVGGYDGTSDLATVESYDPVTNTWQPEVSMGTRRSCLGVAALHGLLYSAGGYDGASCL			

NSAERYDPLTGTWTSVAMSTRRRYVRVATLDGNLYAVGGYDSSSHLATVEKEYEPQVN VWSPVASMLSRSSAGVAVLEGALYVAGGNDGTSLNSVERYSPKAGAWESVAPMNIR RSTHDLVAMDGWLYAVGGNDGSSSLNSIEKYNPRTNKWVAASCMFTRRSSVGVAVLEL LNFPPSPPTLSVSSTSL (SEQ ID NO: 40)			
KRT24	192666	NM_019016	Homo sapiens keratin 24 (KRT24), mRNA
mRNA Sequence			
ACTCTTCGTCATCACCTCTCCTATTTCGCTGGACAAGCTCATGTTTGCAGGAGCACCATGTCTTGTCTCGT CTCGCGCCTCCTCCTCCAGGGCTGGAGGCAGCAGCTCAGCCAGGGTGTCTGCTGGTGAAGCAGCTTCAG CAGTGAAGCAGATGTGGTCTGGGGGCAGCTCGGCCAGGGCTTCCGAGGAGGAGCCAGCAGCTGCAGC CTGAGTGGGGGTCTAGCGGTGCTTTTGGGGGCAGCTTTGGAGGGGGCTTTGGTAGCTGCTCAGTAGGGG GTGTTTTTGGGGGAGCTTCAGGCTCTGGGACAGGATTTGGTGGGGTTCTAGCTTTGGCGGGGTCTCTGG ATTTGGCAGGGGTTCTGGATTCTGTGGGAGTTCTAGATTACGACAGTGGTCTACTGGAGGCTTCTACAGC TATGGTGGTGGTATGGGAGGTGGTGTGGCGATGGGGGCTTTTCTCTGGAGGGGAAAAGCAAACCATGC AGAACCTCAATGACCGCTTGGCCAATTACCTAGACAAGGTCAGAGCCCTGGAGGAGGCTAACACTGATCT GGAGAACAAAATCAAGGAGTGGTATGACAAATATGGGCCTGGGTCTGGAGACGGTGGATCGGGAAGAGAT TATAGCAAATACTATTCAATAATTGAAGATCTCAGAAACCAGATCATTGCTGCCACTGTTGAAAATGCTG GGATCATTITGACATTGACAATGCCAGATTGGCTGCTGATGACTTCAGACTGAAGTATGAGAACGAGCT GTGTCTCCGGCAGAGCGTGGAGGCTGACATCAATGGCCTGCGGAAAGTCCTGGATGACCTGACTATGACC CGCTCTGACCTGGAGATGCAGATTGAGAGTTTACCGAGGAGCTAGCCTACCTGAGGAAGAACCACGAGG AGGAAATGAAGAATATGCAAGGAAGCTCTGGAGGGGAGGTGACCGTAGAAATGAATGCTGCGCCAGGGAC CGACCTGACCAAATTACTGAATGACATGAGGGCGCAGTACGAGGAGCTGGCTGAGCAAAACCGCCGAGAG GCTGAGGAGCGGTTCACAAGCAGAGCGCATCACTACAAGCACAAATCTCCACTGATGCTGGGGCAGCCA CTTCTGCCAAGAATGAGATAACAGAACTAAAACGTACCCTGCAAGCCCTGGAAATTGAGCTTCAGTCCCA ACTGGCCATGAAAAGCTCCCTGGAGGGAACCTGGCTGACACAGAAGCTGGCTACGTGGCTCAGCTGTCA GAAATTCAAACGCAGATCAGTGCCCTGGAGGAGGAGATCTGCCAGATCTGGGGTGAGACTAAATGCCAGA ACGCAGAGTACAAGCAATTGCTGGACATCAAGACACGCCTGGAGGTGGAGATCGAGACCTACCGCCGCCT GCTCGATGGAGAGGGAGGTGGTTCAGTTTTGCGAGAATTTGGTGGTAGAAACTCAGGATCTGTAAACATG GGATCCAGGGATCTGGTATCTGGTGACTCAAGATCTGGAAGCTGTTCTGGTCAAGGACGAGATTCAAGCA AGACTAGAGTGACTAAGACTATCGTAGAGGAGTTGGTGGATGGCAAGGTGTCTCGTCTCAAGTCAGCAG TATTTCTGAGGTGAAAGTTAAATAAGGAACCTCCAGATCAACAAAAGTGCTTTTCAAAGAAAAAAAATC AAGAAGGACACAAGCGAAGAAATGGCATCAATCTAGGCATCTTTCTGGATAATTTCAAGAAAAGCTTCAG TCCAGAAATGGATGACTAGCCAACCTTTCTGCATCTTCTTATTTCTCATTAGAAATGCTCTTGAAAATAGC TGAATTAACAACCTTTGCTTTAATTGTTTCTATGCTTCAATAAATTTACTTTTGCAAGTTAAAAAATC AAAAAA (SEQ ID NO: 41)			
Translated protein sequence			
MSCSSRASSSRAGGSSSRVVSAGGSSFSSGSRCLGGSSAQGFR GGASSCSLSSGSSGAFGGSFGGGFGSCSVGGFGGASGSGTGFGGSSFGGVSGFGRG SGFCGSSRFSSGATGGFYSYGGMGGGVGDGGLFSGGEKQTMQNLNDRNLANYLDKVR LEEANTDLENKIKEWYDKYGPSGDGSGRDYSKYYSIIEDLRNQIIAATVENAGIIL HIDNARLAADDRLKYENELCLRQSV EADINGLRKVLDDLTMTRSDLEMQIESFTEEL AYLRKNHEEEMKNMQSSSGEVTVMNAAPGDTLTKLLNDMRAQYEELAEQNRREAE RFNKQSASLQAQISTDAGAATS AKNEITELKRTLQALEIELQSQLAMKSSLEGT LADT EAGYVAQLSEIQTQISALEEEICQIWGETKCQNAEYKQLLDIKTRLEVEIETYRRLD GEGGSSFAEFGGRNSGSVNMGSRDLVSGDSRSGSCSGQGRDSSKTRVTKTIVEELVD GKVVSQVSSISEVKVK (SEQ ID NO: 42)			
MAD2L1BP	9587	NM_014628	Homo sapiens MAD2L1 binding protein (MAD2L1BP), transcript variant 2, mRNA
mRNA Sequence			
ATTCTAACCGCAAGGAGTAGCGGAGGGGAGGTCTGATGGCGGCGCCGAGGCGGAGGTTCTGTCTCAG CCGCAGTCCCTGATTTGGAGTGGTATGAGAAGICCGAAGAACTCACGCCTCCAGATAGAACTACTTGA GACAAGCTCTACGCAGGAACCTCTCAACGCTTCGGAGGCCCTTTTGCCAAGAGACTGCATGGTACCAGTG GTGTTTCTGGGCCTGTGAGCCAGGAAGGCTGCTGTCAGTTTACTTGTGAACCTTCTAAAGCATATCATGT ATCAACGCCAGCAGCTCCCTCTGCCCTATGAACAGCTTAAGCACTTTTACCGAAAACCTTCTCCCCAGGC AGAGGAGATGCTGAAGAAGAAACCTCGGGCCACCACTGAGGTGAGCAGCAGGAAATGCCAACAAGCCCTG GCAGAACTGGAGAGTGTCTCAGCCACCTGGAGGACTTCTTTGCACGGACACTAGTACCGCGAGTGCTGA			

TTCTCCTTGGGGCAATGCCCTAAGCCCCAAGGAGTTCATGAACCTGACTTGTCTCTGCTGCCCCCTA CAGCGTGGACAGAGCCTGAGCACAGCAGCTTGTTCGCGCTCTCTCCGAGCCATATTCATGGCTGAT GCCTTTAGCGAGCTTCAGGCTCCTCCACTCATGGGCACCGTCGTCATGGCACAGGGACACCGCAACTGTG GAGAAGATTGGTTTCGACCCAAGCTCAACTATCGAGTGCCAGCCGGGGCCATAAACTGACTGTGACCCT GTCATGTGGCAGACCTTCCATCCGAACCACGGCTTGGGAAGACTACATTGGTTCCAGGCACCAAGTGACA TTTAAAGGCTTCCGCGAGTGAATGAGTGCTTCTTAATCCTAAAAACACAATGGCTGAATTATCTTTCTCC ATGTGGCGCTGAATCACCCATCTGGTTTGGAGCTAGAGTTGCTTCCCTGGTGAGAGAGGAAGCAACTCTCC TTCTGGTTGTCTGCCTCCCTCAGATTTCTGATAGGCTGATGGCATGTGGCTGTGACTGTGACTGTAAT CATTGCTGAACAACATCTCTTTGAATCAAAGGTTGATTTTCCAGAGGGTGCTGGGTCAGGCATTTCTAT TAGGAGTTGAAAGCAAAATGGGTCCATAGACACTCTATGGAGGTGTCCTTTCTGCTCTTTGCTGTGT CCTTTTCAAAATTTTACCAGGAACATAATGTGGATGTGACTTATGAACTTAAATATAAAATAAATAGATT CTTATTATATTTTCTGAAAAA (SEQ ID NO: 43)			
Translated protein sequence			
MAAPEAEVLSSAAVPDLEWYKSEETHASQIELLETSSTQEPLN ASEAFCDPRDCMPVFPVPGVPSQEGCCQFTCELLKHIMYQRQQLPLPYEQLKHFYRKPS PQAEEMLKKKPRATTEVSSRKQQAALAELESVLSHLEDFARTLVPRVLILLGNALS PKEFYELDLSELLAPYSVDQSLSTAACLRLRFRAIFMADAFSELQAPPLMGTVMMAQGH RNCGEDWFRPKLNYRVPSPRGHKLTVLSCGRPSIRTAWEDIWFQAPVIFKGFRE (SEQ ID NO: 44)			
MANSC1	54682	NM_018050	Homo sapiens MANSC domain containing 1 (MANSC1), mRNA
mRNA Sequence			
AACCACAAAACCCGCCAGGCCGGTGCGGGAGCTGCGGAGCATCCGCTGCGGTCTCGCCGAGACCCCGC GCGGATTGCGCGGTCTCTCCCGCGGGCGGACAGAGCTGTCTCGCACCTGGATGGCAGCAGGGGCGCGG GGGTCTCTCGACGCCAGAGAGAAATCTCATCTGTGTCAGCCTTCTTAAAGCAAACCTAAGACCAGAGG GAGGATTATCCTTTGACCTTTGAAGACCAAACTAAACTGAAATTTAAATGTTCTTCGGGGGAGAAGGGA GCTTGACTTACACTTTGGTAATAATTGTCTTCTGACACTAAGGCTGTCTGCTAGTCAGAATTGCCTCAA AAAGAGTCTAGAAGATGTTGTCATTGACATCCAGTCATCTCTTTCTAAGGGAATCAGAGGCAATGAGCCC GTATATACTTCAACTCAAGAAGACTGCATTAATTCTTGCTGTTCAACAAAAACATATCAGGGGACAAAG CATGTAACCTGATGATCTTCGACACTCGAAAAACAGCTAGACAACCCAACTGCTACCTATTTTCTGTCC CAACGAGGAAGCCTGTCCATTGAAACCAGCAAAAGGACTTATGAGTTACAGGATAATTACAGATTTTCCA TCTTTGACCAGAAATTTGCCAAGCCAAGAGTTACCCAGGAAGATTCTCTTACATGGCCAATTTTCAC AAGCAGTCACTCCCTAGCCCATCATCACACAGATTATTCAAAGCCACCGATATCTCATGGAGAGACAC ACTTTCTCAGAAGTTTGGATCCTCAGATCACTTGGAGAAACTATTTAAGATGGATGAAGCAAGTGCCAG CTCCTTGCTTATAAGGAAAAAGGCCATTCTCAGAGTTTACAATTTTCTCTGATCAAGAAATAGCTCATC TGCTGCCTGAAAATGTGAGTGCGCTCCAGCTACGGTGGCAGTTGCTTCTCCACATACCACCTCGGCTAC TCCAAAGCCCGCCACCCTTCTACCCACCAATGCTTCAGTGACACCTTCTGGGACTTCCAGCCACAGCTG GCCACCACAGCTCCACCTGTAAACCACTGTCACCTTCTCAGCCTCCACGACCCCTCATTTCTACAGTTTAA CACGGGCTGCGGCTACACTCCAAGCAATGGCTACAACAGCAGTTCTGACTACCACCTTTCAGGCACCTAC GGACTCGAAAGGCAGCTTAGAAACCATACCGTTTACAGAAATCTCCAACCTAACTTTGAACACAGGGAAT GTGTATAACCCCTACTGCACTTCTATGTCAAATGTGGAGTCTTCCACTATGAATAAACTGCTTCTCTGGG AAGGTAGGGAGGCCAGTCCAGGCAGTTCTCCAGGGCAGTGTTCCAGAAAATCAGTACGGCCTTCCATT TGAAAAATGGCTTCTTATCGGGTCCCTGCTCTTTGGTGCTCTGTTCCGGTGATAGGCCTCGTCTCTCTG GGTAGAATCCTCTCGGAATCACTCCGCAGGAAACGTTACTCAAGACTGGATTATTTGATCAATGGGATCT ATGTGGACATCTAAGGATGGAACCTCGGTGTCTCTTAATTCATTTAGTAACCAGAAGCCCCAAATGCAATGA GTTTCTGCTGACTTGCTAGTCTTAGCAGGAGGTTGATTTTGAAGACAGGAAAATGCCCTTCTGCTTT CCTTTTTTTTTTTTGGAGACAGAGTCTTGCTTTGTGCCCAGGCTGGAGTGAGTACGATCTCGGCT CTCACCACAACCTCCGTCTCTGGGTTCAGCGATTCTCTGCCTCAGCCTCCTAAGTATCTGGGATTAC AGGCATGTGCCACCACCTGGGTGATTTTTGTATTTTAGTAGAGACGGGGTTTACCATGTTGGTCAG GCTGGTCTCAAACCTCTGACCTAGTGATCCACCTCCTCGGCCTCCCAAAGTGCTGGGATTACAGGCATG AGCCACCACAGCTGGCCCCCTCTGTTTTATGTTTGGTTTTTGAGAAGGAATGAAGTGGGAACCAATTA GGTAATTTTGGGTAATCTGTCTCTAAATATTAGCTAAAAACAAAGCTATGTAAAGTAATAAAGTATA ATTGCCATATAAATTTCAAAATTCAACTGGCTTTTATGCAAAGAAACAGGTTAGGACATCTAGGTTCCAA TTCAATTCACATTCTTGGTTCCAGATAAAATCAACTGTTTATATCAATTTCTAATGGATTGCTTTTCTTT TTATATGGATTCTTTTAAACTTATTCCAGATGTAGTTCCTTCCAATTAATATTG (SEQ ID NO: 45)			
Translated protein sequence			
MFFGGEGSLTYTLVVICFLTLRLSASQNCLKKSLEDVVIDIQSS			

