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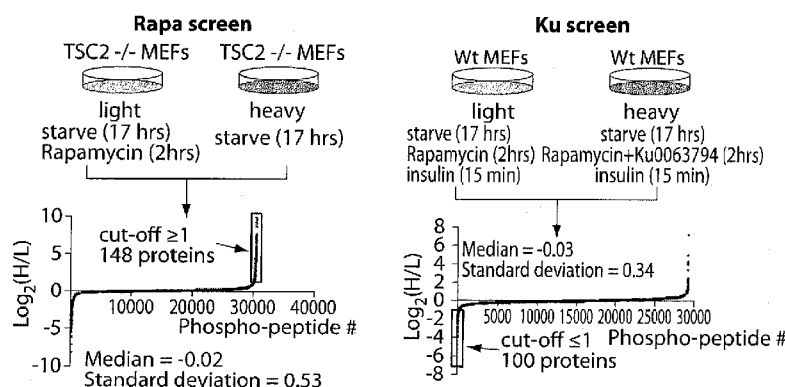


Fig. 1A

(57) **Abstract:** Some aspects of this invention relate to the identification of over 300 mTOR kinase targets by a comprehensive phosphoproteomics assay. Some aspects of this invention relate to targeting mTOR kinase targets, for example, Grb10, FOXK1, ZEB2, NDRG3, LARP1, SRPK2, CDK12, MIB1, or IBTK, in treating hyperproliferative disease. Some aspects of this invention relate to methods to determine the level of mTOR activity by measuring the level of phosphorylation of an mTOR targeted phosphorylation site, for example, a Grb10, FOXK1, ZEB2, NDRG3, LARP1, SRPK2, CDK12, MIB1, and/or IBTK phosphorylation site. Some aspects of this invention relate to methods for distinguishing different classes of mTOR activity in a cell based on phosphoproteomic analysis of mTOR-targeted proteins. Some aspects of this invention relate to the classification of a hyperproliferative disease based on phosphoproteomic analysis of mTOR-targeted proteins. Some aspects of this invention relate to the personalization of therapeutic methods for the treatment of hyperproliferative disease based on phosphoproteomics. Some aspects relate to therapeutic methods including administering to a subject an mTOR inhibitor, an mTOR inhibitor and an additional kinase inhibitor, or a dual inhibitor of mTOR and an additional kinase based on the phosphorylation levels of mTOR targets determined in the subject. Some aspects of this invention relate to the discovery that Grb10 is an mTOR-targeted tumor suppressor gene.

TARGETING mTOR SUBSTRATES IN TREATING PROLIFERATIVE DISEASES

RELATED APPLICATIONS

This application claims priority under 35 U.S.C. § 119(e) to U.S. provisional patent application, U.S.S.N. 61/403,932, filed September 23, 2010, which is incorporated herein by reference.

GOVERNMENT SUPPORT

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BACKGROUND

mTOR is an evolutionarily conserved ser/thr protein kinase that controls many critical cellular processes including growth, protein translation, metabolic flux, and cell survival. mTOR functions as the core catalytic component of two structurally and functionally distinct signaling complexes. mTOR complex 1 (mTORC1) regulates cell growth and is responsible for the well-characterized role of mTOR in controlling protein translation whereas mTOR complex 2 (mTORC2) regulates cell survival and the actin cytoskeleton (1-3). The mechanisms responsible for modulating mTORC1 and mTORC2 activity in response to upstream inputs such as growth factors, energetic status, and amino acid levels have been well studied (1). In contrast, relatively few direct substrates of mTOR have been identified and in many cases the mechanisms underlying mTOR's ability to regulate important aspects of cell biology are not known.

Misregulated mTOR activity is a common feature of most cancers (2). Despite great interest, clinical trials for evaluating the selective mTORC1 inhibitor rapamycin as an anti-cancer agent have met with limited success (3). Rapamycin resistance has emerged as a major challenge to its clinical use (4) and is caused in part by feedback loops that activate the PI3K and MAPK signaling pathways in rapamycin-treated cells through poorly understood mechanisms (5, 6).

SUMMARY OF THE INVENTION

Functional characterization of the mTOR signaling pathways has been hampered by the paucity of substrates that have been identified to date. Identifying novel substrates of mTORC1 and mTORC2 is important for making progress toward our general understanding how mTOR signals to downstream effectors and to specifically define components of the feedback loops involved in rapamycin resistance. The best-characterized mTORC1 substrates include p70S6K and 4EBP, whereas mTORC2 phosphorylates several members of the AGC kinase family, including Akt, SGK, and PKC.

The present invention is based in part on large-scale quantitative phospho-proteomics experiments that were performed to define the entire signaling networks downstream of both mTORC1 and mTORC2. Novel mTORC1 substrates identified herein include, but are not limited to Grb10, FOXK1, ZEB2, NDRG3, LARP1, SRPK2, CDK12, MIB1, and IBTK.

Extensive characterization of a novel mTORC1 substrate, the growth factor receptor-bound protein 10 (Grb10), shows that mTORC1-mediated phosphorylation stabilizes Grb10, leading to feedback inhibition of the PI3K and MAPK pathways. In addition, Grb10 expression was shown to be frequently downregulated in a variety of cancers. Interestingly, loss of Grb10 and the well-established tumor suppressor PTEN are mutually exclusive events. Grb10 has been found to be both a novel mTORC1 substrate and a tumor suppressor with relevance across a broad spectrum of cancer subtypes.