LSKGIRGNEPVYITSTQEDCINSCCSTKNISGDKACNLMIFDTRKTARQPNCYLFFCPN EEACPLKPAKGLMSYRIITDFPSLTRNLPSQELPQEDSLLHGQFSQAVTFLAHHTDY SKPTDISWRDTLSQKFGSSDHLKLFKMDEASQQLLAYKEKGHSQSSQFSSDQEIHL LPENVSLPATVAVASPHHTSATPKPATLLPTNASVTPSGTSQPQLATTAPPVTTVTS QPPTTLISTVFTRAATLQAMATTAVLTTTTFQAPTDSEKGSLETIPFTEISNLTNTGN VYNPTALSMSNVESSTMNKTASWEGREASPGSSSQGSVPENQYGLPFKWLIGSLLF GVLFLVIGLVLLGRILSESLRRKYSRLDYLINGIYVDI (SEQ ID NO: 46)			
MOBK1B	55233	NM_018221	Homo sapiens MOB1, Mps One Binder kinase activator-like 1B (yeast) (MOBK1B), mRNA
mRNA Sequence			
GCGAGGTGGGGTAGGCGGGCAAGGCGGGCGCCGAGGTTTGCAAAGGCTCGCAGCGGCCAGAAACCCGGCT CCGAGCGGCGGGCGGCCCGGCTTCCGCTGCCCCGAGCTAAGGACGGTCCGCTCCCTCTAGCCAGCTCCGA ATCCTGATCCAGGCGGGGGCCAGGGGCCCCCTCGCTCCCTCTGAGGACCGAAGATGAGCTTCTCTTCA GCAGCCGCTCTTCTAAACATTCAAACCAAAGAAGATATCCCTGAAGGATCTCATCAGTATGAACCTT AAAACATGCAGAAGCAACTCTAGGAAGTGGGAATCTGAGACAAGCTGTTATGTTGCCGTGAGGGAGAGGAT CTCAATGAATGGATTGCTGTGAACACTGTGGATTCTTTAACCAGATCAACATGTTATATGGAACATTA CAGAATTCTGCACTGAAGCAAGCTGTCCAGTCATGTCTGCAGGTCCGAGATATGAATATCACTGGGCAGA TGGTACTAATATTAAAAAGCCAATCAAATGTTCTGCACCAAAATACATTGACTATTTGATGACTTGGGT CAAGATCAGCTTGATGATGAACTCTTTTTCTTCTAAGATTGGTGTCCATTTCCCAAAACTTTATGT CTGTGGCAAAGACTATTCTAAAGCGTCTGTTCCAGGGTTATGCCCATATTTATCACCAGCACTTTGATTC TGTGATGCAGCTGCAAGAGGAGGCCCCACCTCAACACCTCCTTTAAGCACTTTATTTCTTTGTTTCAGGAG TTTAATCTGATTGATAGCGGTGAGCTGGCACCTCTCAAGAATTAATAGAGAACTTGGATCAAAAGACA GATAAATGTTTCTTCTAGAACACAGTTACCCCTTGCTTCATCTATTGCTAGAACTATCTCATTGCTATC TGTTATAGACTAGTGATACAACTTTAAGAAAACAGGATAAAAAGATACCCATTGCCGTGTGTCTACTGAT AAAATTATCCCAAAGGTAGGTTGGTGTGATAGTTCCGAGTAAGACCTTAAGGACACAGCCAAATCTTAA GTACTGTGTGACCACCTTGTGTGTTATCACATAGTCATACTTGGTTGTAATATGTGATGGTTAACCTGTA GCTTATAAATTTACTTATTATCTTTTACTCATTACTCAGTCATTTCTTTACAAGAAAATGATTGAATC TGTTTTAGGTGACAGCACAAATGGACATTAAGAATTTCCATCAATAATTTATGAATAAGTTCCAGAACAA ATTTCTAATAACACAATCAGATTGGTTTTATCTTTATTTTACGAATAAAAAATGTATTTTTCAGTAA AAAAA (SEQ ID NO: 47)			
Translated protein sequence			
MSFLFSSRSSKTFKPKKNIPEGSHQYELLKHAEATLGSGNLRQA VMLPEGEDLNEWIAVNTVDFNQINMLYGTITEFCTEASCPVMSAGPRYEHWADGTN IKKPIKCSAPKYIDYLMTWQDQLDDETLFPSKIGVPFPKNFMSVAKTILKRLFRVYA HIYHQHFDSDVMQLQEEAHLNLSFKHFIFVQEFNLIDRRELAPLQELIEKLGSKDR (SEQ ID NO: 48)			
NCP1	4686	NM_002486	Homo sapiens nuclear cap binding protein subunit 1, 80kDa (NCP1), mRNA
mRNA Sequence			
ATTGAGAGGCCACCGGAAACCATTGAGAAGCCCCGAGGACCGGCTGAGCGGAGGCGGAGACTAGAGC GGCCGCCGGCACGACCCGCTTCAGGCGTACGACGACCGCGGCCCGGGGCTCTGAGTGGCCAAAGCGGC GGCATTTCTGCGTGGCCCCGGAAGGACATAGAGCGGAAGCGGGAGAAAGAAGTAGCCGGCAGGCGGAG GCAGCCCGAGGGGCGGTTGCATGTGTGCCAGACGTTCTGAGCCCACTGAGCTTCTCAGCCGGCTGTG GCAGCGCTAGCCCCACCGGCGGCCCTCTCTGCGCTTCCGGGGCCGTGCGGAGCTAGTGCCTGCGTG CCGGCCCATCCGCGCGCCTTGACAGTGTCTTGGCTCGGCCAGCGGCCAGACAGTTCTTGACGCGCTTAC CGCCTGGCCTCTCGGTTCCGCGGCGCACCGGAGGCGAGCATGTGCGGCGGCGGCACAGCGACGAGAACG ACGGTGGGCAGCCTCACAAAAGGAGAAAGACCTCTGATGCAAATGAACTGAAGATCATTGGAATCTTT AATATGTAAGTAGGAGAAAAGAGTGCCTGCTCTTGGAGAGCAACCTAGAAGGCTTGGCTGGTGTGTTG GAAGCTGATCTTCTAACTACAAGAGCAAGATCTTAAGGCTTCTTTGTACAGTTGCACGCTATTACCTG AGAAGCTGACAATTTATACAACATTAGTTGGACTACTGAATGCCAGGAATTACAATTTTGGTGGAGAATT TGTAAGCCATGATTCTCAACTTAAAGAATCATTGAAAGCAAACAATTATAATGAAGCCGTGATTTG GTCCGTTTTTTATCTGATCTTGTGAATTGTCAITGATTGCCGCCCATCAATGGTTGCTATGTTTGAAA ATTTTGTAAGCGTAACTCAGGAAGAAGATGTACCTCAGGTGCGACGAGATTGGTATGTGTATGCATTTCT GTCATCTTTGCCCTGGGTTGAAAGGAGTTGTACGAAAAGAAAGATGCAGAGATGGACCGCATCTTIGCC AACACTGAAAGCTATCTTAAAGACGCCAAAAGACTCATGTACCCATGTTACAGGTATGGACTGCTGATA AACCACATCCACAAGAAGAGTATTTAGATTGCCGTGTGGGCCAGATTTCAGAAATTGAAAAAGGATCGCTG			

GCAGGAACGGCACATCCTAAGACCTTATCTTGCCTTTGACAGCATCCTGTGTGAAGCACTGCAGCACAAT
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 AACTTCCAGCACCCTCATTGATGTGATGTACACAACACTCCTCATGAACTGTGCAAACTTCAACC
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 ACCTGTGTAGACAGGTTTATTAATTGGTTTTCTCATCATCTAAGTAACTTCCAGTTCCGTTGGAGCTGGG
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 AAGGAAACAAAGGGGAAGAGGACAGTGAATGAACATGGCATTACTTTAATTGCCCTGAAAAGCAAATAC
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 GCAGCTTTAGTGTATGAAAAATGAACTAGGAATTGAGTTTTGAAGAAATAAAGGTGTAAGAGCAAACA
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 TTGCAATAAATATTCTGTTAAATTTGTGCTGGTGAATTTAACATGCTTTTGTCAAAGTAAA (SEQ ID NO:

SUBSTITUTE SHEET (RULE 26)

AGGCAGGGCCATGGGCACCCTGCTCAGCCTCCTGTGGAGGAGGCTCCAGTCCCGCTCCGTGTACTGCAT
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GCTGCAGCCTGATGGCTCCCTGGTCAATTAGCCGAGTGGCTGTAGAAGATGGCGGCTTCTACACCTGTGTC
GCTTTCAATGGGCAGGACCCGAGACAGCGATGGGTCCAGCTCAGAGTTCTGGGGGAGCTGACAATCTCAG
GACTGCCCCCTACTGTGACAGTGCCAGAGGTGATACGGCCAGGCTATTGTGTGTGGTAGCAGGAGAAAG
TGTGAACATCAGGTGGTCCAGGAACGGGCTACCTGTGCAGGCTGATGGCCACCGTGTCCACCACTCCCA
GATGGCAGCTGCTCATTTACAACCTTGGGGCCAGGGATGAGGGCTCCTACAGTGCAGTGCCTACCAAG
GGAGCCAGGCAGTCAAGCGCAGCACCCGAGGTGAAGGTGGTCTCACCAGCACCCAGCCAGCCAGGGA
CCCTGGCAGGGACTGCGTCGACCAGCAGAGCTGGCCAACGTGATTGATCCTGAGCCCAAGCTTTGT
GGCAATGAGTATTACTCCAGCTTCTGCTGTGCCAGCTGTTACGTTTCCAGCCTCAGCTCAGCCCATCT
GGCAGTAGGGATGAAGGCTAGTTCCAGCCCCAGTCCAAAATAGTTTATAGGGCTAGGGAGAAAGGAAGAT
GGACTCTTGGCTTCTCTCTCTGGCTGGCAAAGGGAGTTATCTTCTGGAATACATTAGCTCTTTCAAAAA
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TCTCTGACATAACCACAGGCTGCTGTGTTTCAAGAAGAGCAATCTGTTTGGATAAGAAAAACCTTTACTTT
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GGCTGTGACGGTTCACTGACACCTGTGTAAAGCTGACCAGCCTGCTCTGTACAGTGACAATGAGGAGCC
CCTCTCTTCTTAAGTAGGAATCTGTGAAGCAAAATGTTTGTGTCGCAAAAGACAAATCAGACTGTCACTCA
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GGCTTCAGAAATGGTTTGAGTTGGAAGACAACATTCTTCATCTCTCAGGACTTCTAATTCCTTGATGCTA AAAGAAGAGGCATGGATTCTATGAGCTTCCAAGTCCCTTTCCACTTTAACCTTCTACAAATCTTTCAGAG GACTGCCTAGTAGCAAAGGTTATTCTGGACACAGGAAAGACGGGCATTACAGGGACCAAAGCTCTGAAA GGTGACTTTTATTACCAACACACTGGCTGGAAAAGGGACAAACCACATCACGGGTGAGTGATACTTCTCA GTCTTCTCTACTCATTCACAAAGGAAATGTGGGCTGGGGCAGAGGTCTTTTTTTCATTTAATACTGAAA AATATTGAAGAGCATCCATGTTCACTTATGGCTGGTTTTGCTATAGAAATTGGAATAAAGGCCACTTT TTTGAAATCCCCAGTTTAATTAATAAAAAAAAAAAAAAAAAA (SEQ ID NO: 53)			
Translated protein sequence			
MRLLLVPLLLAPAGSSAPKVRQSDTWGPWSQWSPCSRTC GVSRFRERPCYSQRRDGGSSCVGPASRSHRSCRTESCPDGARDFRAEQCAEFDGAEFQGR RWRWLPYYSAPNKCELNCIPKGENFYKHXREAVDGTPEPGKRDVCVDGSCRVDGCD HELDSSKQEDKCLRCGGDGTTCYPVAGTFDANDLSRAVKNVRGEYYLNGHWTIEAARA LPAASTILHYERGAEGDLAPERLHARGPTSEPLVIELISQEPNPGVHYEYHLPLRRPS PGFSWSHGSWSDCSAECGGGHQSRLVFCTIDHEAYPDHMCQRQPRPADRRSCNLHPCP ETKRWKAGPWAPCSASCSSGSSQSRVYCISSDGAGIQEAVEEAECAGLPGKPPAIQAC NLQRCAAWSPEPWGECVSCGVGRKRSVTCRGERGSLHTAACSLEDPRPLTEPCVH EDCPLLSDQAWHVGTWGLCSKSCSSGTRRRQVICAIGPPSHCGSLQHSKFPVDVEPCNT QPCHLPQEVPSMQDVHTPASNPWMPLGPQESPASDSRGQWAAQEHPSARGDHRGERG DPRGDQGTSLALGPAPSLQPPYQQLRSGSGPHDCRHSHPHGCPDGHTASLGPQWQ GCPGAPCQQSRYGCCPDVRSVAEGPHHAGCTKSYGGDSTGGMPRSRAVASTVHNTHQP QAQNEPSECRGSQFGCCYDNVATAAGPLGEGCVGQPSHAYPVRCLLPSAHGSCADWA ARWYFVASVGGQCNRFWYGGCHGNANNFASEQECCMSQGSLSHGPRRPQPGASGRSTHT DGGGSSPAGEQEPSQHRTGAAVQRKPWPSGGLWRQDQPGPGEAPHTQAFGEWPWGQE LGSRAPGLGGDAGSPAPPFHSSSYRISLAGVEPSLVQAALGQLVRLSCSDDTAPESQA AWQKDGQPISSDRHRLQFDGLIIHPLQAEDAGTYSCTGRPRDSQKIQRLRIIGGDM AVLSEAELSRFPQPRDPAQDFGQAGAAGPLGAIPSSHQPANRLRLDQNPQPRVVDASP GQRIRMTCAEGFPFPAIEWQRDQGVSSPRHQLQPDGSLVISRVAVEDGGFYTCVAF NGQDRDQRWVQLRVLGELTISGLPPTVTVPEDTARLLCVVAGESVNIRWSRNLPLVQ ADGHRVHQSPDGTLLIYNLRARDEGSYTC SAYQGSQAVSRSTEVKVVSPAPTAQPRDP GRDCVDQPELANCDLILQAQLCGNEYSSFFCCASCSRFQPHAQPIWQ (SEQ ID NO: 54)			
PCDH1	5097	NM_002587	Homo sapiens protocadherin 1 (PCDH1), transcript variant 1, mRNA
mRNA Sequence			
CGCAAAGCCGCCGGGCTGCTGCGCCAGAGCCAGCCGGAGCCGGAGCCGGAGCCCGAAGTGCAGCTCCAG CCCCAGCCGTGCGGAGCCGAGCCAGCCAGCCGGGCGCGGCGGCTCATGGACAGCGGGCGGGCGGCCG GCGCTGCCCCGAGGCGGCCCTCTGATTCTGGGGCTCCAGGATGGAGCACCTGAGGCACAGCCAGGC CCTGGGGGGAACGGCTACTGCTGCCCTCCATGCTGCTAGCACTGCTGCTCCTGCTGGCTCCATCCCCAG GCCACGCCACTCGGGTAGTGTACAAGGTGCCGGAGGAACAGCCACCCACACCCCTCATTGGGAGCCTCGC AGCCGACTATGGTTTTCCAGATGTGGGGCACCTGTACAAGCTAGAGGTGGGTGCCCCGTACCTTCGCGTG GATGGCAAGACAGGTGACATTTTACCACCGAGACCTCCATCGACCGTGAGGGGCTCCGTGAATGCCAGA ACCAGCTCCCTGGTGATCCCTGCATCCTGGAGTTTGAGGTATCTATCACAGACCTCGTGCAATGGCAG CCCCCGGCTGCTAGAGGGCCAGATAGAAGTACAAGACATCAATGACAACACACCCCAACTTCGCCTACCA GTCATCACTCTGGCCATCCCTGAGAACACCAACATCGGCTCACTCTTCCCCATCCCGCTGGCTTCAGACC GTGATGCTGGTCCCAACGGTGTGGCATCTATGAGCTGCAGGCTGGGCTGAGGCCAGGAGCTATTTGG GCTGCAGGTGGCAGAGGACCAGGAGGAGAAGCAACACAGCTCATTGTGATGGGCAACCTGGACCGTGAG CGCTGGGACTCCTATGACCTACCATCAAGGTGCAGGATGGCGGCAGCCCCCAGCGCCAGCAGTGCCC TGCTGCGTGTCACCGTGCTTGACACCAATGACAACGCCCCCAAGTTTGAGCGGCCCTCCTATGAGGCCGA ACTATCTGAGAATAGCCCCATAGGCCACTCGGTCACTCAGGTGAAGGCCAATGACTCAGACCAAGGTGCC AATGCAGAAATCGAATACACATTCACCAGGCGCCGAAGTTGTGAGGCGTCTTCTTCGACTGGACAGGA ACACTGGACTTATCACTGTTAGGGGCCGGTGGACCGTGAGGACCTAAGCACCTGCGCTCTCAGTGCT TGCTAAGGACCGAGGACCAACCCCAAGAGTGCCCGTGCCAGGTGGTTGTGACCGTGAAGGACATGAAT GACAATGCCCCACCATGAGATCCGGGCGATAGGGCTAGTGACTCATCAAGATGGGATGGCTAACATCT CAGAGGATGTGGCAGAGGAGACAGCTGTGGCCCTGGTGAGGTGTCTGACCGAGATGAGGGAGAGAATGC AGCTGTCACTGTGTGGTGGCAGGTGATGTGCCCTTCCAGCTGCGCCAGGCCAGTGAGACAGGCAGTGAC AGCAAGAAGAAGTATTTCTGCAGACTACCACCCCGCTAGACTACGAGAAGGTCAAAGACTACACCATTG AGATTGTGGCTGTGGACTCTGGCAACCCCCACTCTCCAGCACTAACTCCCTCAAGGTGCAGGTGGTGA			

CGTCAATGACAACGCACCTGTCTTCACTCAGAGTGTCACTGAGGTGCGCTTCCCGGAAAAACAACAGCCT
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 TCCTGGGCCACAGCCTGGACACGCGCTGGATATTGACATTGCTGGGGATCCAGAATATGAGCGCTCCAA
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 CCCAAGCCCGTGAAGCCAGTGGAGGACGAGGATGAGGCCGGGCTGCAGAAGTCCCTCAAGTCAACCTG
 ATGAGCGATGCCCCCTGGGGACAGTCCCCGCATCCACCTGCCCTCAACTACCCAGGCACCCCTGACC
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 GCCAGCCCTTTCAGCTCAGCACACCCAGCCCTACCCACCCCTACCACGAGCCATCTGGACCGAGGT
 GTGGGAGTGATGGAGCAGGTTTACTGTGCTGCCCCGTGTTGGGGGCCAGCCTGAGCCAGCAGTGGGAGGT
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 TCCAAACCTAGGTCTCTATGTGAGACCAGACCTAGGTGCTTCTCTAGGAGGGAAACAGGGAGACCTGGGG
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 GTTCTCTATTTTTGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
 A (SEQ ID NO: 55)

Translated protein sequence

MDSGAGGRRCP EAALLILGPPRMEHLRHSPGPGQRLLLPSMLL
 ALLLLLAPSPGHATRVVYKVPPEEQPNTLIGSLAADYGFDPDVGHLYKLEVGAPYLVRD
 GKTGDIFFTETSIDREGLRECQNQLPGDPCILEFEVSIITDLVQNGSPRLLEGQIEVQD
 INDNTPNFASPVITLAIPENTNIGSLFPIPLASDRDAGPNGVASYLEQAGPEAEQLFG
 LQVAEDQEEKQQLIVMGNLDRERWDSYDLTIKVQDGGSPPRASSALLRVTVLTDNDN
 APKFERPSYEAELSENSPIGHSVIQVKANDSDQGANAEIEYTFHQAPEVVRRLRLDR
 NTGLITVQGPVDREDLSTLRFVSLAKDRGTNPKSARAQVVVTVKDMNDNAPTIEIRGI
 GLVTHQDGMANISEDVAEETAVALVQVSDRDEGENAAVTCVVGADVPFQLRQASETGS
 DSKKKYFLQTTTPLDYEKVKDYTIEIVA VDSGNPPLSSTNSLKVQVVDVNDNAPVFTQ
 SVTEVAFPENNKPGEVIAEITASDADSGSNAELVYSLEPEPAAGLFTISPETGEIQV
 KTSLDREQRESYELKVVAADRGSPLQGTATVLNVNLDNDNDPKFMLS GYNFVSMEN
 MPALSPVGMVTVIDGDKGENAQVQLSVEQDNGDFVIQNGTGILSSLSFDREQQSTYT
 FQLKAVDGGVPPRSAYVGTINVLDENDNAPYITAPSNTSHKLLTPQTRLGETVSQVA
 AEDFDSGVNAELIYSIAGGNPYGLFQIGSHSGAITLEKEIERRHHGLHRLVVKVSDRG
 KPPRYGTALVHLYVNETLANRTLLETLLGHSLDTPLDIDIDAGDPEYERSKQRGNI LFG
 VVAGVVAALLIALAVLVRYCRQREAKSGYQAGKKETKDLYAPKPSGKASKGNKSKGK
 KSKSPKVPKVEDEDEAGLQKSLKFNLMSDAPGDSPRIHLPLNYPGSPDLGRHYRSN
 SPLPSIQLPQSPSASKKHQVVDLPPANTFVGTGDTTSTGSEQSYSDYSYRTNPPKYP
 SKQVGQPFQLSTPQPLPHYPHGAIWTEVWE (SEQ ID NO: 56)