In some aspects, the invention provides methods for determining mTOR kinase activity in a cell, the method comprising obtaining a cancer cell from a subject diagnosed to have a cancer, determining the level of Grb10 phosphorylation in the cell, and comparing the level of Grb10 phosphorylation to a reference level, wherein if the level of Grb10 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity. In some embodiments, the cell is a normal or healthy cell. In some embodiments, the cell is a cell obtained from a subject not diagnosed with a neoplastic disease. In some embodiments, the cell is a cell obtained from a subject not diagnosed with a cancer. In some embodiments, the cell is a neoplastic cell. In some embodiments, the cell is a cancer cell. In some embodiments, the cell is a cell obtained from a subject diagnosed with a neoplastic disease, for example, with a cancer.

In some aspects, the invention provides methods for selecting a treatment of a neoplastic disease, for example, of a cancer, in a subject, the method comprising obtaining a cell from a subject diagnosed to have a neoplastic disease, for example, a cancer, exhibiting an elevated level of mTOR activity; determining the level of Grb10 expression in the cell;

and comparing the level of Grb10 expression to a reference level, wherein if the level of Grb10 expression in the cell is higher than the reference level, then the cell is determined to exhibit a high likelihood of expressing an elevated level of PI3K, Akt, and/or MAPK activity upon being contacted with an mTORC1 inhibitor.

5 Other aspects of this invention provide methods for determining mTOR kinase activity in a cell by determining the level of phosphorylation of a phosphorylation site disclosed in Table 1, 2, 3, 7, 8, or 11 in the cell, and comparing the level of phosphorylation to a reference level, wherein if the level of phosphorylation is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity, or if the level
10 of phosphorylation is equal or lower than the reference level, then the cell is determined to not exhibit an elevated level of mTOR kinase activity. In certain embodiments, if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class I phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTORC1 activity. In certain embodiments,
15 if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class II phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity. In some embodiments, if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class III phosphorylation
20 site, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR activity, or an elevated level of rapamycin-insensitive mTOR activity, or both.

In some embodiments, the methods provided herein further comprise selecting a method of treatment of the subject based on the level of phosphorylation of the phosphorylation site. In some embodiments, if the cell is determined to exhibit an elevated
25 level of mTOR kinase activity, then a method of treatment is selected that includes administering an effective amount of an mTOR kinase inhibitor to the subject. In some embodiments, if the cell is determined to not exhibit an elevated level of mTOR kinase activity, then a method of treatment is selected that does not include administering an mTOR kinase inhibitor. In some embodiments, if the cell is determined to exhibit an elevated level
30 of rapamycin-sensitive mTORC1 activity, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-sensitive mTORC1 kinase activity (*e.g.*, rapamycin or a rapamycin analog) to the subject. In some embodiments, if the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity, then a method of treatment is selected that comprises administering

an effective amount of an inhibitor of rapamycin-insensitive mTORC1 kinase activity to the subject. In some embodiments, if the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR kinase activity, or an elevated level of rapamycin-insensitive mTOR kinase activity, or both, then a method of treatment is selected that comprises
5 administering an effective amount of an inhibitor of rapamycin-sensitive and rapamycin-insensitive mTOR kinase activity or a combination of an inhibitor of rapamycin-sensitive mTOR kinase activity and an inhibitor of rapamycin-insensitive mTOR kinase activity to the subject.

10 In some embodiments, the method of treatment further comprises administering to the subject an effective amount of a compound that stabilizes Grb10 or that inhibits the degradation of Grb10. In some embodiments, the method of treatment further comprises administering an effective amount of an inhibitor of PI3K, Akt, or MAPK to the subject.

Some aspects of this invention provide a phosphoproteomics array that includes a plurality of phosphosensitive antibodies or antibody fragments each of which specifically
15 binds to phosphorylation site disclosed in Table 1, 2, 3, 7, 8, or 11. In some aspects, the invention also provides a method of using a phosphoproteomics array to determine mTOR activity in a cell by contacting a proteinaceous sample derived from a cell, for example, from a cancer cell, with a phosphoproteomics array as described herein under conditions suitable for a protein expressed in the cell to bind to an antibody or antibody fragment of the array,
20 determining the level of phosphorylated protein bound to an antibody or antibody fragment of the array, and comparing the level of phosphorylated protein bound to an antibody or antibody fragment of the array to a reference level. If the level phosphorylated protein in the sample derived from the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

25 In other aspects, the invention provides methods of identifying an mTOR kinase inhibitor by contacting an mTOR kinase with a polypeptide with a phosphorylation site disclosed in Table 1, 2, 3, 7, 8, or 11 under conditions suitable for the mTOR kinase to phosphorylate the phosphorylation site in the presence of a candidate agent, determining the level of phosphorylation at the phosphorylation site, and comparing the level of
30 phosphorylation to a reference level. If the level of phosphorylation is lower than the reference level, then the candidate agent is identified as an mTOR kinase inhibitor.

In some embodiments involving a phosphorylation site disclosed in Table 1, 2, 3, 7, 8, or 11, the phosphorylation site is not a phosphorylation site previously known to be an mTOR target.

The subject matter of this application may involve, in some cases, interrelated products, alternative solutions to a particular problem, and/or a plurality of different uses of a single method or agent. Other advantages, features, and uses of the invention will become apparent from the following detailed description of non-limiting embodiments of the invention when considered in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. Sample preparation and data analysis for quantitative phosphorylation profiling of mTOR signaling. (A) Schematics of the two quantitative mass spectrometry experiments are shown with a plot highlighting the distribution of phosphopeptides identified in each screen. See data summary in Table 5. Note that most of the phosphopeptides have a ratio of 1:1 between the light and heavy populations and hence have a value close to 0 on a Log₂ axis. Proteins with downregulated phosphorylation in each screen are highlighted in the red box. (B) Typical quantitative MS and MS/MS spectra in which LS*SLRAS*TSKSESSQK (SEQ ID NO: 1) from ribosomal protein S6 (S235 and S240) are identified as a rapamycin-sensitive phosphopeptide. Note the light and heavy peptides differ by 26 Da, corresponding to 2 labeled Lys and 1 labeled Arg in this particular peptide. Sequence in lower panel: SEQ ID NO: 1722. (C) Quantitative differences between the rapamycin-sensitive and -insensitive mTOR downstream phosphorylation events. Phosphopeptides identified in both screens were extracted and their corresponding Log₂ ratios (fold-changes) were plotted. (D) The top ten pathways enriched in the downregulated phospho-proteins identified in the rapamycin (Rapa) screen.

Figure 2. Phosphorylation of Grb10 at S501/S503 is sensitive to rapamycin inhibition. (A) Identification of a doubly-phosphorylated rapamycin-sensitive Grb10 peptide (MNILSS*QS*PLHPSTLNAVIHR, SEQ ID NO: 2, * indicates phosphorylation sites) corresponding to S501/S503. (B) Evolutionary conservation of Grb10 S501/S503 among vertebrate species. (C) Phosphorylation of Grb10 at S501/S503 shows rapamycin sensitivity *in vivo*. *TSC2*^{-/-} cells were starved for serum and treated with 20 nM rapamycin for the indicated times. Sequences, from top to bottom: SEQ ID NO: 1723 to SEQ ID NO: 1727, respectively. (D) Phosphorylation of Grb10 at S501/S501 is sensitive to amino acids withdrawal. *TSC2*^{-/-} cells were starved in DMEM overnight and then transferred to D-PBS for the indicated times. (E) Phosphorylation of Grb10 at S501/S503 is not affected by the pan-kinase inhibitor, staurosporine. *TSC2*^{-/-} cells were starved for serum and treated with either 100 nM staurosporine or Ku-0063794 at the indicated concentrations for two hours.

(F) Grb10 phosphorylation is increased upon growth factor stimulation. Wild type (WT) mouse embryonic fibroblasts (MEFs) were starved for serum overnight and then were stimulated with insulin (100 nM) or serum (10%) for 15 min. The cells were preincubated with the indicated compounds for two hours. AktVIII (1 μ M) is a specific inhibitor of Akt whereas AZD (AZD6244, 5 μ M) specifically inhibits MEK. Rapamycin (rapa) was used at 20 nM. (G) Grb10 phosphorylation at S501/S503 is sensitive to various mTOR kinase inhibitors. *TSC2*^{-/-} cells were serum-starved and treated with the indicated compounds for two hours. The concentrations of the compounds were rapamycin 20 nM, LY (LY294002) 20 μ M, BEZ235 (NVP-BEZ235) 500 nM, torin 100 nM, and pp242 1 μ M.

Figure 3. mTOR-mediated Grb10 phosphorylation is important for Grb10 stability.

(A) Grb10 interacts with raptor, but not rictor. HA-tagged Grb10 was co-transfected with Myc-raptor or Myc-rictor in HEK293T cells. Cells were lysed in lysis buffer A, and the lysates were subjected to immunoprecipitation using anti-HA antibody conjugated beads. Raptor and rictor were probed with an antibody against the Myc-tag. (B) Grb10 is phosphorylated by mTOR *in vitro*. Recombinant Grb10 was prepared from bacteria (the GST-fused Grb10 shows a molecular weight of 80 kDa) and was incubated with recombinant mTOR *in vitro*. Phosphorylation of Grb10 at S501/S503 was detected by using the phospho-specific antibody against these two sites. (C) Long-term rapamycin treatment leads to Grb10 degradation in *TSC2*^{-/-} cells. Note that Grb10 protein expression levels inversely correlated with Akt activity. Grb10 is highly overexpressed in *TSC2*^{-/-} cells. mRNA level was determined using quantitative RT-PCR based on three biological replicate experiments. (D) Knockdown of raptor in *TSC2*^{-/-} cells decreased Grb10 protein level. Cells were starved overnight and the lysates were probed with the antibodies indicated. (E) Grb10 is highly overexpressed in *TSC2*^{-/-} cells. (F) S501A/S503A mutant is unstable compared with the wild-type or the S501D/S503D mutant. The same amount of DNA was transfected into HEK293T cells. (G) Rapamycin failed to induce degradation of the S501D/S503D mutant. S501D/S503D mutant (DD) was stably expressed in *TSC2*^{-/-} cells and cells were treated with 20 nM rapamycin for the indicated times. Endogenous Grb10 was detected using an antibody that preferentially recognizes mouse Grb10 whereas the Grb10 DD mutant (of human origin) was detected using an anti-HA antibody.