PDGFB	5155	NM_002608	Homo sapiens platelet-derived growth factor beta polypeptide (simian sarcoma viral (v-sis) oncogene homolog) (PDGFB), transcript variant 1, mRNA
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mRNA Sequence			
<p>CCTGCCTGCCTCCCTGCGCACCCGACGCTCCCCGCTGCCTCCCTAGGGCTCCCCTCCGGCCGCCAGCG CCCATTTTTCATTCCCTAGATAGAGATACTTTGCGCGCACACACATACATACGCGCGCAAAAAGGAAAAA AAAAAAAAAAGCCACCCTCCAGCCTCGCTGCAAAGAGAAAACCGGAGCAGCCGAGCTCGCAGCTCGC AGCTCGCAGCCCGCAGCCCGCAGAGGACGCCAGAGCGGCGAGCGGGCGGGCAGACGACCGACGGACTC GCGCCGCGTCCACCTGTGCGCCGGGCCAGCCGAGCGCGCAGCGGGCACGCCGCGCGCGGGAGCAGCCG TGCCCCGCCCGGGCCCCGCGCCAGGGCGCACACGCTCCCGCCCCCTACCCGGCCCGGGCGGGAGTTT GCACCTCTCCCTGCCCCGGTGCTCGAGCTGCCGTTGCAAAGCCAACTTTGAAAAAGTTTTTTGGGGGAG ACTTGGGCCTTGAGGTGCCAGCTCCGCGCTTTCGATTTTGGGGGCCTTTCAGAAAATGTTGCAAAAA AGCTAAGCCGGCGGGCAGAGGAAAACGCTGTAGCCGGCGAGTGAAGACGAACCATCGACTGCCGTGTTT CTTTTCTCTTGAGAGTTGGAGTCCCTTGGGCGCCCCACACGGCTAGACGCTCGGTGTTTCGCGACG CAGCCCCCGGCCGTGGATGCTACTCGGGCTCGGGATCCGCCCAGGTAGCGGCCTCGGACCCAGGTCCT GCGCCAGGTCTCCCTGCCCCCAGCGACGGAGCCGGGGCCGGGGCGGCGGCCCGGGGGCCATGC GGGTGAGCCGCGGTGCAGAGGCCTGAGCGCCTGATCGCCGCGGACCCGAGCCGAGCCACCCCCCTCCC CAGCCCCCACCCTGGCCGCGGGGGCGGCGCGCTCGATCTACGCGTCCGGGGCCCCGCGGGGCCGGGCC GGAGTCGCATGAATCGCTGCTGGGCGCTCTTCTGTCTCTGTCTGCTACCTGCGTCTGGTCAGCGCCG AGGGGACCCCATTTCCCGAGGAGCTTTATGAGATGCTGAGTGACCACTCGATCCGCTCCTTTGATGATCT CCAACGCTGCTGCACGGAGACCCCGGAGAGGAAGATGGGGCCGAGTTGGACCTGAACATGACCCGCTCC CACTCTGGAGGCGAGCTGGAGAGCTTGGCTCGTGAAGAAGGAGCCTGGGTTCCCTGACCATTGCTGAGC CGGCCATGATCGCCGAGTGCAAGACGCGCACCGAGGTGTTTCGAGATCTCCCGCGCTCATAGACCCGAC CAACGCCAACTTCTGGTGTGGCCGCCCTGTGTGAGGTGCAGCGTGTCTCCGGTGTGCAACAACCCG AACGTGAGTGCCTGCCGCCACCAGGTGCAGCTGCAGCTGTCAGGTGAGAAAGATCGAGATTGTGCGGA AGAAGCCAATCTTTAAGAAGGCCACGGTGACGCTGGAAGACCACCTGGCATGCAAGTGTGAGACAGTGGC AGCTGCACGGCCTGTGACCCGAAGCCCGGGGGTTCCAGGAGCAGCGAGCCAAAACGCCCAAACCTCGG GTGACCATTGCGACGGTGCAGTCCGCGGCCCCCCAAGGGCAAGCACCGGAAATTCAAGCACACGCATG ACAAGACGGCACTGAAGGAGACCTTGGAGCCTAGGGGCATCGGCAGGAGAGTGTGTGGGAGGGTTATT TAATATGGTATTTGCTGTATTGCCCCCATGGGGTCTTGGAGTGATAATATTGTTTCCCTCGTCCGTCTG TCTCGATGCCTGATTTCGACGGCCAATGGTGTCTCCCCACCCCTCCACGTGTCCGTCCACCCTTCCATC AGCGGGTCTCCTCCCAGCGGCTCCGGCGTCTTGCCAGCAGCTCAAGAAGAAAAAGAGACTGAATC CATCGCCATCTTCTTCCCTTAACTCCAAGAACITGGGATAAGAGTGTGAGAGAGACTGATGGGGTCGCTC TTTGGGGAAACGGGCTCCTTCCCTGCACCTGGCCTGGGCCACACCTGAGCGCTGTGGACTGTCTGAG GAGCCCTGAGGACCTCTCAGCATAGCCTGCCTGATCCCTGAACCCCTGGCCAGCTCTGAGGGGAGGCACC TCCAGGCAGGCCAGGCTGCCTCGGACTCCATGGCTAAGACCACAGACGGGCACACAGACTGGAGAAAACC CCTCCCACGGTGCCCAAACACCAGTCACCTCGTCTCCCTGGTGCCCTCTGTGCACAGTGGCTTCTTTTCGT TTTCGTTTTGAAGACGTGGACTCCTCTTGGTGGGTGTGGCCAGCACACCAAGTGGCTGGGTGCCCTCTCA GGTGGGTAGAGATGGAGTTTGCTGTGAGGTGGCTGTAGATGGTGACCTGGGTATCCCTGCCTCCTGC CACCCCTTCTCCCCACACTCCACTCTGATTACCTCTTCTCTGTTTCTTTCATCTCTTACCTCCAC CCTGATTTTCTCTTGTCTGGCCCTTCAGTCTGCTCCACCAAGGGGCTCTTGAACCCCTTATTAAGGC CCCAGATGATCCAGTCACTCCTCTCTAGGGCAGAAGACTAGAGGCCAGGGCAGCAAGGACCTGCICAT CATATTTCAACCCAGCCACGACTGCCATGTAAGTGTGTGACGGGTGTGTACTGCACAAGGACATTGTATG CAGGGAGCACTGTTACATCATAGATAAAGCTGATTGTATATTTATTATGACAATTTCTGGCAGATGTA GGTAAAGAGGAAAAGGATCCTTTTCTAATTCACACAAAGACTCCTTGTGGACTGGCTGTGCCCTGATG CAGCCTGTGGCTTGGAGTGGCCAAATAGGAGGGAGACTGTGGTAGGGGCAGGGAGGCAACACTGCTGTCC ACATGACCTCCATTTCCCAAAGTCTCTGCTCCAGCAACTGCCCTTCCAGGTGGGTGTGGACACCTGGG AGAAGGTCTCCAAGGGAGGGTGCAGCCCTCTTGCCCGCACCCCTCCCTGCTTGCACACTTCCCCATCTTT GATCCTTCTGAGCTCCACCTCTGGTGGCTCCTCTAGGAAACCAGCTCGTGGGCTGGGAATGGGGGAGAG AAGGGAAAAGATCCCCAAGACCCCTGGGGTGGGATCTGAGCTCCACCTCCCTTCCACCTACTGCACT TTCCCCCTTCCGCTTCCAAAACCTGCTTCTTTCAGTTTGTAAAGTCGGTGATTATATTTTGGGGGCT TTCTTTTATTTTTTAAATGTAAATTTATTTATATTCGTATTTAAAGTTGTAAAAAAAATAACCACA AAACAAAACCAATGAAAAAAAAAAAAAAAAAAAA (SEQ ID NO: 57)</p>			
Translated protein sequence			
<p>MNRCWALFLSLCCYLRLVSAEGDPIPEELYEMLSDHSIRSFDDL QRLHGDPEEDGAELDLNMTRSHSGGELESLARGRSLGLSLTIAEPAMIAECKTRTE VFEISRRLIDRTNANFLVWPPCVEVQRCSCCNRNVQCRPTQVQLRPVQVRKIEIVR KKPIFKKATVTLEDHLACKCETVAAARPVTRSPGGSQEQRAKTPQTRVTIRTVRVRP PKGHRKFKHTDKTALKETLGA (SEQ ID NO: 58)</p>			
PHOSPHO2	493911	NM_001008489	Homo sapiens phosphatase, orphan 2 (PHOSPHO2),

			mRNA
mRNA Sequence			
<p>AACAAGGGAGGTGCTGCAGTTGGCGGTCGGGCTAGAGAAGAGAGGGCGCCTGCCTTGCGAGCTGGGCTTG TGAGTGGGGCTGCCGAGAGGGCAGGCGTGGGGCGAGGCCAAAGGACTGAACCCGAGGAGCGTCACGGGC GCCGGGGCGGCTGCCGACGGCGGGACTGGGTTTTCTATCAGATGTTCCACGTAATAATGCTGGAGTTAAG AAGTTTCCATTATTTTGCTCCAAACCAGAAGACTCTGTTCCCTGTATATAGAATAGGAGTAATATTTGAA AACAAC TGGCTGATGTTTAAACTGAAGATTGCATGATTGTTTATCTAATCCCAATGCTGAAGTAAGA TTGTCTTGAAATACTAAGTTGGGGTAATCCAAATCTATTTCTGGAACCATGAAAATTTTGCTAGTTTTT GACTTTGACAATACAATCATAGATGACAATAGTGACACTTGGATTGTACAATGTGCTCCCAACAAAAGC TTCTATTGAACTACGTGATTCTTATCGAAAAGGATTTTGGACAGAATTTATGGGCAGAGTCTTTAAGTA TTTGGGAGATAAGGGTGTAAAGAGAACATGAAATGAAAAGAGCAGTGACATCATTGCCCTTTCACCTCAGGG ATGGTGGAACCTTCAACTTTTATAAGAAAGAAATAAGGATAAATTTGACTGCATTATTATTTTCAGATTCAA ATTCCGCTCTTCATAGATTGGGTTTTAGAAGCTGCCAGTTTTTCATGACATATTTGATAAAGTGTTTACAAA TCCAGCAGCTTTTAAATAGCAATGGTCATCTCACTGTTGAAAATTATCATACTCATCTTGCAATAGATGC CCAAAGAATCTTTGCAAAAAGGTAGTTTTGATAGAATTTGTAGATAAACAGTTACAACAGGGAGTGAATT ATACACAAATTGTTTATATTGGTGATGGTGGAATGATGCTGTCCAGTCACCTTTTTAAAGAATGATGA TGTTGCCATGCCACGGAAAGGATATACCTTACAGAAAACCTTTCCAGAATGTCTCAAAATCTTGAGCCT ATGGAATATTCTGTTGTAGTTTGGTCCTCAGGIGTTGATATAATTTCTCATTTACAATTTCTAATAAAGG ATTAATATGTCAGCAAAAAAAAAAAAAA (SEQ ID NO: 59)</p>			
Translated protein sequence			
<p>MKILLVDFDNTIIDNSDTWIVQCAPNKKLPIELRDSYRKGFV TEFMGRVFKYLGDKGVREHEMKRAVTSLPFTPGMVELFNFIRKNKDKFDCIIISDSNS VFIDWGLEAASFHDIFDKVFTNPAAFNSNGHLTVENYHTHSCNRCPKNLCKKVVLIIEF VDKQLQQGVNYTQIVYIGDGGNDVCPVTFLNDDVAMPRKGYTLQKTLSRMSQNLPEM EYSVVVWSSGVDIISHLQFLIKD (SEQ ID NO: 60)</p>			
PSENE	55851	NM_172341	Homo sapiens presenilin enhancer 2 homolog (C. elegans) (PSENE), mRNA
mRNA Sequence			
<p>CTCGCCCAAAGAAGACTACAATCTCCAGGGAAACCTGGGGCGTCTCGCGCAAACGTCCTATACTGAAAGT AGCTAAGGCACCCAGCCGAGGAAGTGAGCTCTCCTGGGGCGTGGTTGTTCTGTATCCTTGATCTGTT ACTTAGGGTCAAGGCTTGGGCTTGTCCCGCAGACCTTGGGACGACCCGGCCCCAGCGCAGCTATGAAC CTGGAGCGAGTGCCAATGAGGAGAAATTGAACCTGTGCCGGAAGTACTACCTGGGGGGGTTTGTCTTCC TGCTTTTCTCTGTTTGGTCAACATCTTCTGTTTCTTCCGAGAGGCCTTCTTGTCCAGCCTACACAGA ACAGAGCCAAATCAAAGGCTATGTCTGGCGCTCAGCTGTGGGCTTCTCTTCTGGGTGATAGTGTCAAC TCTTGATCACCATCTTCCAGATCTACCGGGCCCGCTGGGGTGCCCTTGGGGACTACCTCTCTTCAACA TACCCCTGGGCACCCCTGACAACCTTCTGCACATACTGGGGCCCTGCTTATTCTCCAGGACAGGCTCCT TAAAGCAGAGGAGCCTGTCTGGGAGCCCTTCTCAAACTCCTAAGACTTGTTTTCATGTCCACGTTCT CTGCTGACATCCCCCAATAAAGGACCCTAATTTCAAAAAAAAAAAAAA (SEQ ID NO: 61)</p>			
Translated protein sequence			
<p>MNLERVSNEEKLNLCKYYLGGFAFLPFLWLVNIFWFFREAFV PAYTEQSQIKGYVWRSVAGFLFWIVLTSWITIFQIYRPRWGALGDYLSFTIPLGTP (SEQ ID NO: 62)</p>			
SATB1	6304	NM_002971	Homo sapiens SATB homeobox 1 (SATB1), transcript variant 1, mRNA
mRNA Sequence			
<p>TTTCTCGCTCGCTCCCGTTCCCGGACGCGCGGATGAGCCGGCCCCGCTGGGGAAGGCTCCGGGCGGCG GCGGGCGGCGGGAGGAGGCTGCGTGCTCGGGGCTGGGGCTGCGAGCGGGTGATTTTGTATTTAAATGA GGAGGAGGAAGAAGAGGCACCCACAGCGGCAGCGCGGCGGCGGCGGCGGCGAGCAGCAGGAGCAGCGGCG GAGAGGGCTGCAGCCCGGGCGGACGCGCGGAGCCGAGCGGGGACGCGGCGGCGGCGAGCAGCAGCGGCGGG ATGAGTCAACTAATAATTTAATGGGGGACAGAGCGGACGCGAGGGGTAGAGCTAGCGAGGGAGAGAGCGA GAGAAGCAGACCCCGTCCGGGACTCGCGCTCACACTCACGCACACACAAACACACACACCTCTCC TGTGCCACCCAGCAACACCCGGCTCGTCAACAACAACAGCCGCGCCCTCTATCTGCCCCGGG GCCAGCCGAAAAGCCAGGGCGACTCTAGAGGACGCTGCCCGCCCCCTCTTTCAATTCGGGAAACTCCTG</p>			