Figure 4. Grb10 is involved in the feedback inhibition loop from mTORC1 to PI3K and MAPK and *GRB10* mRNA expression is significantly down-regulated in many cancers and is negatively correlated with *PTEN* expression. (A) Knockdown of Grb10 in *TSC2*^{-/-}

cells resulted in PI3K and MAPK hyperactivation after insulin or IGF stimulation. (B) Knockdown of Grb10 in *TSC2* $-/-$ cells protected cells against apoptosis. Grb10 knockdown and control cells were starved overnight and then treated with 100 nM staurosporine for 5 hrs to induce apoptosis. (C) Box plots indicating that *GRB10* expression is significantly lower in many tumor types compared to their corresponding normal tissues. (Only the tumor types that showed significantly lower *GRB10* expression in cancer vs. normal in at least three independent microarray datasets are included). (D) Heat maps indicating a strong negative correlation between *GRB10* and *PTEN* expression in breast carcinomas and myelomas. Low levels of *GRB10* expression rarely occurred in tumors that also showed low levels of *PTEN* expression. (E) Scatter plots comparing the expression levels of *GRB10* and *PTEN* levels in the normal and tumor samples, collected overall from 6 different tissue types, where *GRB10* was shown to be significantly down-regulated in cancer vs. normal. The negative correlation between *GRB10* and *PTEN* expression is evident in the tumor ($P < 0.001$) but not in the corresponding normal samples.

Figure 5. Data analysis for the rapamycin screen and Ku-0063794 screen. (A) Phosphopeptides enrichment in the second biological replicate experiment of the rapamycin screen. Number of phospho- and nonphospho- peptides in each SCX fraction was plotted. (B) Number of downregulated proteins in the two biological replicates of the rapamycin screen. (C) Ku-0063794 inhibits insulin-induced Akt phosphorylation. (D) Pathways enriched in the downregulated phospho-proteins identified in the Ku-0063794 screen. The top ten overrepresented pathways were shown. Analysis was performed using DAVID. See Huang DW, Sherman BT, Lempicki RA. *Systematic and integrative analysis of large gene lists using DAVID Bioinformatics Resources*. Nature Protoc. 2009;4(1):44-57; and Dennis G Jr, Sherman BT, Hosack DA, Yang J, Gao W, Lane HC, Lempicki RA. *DAVID: Database for Annotation, Visualization, and Integrated Discovery*. Genome Biol. 2003;4(5):P3; both incorporated herein by reference for disclosure of integrative analysis methods for large datasets.

Figure 6. Examples of protein phosphorylation changes identified in the rapamycin and Ku-0063794 screens. Note that the light cells were treated with rapamycin and the heavy cells were treated with DMSO in the rapamycin screen (2nd biological replicate). For the Ku-0063794 screen, light cells were treated with rapamycin whereas the heavy cells were treated with a combination of rapamycin and Ku-0063794. (A) Phosphorylation changes of different sites on 4EBP in the rapamycin screen and Ku-0063794 screen. Phosphorylation of T36/T45 was partially responsive to rapamycin and was completely abolished as a result of Ku-

0063794 treatment. In contrast, T70 phosphorylation is mTOR-independent (B) NRDG1 phosphorylation at S330/S333 was sensitive to Ku-0063794 but not rapamycin inhibition. (C) GSK3 β phosphorylation at S9 decreased in both rapamycin and Ku-0063794 screen.

Figure 7. Identification of the rapamycin-sensitive phosphorylation sites on mTOR

- 5 (A) Intensities of an mTOR peptide ²⁴⁷¹AGTTVPES*HIS*FIGDGLVKPEALNKK²⁴⁹⁶ (SEQ ID NO: 3, * indicates phosphorylation sites) from the rapamycin-treated (Light) and control (Heavy) *TSC2* ^{-/-} cells (B) Domain structure of mTOR and conservation of S2478 and S2481 across different species. Sequences, from top to bottom: SEQ ID NO: 1728 to SEQ ID NO: 1735, respectively. (C) Immunoblot experiments showing phospho-mTOR at S2481 is
10 inhibited by acute rapamycin treatment. *TSC2* ^{-/-} cells were starved and then treated with 20 nM rapamycin for the indicated times. (D) mTOR kinase inhibitor pp242 completely ablated mTOR phosphorylation at S2481. *TSC2* ^{-/-} cells were starved and were then treated with 1 μ M pp242 for two hours.

Figure 8. Identification of rapamycin-sensitive phosphorylation sites on Grb10.(A)

- 15 MS/MS experiments identified that phosphorylation of residues S501/S503 of Grb10 is strongly inhibited by rapamycin. (B) Phosphorylation at S455/S458 is rapamycin-insensitive. Sequences, from top to bottom: SEQ ID NO: 1736 and SEQ ID NO: 1737, respectively.

Figure 9. Phosphorylation of Grb10 at S501/S503 regulates its stability. (A) An

- 20 antibody showed specificity towards Grb10 phosphorylation at S501/S503. Preincubation of the antibody with the blocking antibody completely eliminated the immunoreactivity. (B) Further validation of the phospho-specific antibody raised against the Grb10 S501/S503 sites. Grb10 WT, S501A/S503A (AA) and S501D/S503D (DD) were transfected into HEK239T cells and were probed with the antibody. Note that this antibody detected wild type (WT) Grb10, but neither of the mutant proteins. (C) Treatment of *TSC2* ^{-/-} cells with various
25 mTOR kinase inhibitors led to Grb10 degradation. (D) Both rapamycin and NVP-BEZ235 treatment led to a decreased level of Grb10 in *TSC1* ^{-/-} cells. (E) Grb10 is highly overexpressed in *TSC1* ^{-/-} cells compared with their wild-type counterparts. (F) rapamycin treatment of *TSC2* ^{-/-} cells stably expressing wild type (WT) Grb10 led to lower levels of both
30 endogenous and exogenous Grb10.

Figure 10. Grb10 is involved in the feedback loop from mTORC1 to PI3K. (A)

Overexpression of Grb10 in HEK293 cells inhibited PI3K activation. W, wild type (WT) Grb10, A, AA mutant and D, DD mutant. Knockdown of Grb10 in *TSC2* ^{-/-} cells led to IRS

hyperphosphorylation after insulin stimulation. (B) Overexpression of Grb10 in HEK239 cells suppressed IRS tyrosine phosphorylation and PI3K recruitment after insulin stimulation. HA-tagged Grb10 was transfected and IRS2 immunoprecipitates were analyzed. Phosphorylation at Y612 of IRS was detected. (C) HA-tagged Grb10 was transfected and p85 immunoprecipitates were analyzed. (D) Knockdown of Grb10 in *TSC2*^{-/-} cells led to increased IRS Y612 phosphorylation upon insulin stimulation. (E) Knockdown of Grb10 in *TSC2*^{-/-} cells protected these cells against etoposide-induced apoptosis. Cells were starved overnight and were treated with 100 μ M etoposide for the indicated times.

DEFINITIONS

In the tables and the database, *, @, ^ and # denote phosphorylation (Ser, Thr and Tyr), heavy Lys, heavy Arg and oxidation (Met), respectively. International Protein Index (IPI) reference numbers are given in some of the tables and the database provided herein. The IPI database can be accessed at the European Bioinformatics Institute homepage (www.ebi.ac.uk/), for example, at (www.ebi.ac.uk/IPI/IPIhelp.html). Each IPI database entry provided by accession number is incorporated herein by reference for disclosure of the respective proteins amino acid sequence and accompanying protein information.

The term “antibody,” as used herein, refers to an immunoglobulin, whether natural or wholly or partially synthetically produced. All derivatives thereof which maintain specific binding ability are also included in the term. The term also covers any protein having a binding domain which is homologous or largely homologous to an immunoglobulin binding domain. These proteins may be derived from natural sources, or partly or wholly synthetically produced. An antibody may be monoclonal or polyclonal. The antibody may be a member of any immunoglobulin class, including any of the human classes: IgG, IgM, IgA, IgD, and IgE. Derivatives of the IgG class, however, are preferred in the present invention.

The term “antibody fragment,” as used herein, refers to any derivative of an antibody which is less than full-length. Preferably, the antibody fragment retains at least a significant portion of the full-length antibody’s specific binding ability. Examples of antibody fragments include, but are not limited to, Fab, Fab’, F(ab’)₂, scFv, Fv, dsFv, diabody, and Fd fragments. The antibody fragment may be produced by any means. For instance, the antibody fragment may be enzymatically or chemically produced by fragmentation of an intact antibody or it may be recombinantly produced from a gene encoding the partial

antibody sequence. Alternatively, the antibody fragment may be wholly or partially synthetically produced. The antibody fragment may optionally be a single chain antibody fragment. Alternatively, the fragment may comprise multiple chains which are linked together, for instance, by disulfide linkages. The fragment may also optionally be a
5 multimolecular complex. A functional antibody fragment will typically comprise at least about 50 amino acids and more typically will comprise at least about 200 amino acids.

Single-chain Fvs (scFvs) are recombinant antibody fragments consisting of only the variable light chain (V_L) and variable heavy chain (V_H) covalently connected to one another by a polypeptide linker. Either V_L or V_H may be the NH_2 -terminal domain. The polypeptide
10 linker may be of variable length and composition so long as the two variable domains are bridged without serious steric interference. Typically, the linkers are comprised primarily of stretches of glycine and serine residues with some glutamic acid or lysine residues interspersed for solubility.

Diabodies are dimeric scFvs. The components of diabodies typically have shorter
15 peptide linkers than most scFvs, and they show a preference for associating as dimers.

An Fv fragment is an antibody fragment which consists of one V_H and one V_L domain held together by noncovalent interactions. The term dsFv is used herein to refer to an Fv with an engineered intermolecular disulfide bond to stabilize the V_H - V_L pair.

A $F(ab')_2$ fragment is an antibody fragment essentially equivalent to that obtained
20 from immunoglobulins (typically IgG) by digestion with an enzyme pepsin at pH 4.0-4.5. The fragment may be recombinantly produced.

A Fab fragment is an antibody fragment essentially equivalent to that obtained by reduction of the disulfide bridge or bridges joining the two heavy chain pieces in the $F(ab')_2$ fragment. The Fab' fragment may be recombinantly produced.

25 A Fab fragment is an antibody fragment essentially equivalent to that obtained by digestion of immunoglobulins (typically IgG) with the enzyme papain. The Fab fragment may be recombinantly produced. The heavy chain segment of the Fab fragment is the Fd piece.

The term "binding agent", as used herein, refers to an agent binding a target molecule,
30 for example, a polypeptide comprising a phosphorylation site provided herein, with high specificity. Examples of binding agents are antibodies, antibody fragments, aptamers, and adnectins.