81

<p>GTCTTAAAGTTTTAAATAGAGAAAATGTGCTTTACACAGTTGCCTATAAAAAGTGCTCTATGTTATCCA AGCAATTCATACTATAAGCTTCACCTCTTATTGTTGATGCAATTTTTACTATCATGCAAAATAGCTTAGG TAAATAAACTAATAGATCACCTTAGAAAAATTATGCAATTAATGTGAAAATAATTGATGTTTGCAATGTG TCTTCCTTTGGTTTACAATCAATTTTAAAGCTACATCTGTATAAAATTTCTGTATAAAGGTGATTCTCT TTTTATGAGTTTATGGCTATGAAAACAGCTATTTTGTACAGCTGGCTGTTTTTATAAGTGATCACAAT TTTCTTTATGCGAGAAATGTTCTGACTAGGAGTGGTTATTGACTGTAACACACAATTAATAATGTTTGTA TCGTATGACATGGTAGGGTTTGTCTGCTTATGTGAAGTAACATAAGGAGTCAAAGGATGGCCCTCTCATT TAGGTGCATGTTAATAACTTGTATTTTCACTGATTTTAAAAAGAGCAATTGACAAGTTACTTGAAACACT GTAAATTTAAATCACAAACACATGCTCATTTTTAAATAGGTATGAAATTCACAATGAAAATAACCTGTT TGGTTAACATTTTGCTTAATAAGTAGAGATAGGATGGTCAAAGACTCTCCGACAAAAACAAATCCAGTC TCTAGCAGTTATGTTGTTAGAATGGA (SEQ ID NO: 63)</p>			
Translated protein sequence			
<p>MDHLNEATQGKEHSEMSNNVSDPKGPPAKIARLEQNGSPLGRGR LGSTGAKMQGVPLKHSGLHMKTNLRKGTMLPVFCVVEHYENAIEYDCKEEHAEFVLVR KDMLFNQLIEMALLSLGYSHSSAAQAKGLIQVGKWNVPVLSYVTDAPDATVADMLQDV YHVVTLKIQLHSCPKLEDLPPEQWSHTTVRNALKDLLKDMNQSSLAKECPLSQSMISS IVNSTYANVSAAKQEFGRWYKHFKTKDMMVEMDSLSELSQQGANHVNFQQPVPG NTAEQPPSPAQLSHGSQPSVRTPLPNLHPGLVSTPISPQLVNQQLVMAQLLNQQYAVN RLLAQQSLNQQYLNHPPVSRSMNKPLEQQVSTNTEVSSEIYQWVRDELKRAGISQAV FARVAFNRTQGLLSEILRKEEDPKTASQSLVNLRAMQNFLQLPEAERDRIYQDERER SLNAASAMGPAPLISTPPSRPPQVKTTATERNKGKPNNTMNNINASIYDEIQQEMKR AKVSQALFAKVAATKSQGWLCCELLRWKEDPSPENRTLWENLSMIRRFSLPQPERDAI YEQESNAVHHGDRPPHIIHVPAEQIQQQQQQQQQQQQQQAPPPPQPQQQPQTGPRL PPRQPTVASPAESDEENRQKTRPRTKISVEALGILQSFIQDVGLYPDEEAIQTLQAQL DLPKYTIKFFQNRYYLKHGKLDNSGLEVDVAEYKEEELLKDLEESVQDKNTNTL FSVKLEEELSVEGNTDINTDLKD (SEQ ID NO: 64)</p>			
SNX11	29916	NM_013323	Homo sapiens sorting nexin 11 (SNX11), transcript variant 2, mRNA
mRNA Sequence			
<p>CCGGCGTCCCAAGTGAGTGGAGGGGGGATCCCGACTCCAGTCCGGGGCCTTGGCCAGCGGAGCCGCGCTA TTCGGAAGCGGGAATCCCACTCAGAGCCCAGGGCCTGTAGGGGCGGGGCGTCCCGGGCACCAGGGATTGGG GCGTCTCCCGTCGTGCACCGGGGCACCGGCGACTCACCCGGAAGGAGAAGCCGTGATCTGCTATAATGGT GGGGCGCGGGCGGTGTCGCTGTGGGGAGCTGGTGCTGTTCTCAGATGTTTCTTCCAATGGGCTTTTGGT GTAGGATGTCGGAGAACCAAGAACAGGAGGAGGTGATTACAGTGCCTGTTTACAGACCCCCGAGTGCAGAA TGAGGGCTCCTGGAACCTTTATGTGGATTATAAGATATTCTTCCATACCAACAGCAAAGCCTTTACTGCC AAGACTTCTGTGTGCGGCGCCGCTACCGTGAGTTCTGTGTGGCTGAGAAAGCAGCTACAGAGAAATGCTG GTTTGGTGCTGTTCTTGAACCTTCTGGGAAGTCAACCTTCTTCGGCACCTCAGATGAGTTTATTGAGAA GCGACGACAAGGTCTGCAGCACTTCTTGAAGGTCCTGCAGAGTGTGGTTCTTCTGTCAGACAGCCAG TTGCACCTATTCTGCAAAGCCAGCTCTCGGTGCTGAGATAGAAGCCTGTGTCCAGGGCCGAAGTACCA TGACTGTGTCTGATGCCATTCTTCGATATGCTATGTCAAAGTGTGGCTGGGCCAGGAAGAGAGGCAGAG CTCTTCTACCTGGCTAAAGGAGAGACCAGCCTAAGAGTTGCTGCTTTCTTCCAAGATCGGGTAGGAGGAGC TCTCCCTCACCGCCTCCAGTGAAGAAAAGGACCATTTAGAAGTGTGGGCTCCAGTTGTTGACTCTGAGG TTCCTTCTTGGAAAGTCCCACTCTCCACCCCTCTCTCACCATTATGCTGTGATTTTGGAAAGACCCAA AGAGGGAACTCCACTCTTCACTGTGTGAGGAGGGCTGTGGGAGGAGATCATGCTGTGCCCTTTGGACCCT GGTCAGTTAGAAACAGTTTTGAAAAGTGAGCTCTGGGTTCTGCTCTGAGATGGTCAGAGAAGATGCGGG CCAGGAGACTTACTCAGGTGGGACTGGGCACAGGGCAGGTATGTGGGAGGCTGGGCTGCTTAGTGTCTTC TAGTCACCTCTGCTTGGGCTGATTGACAGAGGTCAGTCATTACAGCCCCCTATGCCTCTTCCATGGGAAC AAATACTGTGCAGATGTTTGAAGTTAAACATAAGACACAGGGGCTGTGCTTTTGAACAGAACCCTATA TTACTCTCTGGGATCTGAGTTCTGTCAGGTCATTGTATGTAGGACCAGGAGTATCTCTCAGGTGACC AGTTTTGGGGACCCGATGTGCAAAATTCTAAGCTGCCATATTGAACATCATCCCACTGGGAGTGGTTAT GTTGTATCCCCATCTTGGCTGGCTTCAGTTTTTGTCTGTAGCCCTAGAGCACTTTGTTTGTGGGAGGCTGG CCTCTTGCTTACCTCCTTGCAATGGACAGGGGGATGAATATTTACTTTCCACCTCCTTGCTTTTTCTTTC ACTGATACCACTGAATGGAACGGTGTGTGACTCTGTGCTGGGGATTTATGTCCCGAGACCTTAGCC TGGCTGAGTGGAGCCTGAGACCTGCACAACAGCTCATGGTCATGCATGAGAGAGAAGTGGCTGGCCACAG CCAGAGGGAACAGTAACAGCCAGGGGCCCTTTATTTGGGAAAGGCTGTCCCGGGCTGTTACTGTCTCTT CTGTTTATAAAGCAGACATGTGGCCATCTTTCCGAGGGTTAGAGTGGGCTCCTTTCTTTTGGAAATCC</p>			

<p>TTTTCTTCTCCTTTGGTAGCAGCTCCCTGCCTCCAGGGCTTCCGCCACCAGCGTCTCTGCTGTGTTGCGC AGTGCAGTGGGGTGCAAGGGCTTTGTTTCTGCCTGCCTGAAAGAGAGGGCTCTGGGGATGGAGATGAGAA ACAACACGCTCTCCTTCAGACAATGAGGCATTCTGCTCCTGCTGCCATTCTTCATCTCCACTGAGAGC CAGAGCTGGTAGGAGCCGAGTGCCACAGGCATTCTGCATTGCTCTACTCTTAGGTTTGTGTGTGATCC TTCCCCCTCCTGTGCGCCACTCCTCCCTCCTCTGGCTATCCTACCCTGTCTGTGGGCTCTTTTACTACCA GCCTATGCTGTGGGACTGTCAATGGCATTAGTTTCAAGAGTGGAGGGGCTTGGCCTGAAATAAAATGCAAG TATTT (SEQ ID NO: 65)</p>			
Translated protein sequence			
<p>MGFWCRMSENQEQEEVITVRVQDPRVQNEGSWNSYVDYKIFLHT NSKAFTAKTSCVRRRYREFVWLRLKQLQRNAGLVPPELPGKSTFFGTSDEFIEKRRQG LQHFLEKVLQSVVLLSDSQLHLFLQSQLSVPEIEACVQGRSTMTVSDAILRYAMSNCG WAQEERQSSSHLAKGDQPKSCFLPRSGRRSSPSPPPSEEKDHLEVWAPVVDSEVPSL ESPTLPPLSSPLCCDFGRPKEGTSTLQSVRRVGGDHAVPLDPGQLETVLEK (SEQ ID NO: 66)</p>			
SPTA1	6708	NM_003126	Homo sapiens spectrin, alpha, erythrocytic 1 (elliptocytosis 2) (SPTA1), mRNA
mRNA Sequence			
<p>TATGTCTTCTAAAGATAATGTCGATTGTGTATGGCTGATGGGATTCTAGGACCAAGCAAGAGGTTTTTTT TTTTCCCCACATACTTAACGTTTCTATATTTCTATTTGAATTCGACTGGACAGTTCCATTGGAATTATT TCTCTCTCTCTCTCTCTGACACATTTTATCTTGCCAGGTTCTAAACCTTTAGGAAAAATGGAGCAATT TCCAAAGGAAACCGTTGTGGAGAGCAGTGGGCCAAAGGTTTTGGAACAGCAGAAGAGATCCAGGAGAGG CGTCAGGAAGTGTGACTCGGTATCAAAGTTTCAAGGAGCGGGTCGCTGAGAGGGGTGAGAAGCTTGAGG ATTCCTATCACTTACAAGTTTCAAGCGAGATGCAGATGATCTGGGGAAGTGGATCATGGAGAAAGTCAA TATCTTAACCGATAAGAGCTATGAAGACCCAACTAATATACAGGGGAAATATCAGAAGCATCAATCCCTT GAAGCAGAGGTGCAAAACAAAAAACAAGACTCATGTCTGAAGTGGAAAAACAAGGAAGAACGATTTACCA TGGGTCTATTCTGCCACGAAAGAAACGAAGGCCATATAGAGGAGCTACGCCACCTGTGGGACCTGCTGTT AGAGCTGACCCTGGAGAAGGGTGACCAGTTGCTGCGGGCCCTGAAGTTCCAGCAGTATGTACAGGAGTGT GCTGACATCTTAGAGTGGATTGGAGACAAGGAGGCTATAGCGACATCAGTGGAGCTAGGTGAAGACTGGG AGCGCACCGAAGTTCTGCATAAGAAATTTGAAGACTTCCAAGTGGAGCTGGTAGCTAAAGAAGGGAGAGT TGTTGAAGTGAACCAATATGCCAATGAGTGTGCCGAGGAAACCATCCTGACCTACCTTAATTCAGTCT AAGCAAAATGAGGTGAATGCTGCCTGGGAGCGCCTTCGTGGTTTGGCTCTCCAGAGACAGAAAGCTCTGT CCAATGCTGCAAACTTACAACGATTCAAAAGGGATGTGACTGAAGCCATCCAGTGGATCAAGGAGAAGGA ACCTGTACTACCTCTGAGGACTATGGCAAAGACCTTGTTCCTCTGAAGGACTGTTTCACAGTCAACAAG GGACTTGAGAGAAATCTTGCTGTCATGAGTGACAAGGTGAAGGAGTTATGTGCTAAAGCAGAGAAGCTGA CACTTTCCCATCCTTCAGATGCACCTCAGATCCAGGAGATGAAAGAAGATCTGGTCTCCAGCTGGGAGCA TATTCGTGCCCTGGCCACCAGCAGATATGAAAACTGCAGGCTACTTATTTGGTACCATCGATTTTTCATCT GACTTTGATGAACTCTCAGGCTGGATGAACGAGAAGACTGCTGCGATCAATGCTGATGAGCTGCCAACAG ATGTGGCTGGTGGAGAAGTTCTGCTGGACAGGCATCAGCAGCATAAGCATGAGATTGACTCTTACGATGA CCGATTTCAATCTGCTGATGAGACTGGTCAAGACCTCGTGAATGCCAATCATGAAGCCTCTGATGAAGTT CGGGAAAAGATGGAAATACCTTGACAACAACGGACTGCCCTGCTGGAACGTGGGACGAGCGTCATCGTC AGTATGAGCAGTGTCTGGACTTTCATCTCTTACAGAGACAGTGAAGTGGACAGTTGGATGAGTAG ACAAGAGGCCTTCTGGAAAACGAGGATCTGGGAACTCACTGGGCAGTGCAGAAGCCCTTCTTCAGAAG CATGAAGACTTTGAGGAAGCCTTACTGCCCCAGGAAGAGAAGATCATAACTGTAGACAAGACTGCAACCA AATTGATTGGTGATGACCATTATGATTAGAGAACATCAAGGCTATCCGTGACGGGCTGTAGCCCCGGCG GGATGCCCTACGTGAAAAGGCTGCCACTAGACGTAGATTGCTGAAGGAGTCAATTGCTTCTGCAAAAACTG TATGAGGACTCAGATGACCTAAAGAACTGGATCAACAAGAAGAAAAAGTTGGCAGATGATGAAGATTACA AGGACATACAGAACTTGAAGAGCAGGGTTCAAAGCAGCAAGTCTTTGAAAAGGAGTTGGCAGTTAATAA GACCCAGCTGGAAAACATACAGAAAACGGCCAAAGAGATGATTGAGGGTGGTCACTATGCCTCTGACAAT GTGACCACTCGTCTGAGTGAAGTTGCCAGCCTCTGGGAGGAGTTGCTGGAGGCTACAAAACAGAAAGGGA CCCAGTTGCATGAGGCCAACCAGCAGCTGCAATTTGAAAATAATGCAGAAGATTTGCAGCGCTGGCTGGA GGATGTTGAGTGGCAAGTCACCTCTGAGGATTATGGGAAAGGCCTGGCCGAGGTACAGAAATCGACTCAGG AAACACGGCCTCCTGGAGTCGGCTGTGGCTGCTCGTCAGGATCAGGTGGATATCCTTACAGACCTGGCTG CATATTTTGAAGAAATAGGCCATCCTGATTCTAAGGATATAAGGGCAAGGCAAGAGTCCTTGGTATGCCG ATTTGAAGCTCTGAAAGAGCCACTGGCCACCCGAAAGAAGAAGCTCTTAGACCTTCTCCATCTGCAGCTG ATTTGTAGAGACACAGAGGATGAGGAGGCTGGATCCAAGAGACTGAACCTCAGCTACTTCCACCTACC TTGGAAGGACCTGATTGCTTCCAAAAGCTTCTGAATAGGCATAGAGTCATCCTGGAGAACATTGCCAG CCATGAACCACGCATTCAAGAGATAACAGAAAGGGGAAACAAAATGGTAGAGGAAGGACACTTGTGCA GAAGATGTGGCCTCTAGGGTCAAGAGTTTGAACCAGAATATGGAGTCTCTCCGTGCTCGAGCTGCTAGGC</p>			