The term "phosphosensitive", as used herein in the context of a binding agent, refers to a binding agent that specifically binds to a phosphorylation site, for example, a

phosphorylation site provided herein, in either the phosphorylated or non-phosphorylated state. In some embodiments, a phosphosensitive binding agent provided herein binds to the phosphorylation site in its phosphorylated state, but does not significantly bind the phosphorylation site in a non-phosphorylated state. Phosphosensitive binding agents, for example, phosphosensitive antibodies or antibody fragments, accordingly, allow for the detection of phosphorylation at a specific phosphorylation site.

The term “cancer”, as used herein, refers to a malignant neoplastic disease. Most cancers are characterized by hyperproliferation of a cell population. In some embodiments, a cancer manifests as a solid tumor. In some embodiments, a cancer manifests as a liquid tumor. Non-limiting examples of cancers include carcinomas (derived from epithelial cells, e.g., some forms of breast, prostate, lung and colon cancer), sarcomas (derived from connective tissue or mesenchymal cells), lymphoma and leukemia (derived from hematopoietic cells) and seminomas (derived from germ cells).

The term “cancer cell”, as used herein, refers to a malignant neoplastic cell. In some embodiments, a cancer cell is part of a neoplastic cell population. In some embodiments, a cancer cell is a cell of a solid tumor. In some embodiments, a cancer cell is a cell of a liquid tumor. In some embodiments, a cancer cell carries a mutation that affects regulation of cell cycle control. In some embodiments, a cancer cell is a cell obtained from a tumor in a subject.

The term “candidate agent”, as used herein refers to a molecule to be tested for a specific property, for example, for its ability to inhibit mTOR kinase activity. In some embodiments, a candidate agent is a small molecule. In some embodiments, a candidate agent is a polypeptide or protein. In some embodiments, a candidate agent is a binding agent. In some embodiments, a candidate agent is a nucleic acid.

The term “determining a level of expression”, as used herein, refers to performing an assay to determine the level of a gene product expressed in a cell or tissue, for example, in a cancer cell or tumor tissue. In some embodiments, the assay includes obtaining a cell from a subject, for example, by biopsy. In some embodiments, the gene product is a transcript, for example, an mRNA. In other embodiments, the gene product is a protein, for example, an mTOR substrate disclosed herein, or a protein comprising a phosphorylation site disclosed herein. In some embodiments, the gene product is a protein that is phosphorylated at a specific phosphorylation site. In some embodiments, the gene product is a protein that is not phosphorylated at a specific phosphorylation site. Methods, assays, and reagents to determine the level of a gene product in a cell or tissue are described herein and are well known to those of skill in the art. See, for example, Sambrook *et al.*, *Molecular Cloning*,

second edition, Cold Spring Harbor Laboratory, Plainview, N.Y.; (1989), or Ausubel *et al.*, *Current Protocols in Molecular Biology*, *Current Protocols* (1989), and *DNA Cloning: A Practical Approach*, Volumes I and II (ed. D. N. Glover) IREL Press, Oxford, (1985); each of which is incorporated herein by reference.

5 Methods to determine transcript levels include, for example, RT-PCR, northern blot, *in situ* hybridization, microarray assays, and massive parallel sequencing assays. Methods to determine protein levels include, for example, western blot, immunohistochemistry, ELISA, protein array assays, and mass spectrometry.

10 The term “high risk of expressing an elevated level of PI3K, Akt, and/or MAPK activity”, as used herein in the context of cells, refers to a condition in a cell that is likely to result in upregulation of PI3K, Akt, and/or MAPK kinase activity, when the cell is contacted with a therapeutic agent, for example, with an mTOR inhibitor. The term “risk” is used interchangeably with the term “likelihood” in this context. Such risk can be conferred through feedback-relief triggered by the therapeutic target. For example, in some
15 embodiments, a cell, for example, a cell derived from a tumor in a subject, is determined to have a high likelihood of expressing an elevated level of PI3K, Akt, and/or MAPK, if it is established that the cell highly expresses a feedback-mediator, for example, phosphorylated Grb10, that limits PI3K, Akt, and/or MAPK expression. If the feedback-mediator is a known substrate of an oncogenic kinase, for example, if the feedback-mediator is the mTOR kinase
20 substrate Grb10, then the cell is likely to exhibit feedback relief upon administration of an inhibitor of the kinase, for example, an mTOR kinase inhibitor, which, in turn, may increase the cell’s proliferation and/or survival capacity.

25 The term “inhibitor” as used herein in the context of kinases, refers to a molecule that inhibits the activity of a kinase. In some embodiments, an inhibitor diminishes the catalytic activity of a kinase. In some embodiments, an inhibitor abolishes the catalytic activity of a kinase. In some embodiments, the inhibitor is a small molecule. In some embodiments, the inhibitor is a nucleic acid or a polypeptide. In some embodiments, the inhibitor is a binding agent. In some embodiments, a kinase inhibitor effects inhibition by downregulating expression of the kinase. In some embodiments, a kinase inhibitor effects inhibition by
30 binding the kinase and interfering with the kinase reaction. In some embodiments, a kinase inhibitor is an allosteric kinase inhibitor. The term “allosteric kinase inhibitor” refers to a kinase inhibitor, for example, a small molecule, that binds its target kinase, wherein the binding of the inhibitor results in an allosteric change in the kinase molecule, leading to diminished kinase activity. Allosteric changes leading to diminished kinase activity can be

changes resulting in a reduction of the kinase's ability to bind a substrate molecule, or changes resulting in a reduction of the kinase's ability to transfer a phosphate group to a substrate molecule. In some embodiments, the kinase inhibitor is a catalytic kinase inhibitor. In some embodiments, a catalytic inhibitor, which itself cannot partake in a kinase reaction, competes with a kinase substrate for binding. In some embodiments, a catalytic kinase inhibitor is an ATP-competitive inhibitor.