GACAAAATGATCTTGAAGCCAATGTCCAGTTCAGCAGTACCTGGCTGACCTGCATGAAGCAGAAACATG
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 GTGAGTGAAGAGACTCTAAAGGAATTTAGCACAATCTATAAACACTTTGATGAGAATTTGACAGGGCGCC
 TGACTCACAAGAGTTCCGGTCTGCTGAGAGGACTCAATTACTACTTGGCCATGGTGGAGGAGGATGA

			(TMEM79), transcript variant 1, mRNA
mRNA Sequence			
AGGTTTTGAGACACAGGTAAAGGGAGGGAGACAGAGAGAAATACTTGCAGAGCCAGCAGGTAGCTGGGCA GCTCCTTCCCGGACGGACGGATGGACAGACGCTGGGGACCCTCCACTCCATATGGAAGATGACATGACC TTGTGGTAGATCCCAGAACTGAGGCCCCAGGATGACAGAACAGGAGACCCTGGCCCTACTGGAAGTGAAG AGGTCTGATTCCCCAGAGAAGAGCTCACCCCAGGCCCTTGGTTCCCAATGGCCGGCAGCCAGAAGGGGAAG GTGGGGCCGAATCCCCGGGAGCTGAGTCCCTCAGAGTGGGGTCTTCAGCTGGATCTCCACAGCCATAGA GGGGGTGAGGATGGTCTAGACAGCACAGTAAGTGAGGCTGCCACCTTGCCCTGGGGGACTGGCCCTCAG CCCAGTGTCCGTTCCCGGATCCCCCTGGCTGGCGGGACATTGAACCAGAGCCCCCTGAGTCAGAACCCAC TTACCAAGCTAGAGGAGCTGCCCCAAGACGATGCCAACCTGCTGCCTGAGAAAGCGGCCCCGTGCCTTCGT GCCTATTGACCTACAGTGCATTGAGCGGCAGCCCCAAGAAGACCTTATCGTGCGCTGTGAGGCAGGCGAG GGCGAGTGCCGAACCTTCATGCCCCCCCCGGGTACCCACCCCGACCCCACTGAGCGCAAGTGGGCTGAGG CAGTGGTGAGGCCCGCTGGCTGTTCTGTGGGGGTGCGGGAGCTGTGGAGACCGTGAGTGGCTAAGGGC TGTGGCTCCGTTGGGAGCCGCACTCATTTCTCTCCCTTGCCCTACTATACGGGGCATATGCCTTCCTGCCG TTTGATGTCCACAGGCTGCCCACCATGAGTTCCTCGCTGATCTACACACTGCGCTGCGGGGTCTTTGCCA CCTTCCCCATTGTGCTGGGGATCCTGGTGTACGGGTGAGCCTGTTATGCTTTTCTGCCCTTCGGCCCTT TGGGGAGCCACGGCGGGAGGTGGAGATCCACCGCGATATGTGGCCAGTCGGTCCAGCTCTTTATTCTC TACTTCTTCAACCTGGCCGTGCTTTCCACTTACCTGCCCCAGGATACCCCAAACCTGCTCCCTCTGCTCA CTGCTCTCTTTGCCGTCTCCCGGTGATCTACIGGCTGACCTTTGCCGTGGGCCGCTCCTTCCGAGGCTT CGGCTACGGCCTGACGTTTCTGCCACTGCTGTGATGCTGTGTAACCTCTACTACATGTTCTGTTG GAGCCGGAGCGCATGCTCACTGCCACCGAGAGCCGCTGGACTACCCGACCAAGCCGCTCGGCCCTCCG ACTACAGGCCCGCCCCCTGGGGCTGAGCCTCTCCGCCCTCGCCCTCGGAGTAGGGGTAGCGGCTTGGGT CTGACACATCTTTGAACCTTGTGGCCAGGCTTGACTTCGCCCCAGGCTAGGACCGCGGTGGGTGGAA CCCTGCTACTGCCCCAACAGGGACTCCAATCAATCGGAGTTCTCCCTTGCCGGAGCTGCCCTTACCTT TGGGGCCCCGAGACAGTCATAAGGGATGGAAGTATGTTTCTTGCAGGGAAAAAGGTGGACAGCCGTGTTTC TTAAGGATGCTGAGGGCATGGGGCCAGGACCAGGGGAGAGGCACAGCTCCTTCCTGAGCAGCCTCTCACC ACTGCCACAAGGCTCCCTAATGCTGGTCTCTGCTCCACTCCCCGGCTTCCCGTGAGGCAGGAGGCAGAGC CACAGCCAAGGCCCTGACCACTTCTGTGCCAGTTGTCTAAGCAGAGCGCCTCAGGGACGCTGGAAATGCC TTAAGGATAGAGGCTGGGCATCACATCAAATGGGACTGTGGTGTGTTGGTGAAAACCTTCTGAGGATCTG GATTACAGGACCTCCATGACTGGCCTATTTACGTTTACAGCTGGCCAGTGACAGCTGCTGCTCTTTTA CCTTTTTAGGCCCTGTAACTTCCACCTTTAACTGCCAGAGGATGCCTCTCCACAGGAAGAGGG GAGCAGACAGGGAAATCTGCCTACCAAGAGGGGTGTGTGTGCTTTGTGCCACACGTGGTGGCTGGGGA GTGCCTGGATGGTGCAGTGGTTGATGTTAACCTAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT GTGTGTGTGTAACAATAAATTACTACCAGTCAAAAAAAAAAAAAA (SEQ ID NO: 69)			
Translated protein sequence			
MTEQETLALLEVKRSDSPEKSSPQALVPNGRQPEGEGGAESPGA ESLRVGSSAGSPTAIEGAEDGLDSTVSEAATLPWGTGPQPSAPFPDPPGWRDIEPEPP ESEPLTKLEELPEDDANLLPEKAARAFVPIDLQCIERQPQEDLIVRCEAGEGECRTFM PPRVTHPDPFTERKWAEAVVRPPGCSGCGSGCDREWLRAVASVGAALILFPCLLYGA YAFLPFDVPRLPMTSSRLIYTLRCGVFATFPFIVLGILVYGLSLLCFSAIRPFGEPRRE VEIHRRYVAQSVQLFIFYFNLAVLSTYLPQDTLKLPLLTGLFAVSRLIYWLTFVVG RSFRGFGYGLTFLPLLSMLMWNLYMFVVEPERMLTATESRLDYPDHARSASDYRPRP WG (SEQ ID NO: 70)			
TMIGD2	126259	NM_144615	Homo sapiens transmembrane and immunoglobulin domain containing 2 (TMIGD2), mRNA
mRNA Sequence			
GGAAGTCTGTCAACTGGGAGGGGGAGAGGGGGGTGATGGGCCAGGAATGGGGTCCCCGGGCATGGTGCTG GGCCTCCTGGTGAGATCTGGGCCCTGCAAGAAGCCTCAAGCCTGAGCGTGACAGAGGGGCCAACTTGC TGCAGGTGAGGCAGGGCAGTCAGGCGACCCCTGGTCTGCCAGGTGGACCAGGCCACAGCCTGGGAACGGCT CCGTGTTAAGTGGACAAAGGATGGGGCCATCCTGTGTCAACCGTACATACCAACGGCAGCCTCAGCCTG GGGGTCTGCGGGCCCCAGGGACGGCTCTCCTGGCAGGCACCCAGCCATCTCACCTGCAGCTGGACCCTG TGAGCCTCAACCACAGCGGGCGTACGTGTGCTGGCGGCCGTAGAGATTCTGAGTTGGAGGAGGCTGA GGGCAACATAACAAGGCTCTTTGTGACCCAGATGACCCACACAGAACAGAAACCGGATCGCAAGCTTC CCAGGATTCTCTTCTGTGCTGCTGGGGGTGGGAAGCATGGGTGTGGCTGCGATCGTGTGGGGTGCTGGT TCTGGGGCCGCCGAGCTGCCAGCAAAGGGACTCAGGTAACAGCCCAGGAAATGCATTCTACAGCAACGT			

CCTATACCGGCCCCGGGGGGCCCCAAAGAAGAGTGAGGACTGCTCTGGAGAGGGGAAGGACCAGAGGGGC CAGAGCATTATTCAACCTCCTTCCCGCAACCGGCCCCCGCCAGCCGACCTGGCGTCAAGACCCGTGCC CCAGCCCGAGACCCTGCCCCAGCCCCAGGCCCGGCCACCCCGTCTCTATGGTCAGGGTCTCTCTAGACC AAGCCCCACCCAGCAGCCGAGGCCAAAAGGGTTCCTCCAAAGTGGGAGAGGAGTGAGAGATCCCAGGAGAC CTCAACAGGACCCCCACCCATAGGTACACACAAAAAGGGGGGATCGAGGCCAGACACGGTGGCTCACGCC TGTAATCCCAGCAGTTTGGGAAGCCGAGGCGGGTGGAAACACTTGAGGTCAGGGGTTTGGAGCCAGCCTGG CTTGAACCTGGGAGGCGGAGGTTGCAGTGAGCCGAGATTGCGCCACTGCACTCCAGCCTGGGCGACAGAG TGAGACTCCGTCTCAAAAAAACAAAAAGCAGGAGGATTGGGAGCCTGTCAGCCCCATCTGAGACCCCG TCCTCATTCTGTAAATGATGGATCTCGCTCCCACTTTCCCCCAAGAACCTAATAAAGGCTTGTGAAGAAA AAGCAAAAAAAAAAAAAAAAAA (SEQ ID NO: 71)			
Translated protein sequence			
MGSPGMVLGLLVQI WALQEASSLSVQQGPNLLQVRQGSQATLVC QVDQATAWERLRVKWKD GAILCQPYITNGSLSLGVC GPQGRLSWQAPSHLTLQLDPV SLNHSGAYVCWAAVEIPELEEAEGNITRLFVDPDDPTQNRNRIASFPGFLFVLLGVGS MGVAAI VWGAWFWGRRSCQQRDSGNSPGNFYSNVLYRPRGAPKKSEDCSGEGKDQRG QSIYSTSFQ PAPRQPHLASRPCSPRPCSPRPGHPVSMVRVSPRPSPTQQPRPKGF PKVGEE (SEQ ID NO: 72)			
TUBB6	84617	NM_032525	Homo sapiens tubulin, beta 6 (TUBB6), mRNA
mRNA Sequence			
GGGCACGAGGGCAGAGCCAGTTCTTAGCGCAGAGCCGCGCCCGCCATGAGGGAGATCGTGCACATCCAGG CGGGCCAGTGC GGGAACCAGATCGGCACCAAGTTTGGGAAGTGATCAGCGATGAGCACGGCATCGACCC GGCCGGAGGCTACGTGGGAGACTCGGCGCTGCAGCTGGAGAGAATCAACGTCTACTACAATGAGTCATCG TCTCAGAAAATATGTGCCAGGGCCGCCCTGGTGGACTTAGAGCCAGGCACCATGGACAGCGTGC GGCTCTG GGCCTTTTGGGCAGCTTTTCCGGCTGACAACITCATCTTTGGCCAGACGGGTGCAGGGAACAACCTGGGC GAAAGGGCACTACACGGAGGGCGCGGAGCTGGTGGACGCAGTGCTGGACGTGGTGC GGAAGGAGTGC GAG CACTGCGACTGCCTGCAGGGCTTCCAGCTCACGCACTCGCTGGGCGGCGGCACGGGCTCAGGCATGGGCA CGCTGCTCATCAGCAAGATCCGTGAGGAGTTCCCGGACCGCATCATGAACACCTTCAGCGTCATGCCCTC GCCCAAGTGTCGGACACGGTGGTGGAGCCCTACAATGCCACACTGTCGGTGCACCAGCTGGTGGAGAAT ACAGACGAGACCTACTGCATCGACAACGAGGCGCTCTATGACATCTGCTTCCGCACTCTGAAGCTGACAA CGCCACCTACGGGGACCTCAACCACCTGGTGICCGCCACCATGAGTGGGGTCACCACCTCGCTGCGCTT CCCGGGCCAGCTCAATGCTGACCTGCGCAAGCTGGCGGTGAACATGGTGCCTTCCCGCGCTGCACTTC TTATGCTGGCTTCGCGCCGCTCACCAGCCGCGGCAGCCAGCAGTACCGGGCCCTGACCGTGCCCGAGC TCACCCAGCAGATGTTTCGACGCCAGGAACATGATGGCCGCTGCGATCCGCGCCATGGCCGCTACCTGAC CGTGGCCACCGTGTTCCGCGGGCCCATGTCCATGAAGGAGGTGGACGAGCAGATGCTGGCCATCCAGAGT AAGAACAGCAGCTACTTCTGTGGAGTGGATTCCCAACAACGTGAAGGTGGCCGTGTGCGACATCCCGCCCC GCGGCTGAAGATGGCCTCCACCTTCATCGGCAACAGCACGGCCATCCAGGAGCTGTTCAAGCGCATCTC CGAGCAGTTCTCAGCCATGTTCCGGCGCAAGGCTTCTCTGCACTGGTTACGGGTGAGGGCATGGATGAA ATGGAGTTCACCGAGGCGGAGAGCAACATGAACGACCTGGTATCCGAGTACCAGCAGTACCAGGATGCCA CCGCCAATGACGGGGAGGAAGCTTTTGAGGATGAGGAAGAGGAGATCGATGGATAGTCGGAATAGAGCCG CCCCAACTCAGATCTTACAACACGCAAGTTCTTCTGAACCTGGTGCCTCTACCTATGGCCCTGAA TGGTGCCTGTTTAAATTGTGTTGGTGTGCGCCCCTCACAAATGCAGCAAGTCATGTAATTAGTCATCT GGAACAAAGACTAAAAACAGCAGAGAATTGCGGGTCTACCCAGTCAGAAGATCACACCATGGAGACTTT CTACTAGAGGACTTGAAAGAGAACTGAGGGGCCACAAAATAAACTTCACCTTCCATTAAAGTGTTCAGCA TGTCTGCAAATTAGGAGGGAGTTAGAAACAGTCTTTTTCATCCTTTGTGATGAAGCCTGAAATTGTGCCG TGTTGCCCTTATATGAATATGCAGTATGGGACTTTGAAATAATGATTCAATAATAAATACTAAACGTGTGT CTTCAAAAAAAAAAAAAAAAAA (SEQ ID NO: 73)			
Translated protein sequence			
MREIVHIQAGQCGNQIGTKFEVISDEHGIDPAGGYVGDSALQL ERINVYNESSSQYVPRAALVDLEPGTMDSVRS GPFQ LFRPDNFIFGQTGAGNNWA KGHYTEGAELVDAVL DVVRKECEHCDCLQGFQLTHSLGGGTGSGMGTLLISKIREEF DRIMNTFSVMPSPKVSDTVVEPYNATLSVHQLVENTDETYCIDNEALYD ICFRTLKLT TPTYGDLNLHVSATMSGVTSLRFPQQLNADLRKLAVNMVFPRLHFFMPGFAPLTSR GSQQYRALTVPELTQQMFDARNMMAACDPRHGRYLT VATVFRGPMSMKEVDEQMLAIQ SKNSSYFVEWIPNNVKVAVCDIPPRGLKMASTFIGNSTAIQELFKRISEQFSAMFRRK AFLHWFTEGEMDEMEFTEAESNMNDLVSEYQQYQDATANDGEEAFEDEEEIDG (SEQ ID NO: 74)			
TYROBP	7305	NM_198125	Homo sapiens TYRO protein tyrosine kinase

			binding protein (TYROBP), transcript variant 2, mRNA
mRNA Sequence			
AGACTTCCTCCTTCACTTGCTGGACGCTGCGCCACATCCCACCGGCCCTTACACTGTGGTGTCCAGCAG CATCCGGCTTCATGGGGGACTTGAACCTGCAGCAGGCTCCTGCTCCTGCCTCTCCTGCTGGCTGTAAAG TGGTCTCCGTCCTGTCCAGGCCAGGCCAGAGCGATTGCAGTTGCTCTACGGTGAGCCCGGGCGTGCTG GCAGGGATCGTGATGGGAGACCTGGTGCTGACAGTGCTCATTGCCCTGGCCGTGTACTTCTGGGCCGGC TGGTCCCTCGGGGCGAGGGGCTGCGGAGGCGACCCGAAACAGCGTATCACTGAGACCGAGTGCCTTA TCAGGAGCTCCAGGGTCAGAGGTCGGATGTCTACAGCGACCTCAACACACAGAGGCCGTATTACAAATGA GCCCCAATCATGACAGTCAGCAACATGATACCTGGATCCAGCCATTCTGAAGCCACCTGCACCTCAT TCCAACTCTACCGGATACAGACCCACAGAGTGCCATCCCTGAGAGACCAGACCGCTCCCAATACTCT CCTAAATAAACATGAAGCACAAAAACAAAAA (SEQ ID NO: 75)			
Translated protein sequence			
MGGLEPCSRLLLLPLLLAVSGLRPVQAQAQSDCSCSTVSPGVLA GIVMGDLVLTVLIALAVYFLGRLVPRGRGAAEATRKQRITETESPYQELQGQRSDVYS DLNTQRPYYK (SEQ ID NO: 76)			
YTHDF1	54915	NM_017798	Homo sapiens YTH domain family, member 1 (YTHDF1), mRNA
mRNA Sequence			
GCGTGACGCTGACGCCGCGCAGTCTCGTCCCTGCCGCCGCCGTCGCCGCTGCTGTGCCGCCGCCGCC GCCATTGGAGTCGACGCCCTCTCAGTGCGTCCGCGTCCCGGGCTCACCGCCGCTGCCGCCTCGCCAGGG CCCGCGCGCCAGCAGCCGCCGCCGCCGCCGCCGCCGGCGCCCGGGGAATTGGCGCGGGGCGCCGGGGCCG CGCGAGCTAGGGTGACAGGCCCGGCTCTAGGGGAGGCCGAGCCGGCGGGCGCCCGGCCCGCGCTCTA GTTGTTTCATGAAGCATGTCGGCCACCAGCGTGGACCCAGAGAACAAAAGGACAAGATAATAAAGTACA AATGGTTCGTTACATCAGAAGGATACAGTTATGACAATGACTTTGAGCCCTACCTTACTGGACAGTCA AATCAGAGTAACAGTTACCCCTCAATGAGCGACCCCTACCTGTCCAGCTATTACCCGCCGTCCATTGGAT TTCTTACTCCCTCAATGAGGCTCCGTGGTCTACTGCAGGGGACCCCTCCGATTCCATACCTCACCACTA CGGACAGCTCAGTAACGGAGACCATCATTTTTATGCACGATGCTGTTTTTGGGCAGCCTGGGGCCTGGGG AACAACATCTATCAGCACAGGTTCAATTTTTTCCCTGAAAACCCTGCGTTCTCAGCATGGGGACAAGTG GGTCTCAAGGTCAGCAGACCCAGAGCTCCGCGTATGGGAGCAGCTACACCTACCCCCGAGCTCCCTGGG TGGCACGGTGGTTGATGGGCAGCCAGGCTTTACAGCGACACCCTCAGCAAGGCCCGCGGATGAACAGC CTGGAGCAGGGCATGGTTGGCCTGAAGATTGGGGACGTCAGCTCCTCCGCCGTCAGACGGTGGGCTCTG TCGTACAGCAGCGTGGCACTGACTGGTGTCTTTCTGGCAACGGTGGGACAAATGTGAACATGCCAGTTTC AAAGCCGACCTCGTGGGCTGCCATTGCCAGCAAGCTGCAAAACCACAGCTAAAATGAAACAAAGAGC GGGCCTGTCTAGGGGGTGGGCTGCCCCCTCCACCCATAAAGCATAAATGGACATTGGACCTGGGATA ACAAGGGGCTGTGCCGAAGGCCCCAGTCCCCCAGCAGGCACCCTCTCCACAGGCTGCCCCACAGCCCCA GCAGGTGGCTCAGCCTCTCCAGCACAGCCCCAGCTTTGGCTCAACCGCAGTATCAGAGCCCTCAGCAG CCACCCGAGCCCGCTGGGTTGCCCCACGCAACAGAAACGCGGCGTTTGGGCAGAGCGGAGGGGCTGGCA GCGATAGCAACTCTCTGGAAACGTCCAGCCTAATCTGCCCCACAGCGTCGAATCCCACCCCGTCTTGA AAACTGAAGGCTGCTCAGACTACAACCCGAAAGAGTTTGAGTGGAACTGAAAAGCGGGCGTGTGTTT ATCATCAAGAGCTACTCTGAGGACGACATCCACCGCTCCATTAAGTACTCCATCTGGTGTAGCACAGAGC ACGGCAACAAGCGCTGGACAGCGCTTCCGCTGCATGAGCAGCAAGGGGCCGCTTACCTGCTCTTCAG CGTCAATGGGAGTGGGCATTTTGTGGGGTGGCCGAGATGAAGTCCCCCGTGACTACGGCACCAGTGCC GGGCTCTGGTCTCAGGACAAGTGGAAGGGGAAGTTGATGTCCAGTGGAATTTTGTAAAGATGTACCCA ATAACCAGCTCCGGCACATCAGGCTGGAGAATAACGACAACAAACCGGTCAAACTCCCGGGACACCCA GGAGGTGCCCTTAGAAAAAGCCAAGCAAGTGCTGAAAATTATCAGTTCTACAAGCACACAACCTCCATC TTCGACGACTTTGCTCACTACGAGAAGCGCCAGGAGGAGGAGGTGGTGCAGCAAGGAACGGCAGAGTC GAAACAAACAATGAGGGCGAACCAAGTTTCTTACATGTTCTAACGTTTGACTTTGAAAACAGTTTAAACA CGTGTGCTTGGTCAGCTCCAGTGTGTGCTCCCGTGCAGGGGTTGAGTGTGCATCTTTGCCTTTCTTGTC GTTGATTTTTGCCCAGATGGATCTGCATTTATTTGTACTTTTTCTATGTATTATAATCCTGTAGAAGTCA CTAATAAAGGAGTATTTTTTTGTGAGCTTATCAATCAGACTGATCTAATGTGAAATGTAAGTATCCTTA AAAACAAAGCATCTATTTTGGCAGAAATGTGTCTTAAATTCAGTCATTTGATATTCTGTGAGACTTCA TATTTCTCATCCCTTTATTGCTTTTGTAGCAACATAAGAAACCATGAGTCATTTTGTCTTTAGAGTATT CTGATAAAATCTCTTGAATACTGAAATCAAAAGGTTAATGATTTTTTGTTCATTCTGATTGTGATTT TATTATCTGTTATCGGTCTAAAGTGCTAATTTACCCATTTGATTTTTCTGCTAGACAGATAACTTTTAAAT			

SUBSTITUTE SHEET (RULE 26)