The term "effective amount", as used herein in the context of kinase inhibitors, refers to an amount of kinase inhibitor sufficient to achieve a measurable inhibition of kinase activity, or an amount of kinase inhibitor sufficient to achieve a clinically desirable outcome.

For example, an effective amount of the mTOR inhibitor rapamycin is, in some embodiments, an amount of rapamycin that, when administered to a cell or tissue, results in a measurable decrease in mTOR kinase activity in the cell or tissue. In some embodiments, an effective amount of a kinase inhibitor is an amount that is effective to reduce the activity of the target kinase in a cell or tissue to less than 75%, less than 50%, less than 40%, less than 30%, less than 25%, less than 20%, less than 10%, less than 5%, less than 2.5%, less than 2%, or less than 1% of the activity in the cell or tissue not treated with the inhibitor. Assays for measuring kinase activity are well known in the art and described in more detail elsewhere herein. In some embodiments, an effective amount of a kinase inhibitor, for example, of rapamycin, is an amount that, when administered to a subject, for example, a subject having a cancer with elevated mTOR activity, results in a clinically desirable outcome. In some embodiments, a clinically desirable outcome is reversal of a disease, for example, a decrease in neoplastic or malignant cell number, tumor size, or cell proliferation rate, for example, in a subject having a proliferative disease, *e.g.*, a neoplastic disease or a cancer, or a delay in the progression of a disease, for example a progression from one tumor stage to the next, or from a benign to a malignant neoplastic disease.

The term "mTOR kinase inhibitor" as used herein, refers to a molecule inhibiting a kinase activity of the mTOR kinase. Examples of mTOR kinase inhibitors are mTORC1 kinase inhibitors and mTORC1/2 inhibitors. Examples of mTORC1 kinase inhibitors are rapamycin and rapamycin analogs (*e.g.*, Ridaforolimus, Sirolimus or Everolimus). Examples of mTORC1/2 inhibitors are PP242, PP30, AZD8055, OSI-027, WYE354, INK-128, XL388, and torin1. Further examples of mTOR inhibitors are inhibitors that target mTOR and an additional kinase or additional kinases, for example, dual PI3K/mTOR kinase inhibitors (*e.g.*, NVP-BEZ235, BGT-226, XL-765, GSK2126458, or SF1126).

The term “PI3K kinase inhibitor”, as used herein, refers to a molecule that inhibits PI3K kinase activity. Examples of PI3K inhibitors are ZSTK474, TGX221, GDC0941, LY294002, XL147, PX147, BKM120, GSK 615, CAL101, and PX-866.

The term “mutation”, as used herein, refers to a change in a gene sequence, for example, a deletion, insertion, inversion, transposition, or substitution. In some embodiments, the mutation results in a change of the expression level of the gene product encoded by the respective gene. In some embodiments, a mutation is a mutation in a gene involved in an mTOR signaling pathway, for example, a gene encoding a protein that regulates, directly or indirectly, mTOR kinase activity. Examples of genes involved in an mTOR signaling pathway are Ras, Raf, MAPK, RSK, receptor tyrosine kinases, PI3K (Phosphoinositide 3-kinase), PTEN (phosphatase and tensin homolog), Akt (Protein Kinase B), TSC1/2 (Tuberous sclerosis protein 1, Tuberous sclerosis protein 2, respectively), MEK (Dual specificity mitogen-activated protein kinase kinase 1, MAPK21), LKB (, and NF2 (Neurofibromatosis 2). Methods to determine whether a cell carries a mutation in a gene are well known to those of skill in the related arts.

The term “phosphoproteomic profile”, as used herein, refers to a dataset comprising information regarding the level of phosphorylation of a plurality of phosphorylation sites in a biological sample, for example, a proteinaceous sample derived from a cell or tissue sample. Phosphoproteomic profiles of multiple samples can be compared and similarities and dissimilarities in such profiles can be detected and quantified by methods well known to those of skill in the art, including, but not limited to, supervised and non-supervised learning, hierarchical clustering, nearest neighbor analysis. In some embodiments, a phosphoproteomics profile of a clinical sample, for example, of a sample derived from a malignant cell or tissue sample of a subject is compared to a reference sample from healthy cells or tissue, for example, to determine aberrations in protein phosphorylation in the malignant cell or tissue sample. In some embodiments, a phosphoproteomics profile of a clinical sample at issue is compared to phosphoproteomics profiles of clinical samples of known character, for example, to classify the clinical sample at issue. Phosphoproteomic profiles can be classified by methods well known in the art, including the building and application of predictors for the classification.

The term “phosphorylation level”, as used herein, refers to the proportion of phosphorylated polypeptides carrying a certain phosphorylation site in a sample relation to all polypeptides carrying the phosphorylation site in the sample. For example, if the total number of polypeptides carrying a specific phosphorylation site in a sample is 10, and 3 of

these proteins are phosphorylated at that site, while 7 are not, then the phosphorylation level of this phosphorylation site in the sample would be 30%. Phosphorylation levels can be detected and quantified by methods known to those in the art, for example, by protein detection using phosphosensitive binding agents, *e.g.*, phosphosensitive antibodies or antibody fragments. Most protein quantitation methods known to those of skill in the art do not allow for precise molecule counting, so phosphorylation levels are often approximated based on estimations of the number or fractions of phosphorylated proteins in a sample, for example, after western blot or protein microarray analysis using phosphosensitive antibodies or antibody fragments.