GAATTTATTATTAATAATAATAAGTGAATAATAAGTGGGAGTCCTTGGACCACATCCTAACCTGAGACA
 ATGCCGAGCCTGAGACAAACCCGTGACTCAGACTTGCCACCGGGTCTAATTAGCCCTATTATTTCAGTAT
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 AAAAAACAAACAAAAACAACCAAGCTGGACTTGTACATTGCAGGAGGATGGGGCTGGGGGCAAAATGTA
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 CAGCACCAAGGCCCTCTGCATTTCCAGAGTGCTCTCAAATGCCTTTGACACCATAACCATGGGCTGCTT
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 CAACAGATCCTGTTCCGTACCTGTGTCCAAAAACATTTGTAAAAACCCCTTTGAGTTTAATATTGTAAAT
 TTTAATTTCCACTCTTTTATTACTGATCTTAGCTTAATACAATATTTTATACAGGATTATTCTTCAGT
 ATCCTACTGTGTGATTTTTAAAAAAGATGCAGCAACCTTAATATATCTCCATATCTTGTGCTACTGTGAT
 TGTTCAAGCAAAAGTGGAGAGAAGAAAAGCTGCTGCAAAAGACAACGTGAAACTGTGATATTTATAAAA
 ATAGAAGAAATTCAGTGCTTTCTTTTTTCTATATGTTTTTTTTTTTTTATCTGAATTCAGATACTGC
 CTCCTAACTGTGTCCAAACTTCTTGTGTAATAAGAGATTCTGTTTTTCGATCCTAAGTTCTTTGGGATGC
 CAACATTACAGTCAAGTCTTGAGGAGGTGTGATGATGGCATCATGCCTATTTTTTTGGAAAGCTGTTGT
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 GAAACTGCATTTTAATGCATTTCTTCCACCTGAGCACTGAGCACACCAAACCTGGAATCCATTTGAAAAAT
 GACAGTGTGTGAAGTGTATGATTTACATTAAAAAGAGGGGAGGGAGTTGCCATACATATAAAAATTTTTA
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 AAAGGTCAAGGACCTAGGACAATAACTCTTAGTCGATTTATTTTCGGTTGGTACAACACATCTCCTGTGC
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 GACACCCCTCCCCAGGGTTTGTAGAAATTTGTTTTGTGTGCTGTGAGTGGTTGATGTAGTCTTGTCAAT
 GTTAATAACTTGTATGTGAACACTATTATTTGTACAGTTGAATTAATTTATTTTCAGACATCATCTTTT
 TTTTTTCTTCTTGAAGAGTTCAAAGCACACCAAAGAATTATATTATACATTTTGGTGAAAGATTGTC
 ATTTATGATCCATGGTTTATTTAAAAAAGGAAAGAAAATGGAAAAATATATTTTAAAGCTTACTTG
 AATGAACAACGTAATGTGAAAACCAAGACTCTTCTGCATGTCTTTTTTGCATTGTGTTGATAAGATTAT
 ATATAGTTTATAGATATATTATATTACTAGTACAGTGCATGGTGTGCTCACTTGGAAAGCCTTCAATGT
 TGTCTTCAGATTGTTGTGATGAATATGAAACATGCAGACCCTCCTTTATAAAGAAAAAGACCTTAAACT
 TGAATATGAGATAATTTTACATTTTAAAGTTTATTTGATTTTCATATTATTCATTTCAAAGCCCTTTC
 AAATAGAAAAGGTATGAACTTTGGGGGGATAATTTATGTATCGTAACTTATTAGAACAAAATATTCCT
 GATGTATAATGAGTTGTTTTATTTATACAACCTTTTCAATGGTAGTTTGCACTATTCTTTATTATGCTAC
 AGGTTTATTATTATGAAACAAAGGAATATGTATTTATGTATTTTACCATGCATAGGTAACTCTTTGC
 CACAGATTTATTGGTCTTGTATACACCTAAATAAAAAAATGTGTACCTCCAATAGAGAGCAAGCAAG
 AATGATTATGAAGTAACAAATTTAATAAAGGTATTCTTGTATTATTAAAAA (SEQ ID NO: 79)

Translated protein sequence

MFLKAGRGNKVPPVRVYGPDCVVLMEPPLSKRNPPALRLADLAT
 AQVQPLQNMGTGFPALAGPPAHSQLRAAVAHLRLDLGADPGVATTPLGPEHMAQASTL
 GLSPPSQAFPAHPEAPAAAAAALVAHPGAGSYPCGGSSGAQPSAPPPAPPLPPT
 PSPPPPPPPPPALSGYTTNSGGGGSGKGHSRDFVLRDLSATAPAAAMHGAPLG
 GEQRSGTGSPQHPAPPPHSAGMFIASGTYAGPDGSGGPALFPALHDTGAPGGHHP
 LNGQMRLGLAAAAAAAEELYGRAEPPFAPRSGDAHYGAVAAAAAALHGYGAVNLNL
 NLAAAAAAGPGPHLQHHAPPPAPPPPPAPAQHPHQHHPHPLGAAGAFRLYMRQPI
 KQELICKWIDPELAGLPPLPPPPPPPPPPAGGAKPCSKTFGTMHELVNHVTVHEV
 GGPEQSSHVCFWEDCPREGKPFKAKYKLINHIRVHTGEKPFPCFPFGCGKVFARSEN
 KIHKRHTHGEKPFKCEFDGCDRKFANSSDRKKHSHVHTSDKPYCKIRGCDKSYTHPS
 SLRKHMKIHCKSPPPSPGPLYSSVGTVPVGLPSVLDPARSHSSTLSPQVTNLNEWY
 VCQASGAPSHLHTPSSNGTTSETEDEEIIYGNPEVVRTIH (SEQ ID NO: 80)

CLAIMS

What is claimed is:

- 5 1. A method for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat a subject having breast cancer, the method comprising
- determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1 in a sample derived from said subject, wherein a low level
- 10 of expression of the biomarker is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, will be effective in treating said subject.
2. A method for determining whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat a subject having breast
- 15 cancer, the method comprising
- assaying a sample derived from said subject to determine the level of expression in said sample of a biomarker selected from the group of biomarkers listed in Table 1, wherein a low level of expression of the biomarker is indicative that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, will be effective in treating said
- 20 subject.
3. A method for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat a subject having breast cancer, the method comprising
- 25 determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1 in a sample derived from said subject, and
- predicting that eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, will be effective in treating a subject having breast cancer when said sample is determined to have a low level of expression of said biomarker.
- 30 4. A method for determining the sensitivity of a breast tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, the method comprising

determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1 in said tumor, wherein a low level of expression of the biomarker in said tumor indicates that said tumor is sensitive to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof.

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5. A method for determining the sensitivity of a breast tumor to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, the method comprising

determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1 in said tumor, and

identifying said tumor as being sensitive to treatment with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, when there is determined to be a low level of expression of said biomarker in said tumor.

6. The method of claim 4 or 5, wherein a sample of the breast tumor is obtained from a subject having breast cancer.

7. A method of treating a subject having breast cancer, the method comprising

identifying a subject having breast cancer in which a biomarker selected from the group of biomarkers listed in Table 1 has a low level of expression, and

administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, to said subject.

8. A method of treating a subject having breast cancer, the method comprising

assaying a sample derived from said subject to determine the level of expression in said sample of a biomarker selected from the group of biomarkers listed in Table 1, and

administering a therapeutically effective amount of eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, to said subject when a low level of expression of the biomarker is detected in said sample.

9. The method of any one of claims 1-8, wherein the pharmaceutically acceptable salt of eribulin is eribulin mesylate.

5 10. The method of any one of claims 1-3 or 6-8, wherein said subject has not been previously treated with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof.

10 11. The method of any one of claims 1-3 or 6-8, wherein said subject has been previously treated with eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof.

12. The method of any one of claims 1-3 or 6-8, wherein said breast cancer is an Estrogen Receptor (ER) negative breast cancer.

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13. The method of any one of claims 1-3 or 6-8, wherein said breast cancer is a Progesterone Receptor (PR) negative breast cancer.

14. The method of any one of claims 1-3 or 6-8, wherein said breast cancer is a HER-2 negative breast cancer.

20

15. The method of any one of claims 1-3 or 6-8, wherein said breast cancer is an Estrogen Receptor (ER) negative and Progesterone Receptor (PR) negative breast cancer.

25

16. The method of any one of claims 1-3 or 6-8, wherein said breast cancer is an Estrogen Receptor (ER) negative and HER-2 negative breast cancer.

17. The method of any one of claims 1-3 or 6-8, wherein said breast cancer is a Progesterone Receptor (PR) negative and HER-2 negative breast cancer.

30

18. The method of any one of claims 1-3 or 6-8, wherein said breast cancer is an Estrogen Receptor (ER) negative, Progesterone Receptor (PR) negative and HER-2 negative breast cancer.

5 19. The method of any one of claims 1-8, wherein at least 2 biomarkers selected from the group of biomarkers listed in Table 1 have a low level of expression

20. The method of any one of claims 1-8, wherein the level of expression of at least 3 biomarkers selected from the group of biomarkers listed in Table 1 have a low
10 level of expression.

21. The method of any one of claims 1-8, wherein the level of expression of at least 4 biomarkers selected from the group of biomarkers listed in Table 1 have a low level of expression.

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22. The method of any one of claims 1-8, wherein the level of expression of at least 5 biomarkers selected from the group of biomarkers listed in Table 1 have a low level of expression.

20 23. The method of any one of claims 1-8, wherein there is a low level of expression of said biomarker as compared to a control.

24. The method of claim 23, where said biomarker is not expressed at a detectable level.

25

25. The method of any one of claims 1-8, wherein the level of expression of said biomarker is determined at the nucleic acid level.

26. The method of claim 25, the level of expression of said biomarker is
30 determined by detecting cDNA.

27. The method of claim 25, the level of expression of said biomarker is determined by detecting mRNA or miRNA.

28. The method of claim 25, the level of expression of said biomarker is
5 determined by detecting DNA.

29. The method claim 25, wherein the level of expression of said biomarker is determined by using a technique selected from the group consisting of polymerase chain reaction (PCR) amplification reaction, reverse-transcriptase PCR analysis, quantitative reverse-transcriptase PCR analysis, Northern blot analysis, RNAase
10 protection assay, digital RNA detection/ quantitation, and combinations or sub-combinations thereof.

30. The method of any one of claims 1-8, wherein the level of expression of
15 said biomarker is determined at the protein level.

31. The method of claim 30, wherein the presence of the protein is detected using an antibody or antigen binding fragment thereof, which specifically binds to the protein.

20

32. The method of claim 31, wherein the antibody or antigen binding fragment thereof is selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab', F(ab')₂, ScFv, SMIP, affibody, avimer, versabody, nanobody, a domain antibody, and an
25 antigen binding fragment of any of the foregoing.

33. The method of claim 31, wherein the antibody or antigen binding fragment thereof is labeled.

30 34. The method of claim 33, wherein the antibody or antigen binding fragment thereof is labeled with a label selected from the group consisting of a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, and an enzyme-label.

35. The method of claim 28, wherein the level of expression of said biomarker is determined by using a technique selected from the group consisting of an immunoassay, a western blot analysis, a radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion, electrochemiluminescence immunoassay (ECLIA), ELISA assay, immunopolymerase chain reaction and combinations or sub-combinations thereof.

36. The method of claim 35, wherein the immunoassay is a solution-based immunoassay selected from the group consisting of electrochemiluminescence, chemiluminescence, fluorogenic chemiluminescence, fluorescence polarization, and time-resolved fluorescence.

37. The method of claim 35, wherein the immunoassay is a sandwich immunoassay selected from the group consisting of electrochemiluminescence, chemiluminescence, and fluorogenic chemiluminescence.

38. The method of any one of claims 1-3, 6 or 8, wherein said sample comprises a fluid, or component thereof, obtained from said subject.

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39. The method of claim 38, wherein the fluid is selected from the group consisting of blood, lymph, serum, plasma, cystic fluid, nipple aspirates, urine, sputum, and fluid collected from a biopsy.

40. The method of any one of claims 1-3, 6 or 8, wherein the sample comprises a tissue, or component thereof, obtained from said subject.

41. The method of claim 40, wherein said tissue is selected from the group consisting of breast tissue, connective tissue, lymphatic tissue, tissue obtained from a biopsy and tissue obtained from a lump biopsy.

30

42. The method of claim 40, wherein the tissue is breast tissue or a component thereof.

43. The method of claim 42, wherein said component of said breast tissue comprises breast tissue cells.

5 44. The method of claim 43, wherein said breast tissue cells are circulating breast tumor cells.

45. The method of any one of claims 1-3 or 6-8, wherein said subject is a human subject.

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46. A kit for predicting whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat a subject having breast cancer, the kit comprising

15 reagents for determining the level of expression of a biomarker selected from the group of biomarkers listed in Table 1; and

instructions for use of the kit to predict whether eribulin, an analog thereof, or a pharmaceutically acceptable salt thereof, may be used to treat a subject having breast cancer.

20 47. The kit of claim 46, wherein the pharmaceutically acceptable salt of eribulin is eribulin mesylate.

48. The kit of claim 46, wherein the reagent for determining the level of expression of the biomarker is a probe for identifying a null mutation in the biomarker.

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49. The kit of claim 46, wherein the reagent for determining the level of expression of the biomarker is a probe for amplifying and/or detecting the biomarker.

30 50. The kit of claim 46, wherein the reagent for determining the level of expression of the biomarker is an antibody.

51. The kit of claim 46, further comprising reagents for obtaining a biological sample from a subject.

52. The kit of claim 46, further comprising a control sample.

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