The term “phosphorylation site”, as used herein, refers to an amino acid residue within an amino acid sequence, or motif, that can be phosphorylated, for example, by a kinase targeting the respective site. A phosphorylation site is a substrate of a kinase if it can be phosphorylated by that kinase. For example, S421 and S432 are phosphorylation sites in Grb10 isoform 3 within the motif MSNILSS*QS*PLHPSTLNAVIHR (SEQ ID NO: 4), and are both mTOR substrates, as described elsewhere herein. mTOR phosphorylation sites can further be classified into three classes, as used herein. The term “class I phosphorylation site”, as used herein, refers to a phosphorylation site that is targeted by rapamycin-sensitive mTORC1 activity. The term “class II phosphorylation site,” as used herein, refers to a phosphorylation site that is targeted by rapamycin-insensitive mTORC1 and/or mTORC2 activity. The term “class III phosphorylation site,” as used herein, refers to a phosphorylation site that is targeted by rapamycin-sensitive mTOR activity, rapamycin-insensitive mTOR activity, or both.

The term “proliferative disease,” as used herein, refers to any disease in which cell or tissue homeostasis is disturbed in that a cell or cell population exhibits an abnormally elevated proliferation rate. Proliferative diseases include hyperproliferative diseases, such as pre-neoplastic hyperplastic conditions and neoplastic diseases. Neoplastic diseases are characterized by an abnormal proliferation of cells and include both benign and malignant neoplasias. Malignant neoplasia is also referred to as cancer.

The term “reference”, interchangeably used with the term “control” herein, refers to a value, sample, or parameter that serves as a baseline for comparing a value, sample, or parameter of interest to. The use of a reference can be of value in many methods that allow for the detection of absolute levels, for example, of expression, phosphorylation, or protein binding, and is essential in methods that yield semi-quantitative or relative results.

Comparing an assay result obtained for a cell or tissue in question, for example, a cell or

tissue obtained from a tumor in a subject, to a reference result allows a determination whether the result is abnormal. Depending on their nature, abnormal results can support the inference of specific molecular or cellular aberrations and, in some embodiments, a selection of a course of treatment over another. In some embodiments, a reference value is obtained from
5 cells of the same cell type or the same tissue of origin as the cell in question. For example, in some embodiments, a diseased and a healthy cell is obtained from a subject, and the cells are assayed by methods provided herein in parallel. The value observed in the healthy cell, for example, a level of phosphorylation of a protein then typically serves as the reference level to which the level observed in the cell in question is compared. In other embodiments, the
10 reference level is an average level observed or expected in normal cells. In some embodiments, the reference level is a range typically observed in healthy cells. A suitable reference depends, of course, on the type of assay and sample involved. A suitable reference for a given assay or sample will readily be apparent to those of skill in the art. The following list of exemplary references is for illustration only, since the invention is not limited in this
15 respect.

In some embodiments, a suitable reference level, for example, a suitable reference phosphorylation or expression level, is a level observed or expected in a healthy cell or tissue of the same type as the cell or tissue in question. In some embodiments, for example, in some embodiments where a tumor biopsy is assayed, a suitable reference level is a level
20 observed or expected in healthy cells or tissue of the same tissue the tumor originated from, or in cells or tissue adjacent to the tumor. In some embodiments, for example, in some embodiments where a cell is assayed, a reference cell is a healthy cell that is of the same cell type or tissue of origin as the cell in question. In some embodiments, a reference cell is a cell exhibiting normal mTOR kinase activity. In some embodiments, a reference cell is a
25 malignant cell of known phenotype, for example, a malignant cell known to exhibit elevated mTOR kinase activity, a cell known to exhibit elevated mTORC1 kinase activity, or a cell known to exhibit elevated mTORC1/2 kinase activity. In some embodiments, a reference cell is a malignant cell of known phenotype, for example, a rapamycin-sensitive cancer cell or a rapamycin-sensitive cancer cell.

30 In some embodiments, a suitable reference level is an average level calculated or approximated from historic data. In some embodiments, a reference level is a level obtained from a reference cell or tissue assayed in parallel to the cell or tissue in question. In some embodiments, a level obtained from a cell or tissue sample is determined to be different (higher or lower) than the reference level, if it is statistically significantly different (higher or

lower) than the reference level. In some embodiments, a level obtained from a cell or tissue sample is determined to be higher than the reference level, if the level is at least about 1.25-fold, at least about 1.5-fold, at least about 2-fold, at least about 3-fold, at least about 5-fold, or at least about 10-fold the reference level. In some embodiments, a level obtained from a cell or tissue sample is determined to be lower than the reference level, if it is less than about 0.75-fold, less than about 0.70-fold, less than about 0.60-fold, less than about 0.50-fold, less than about 0.40-fold, less than about 0.30-fold, less than about 0.25-fold, less than about 0.10-fold, less than about 0.05-fold, or less than about 0.01-fold the reference level. In some embodiments, a level obtained from a cell or tissue is determined to be substantially similar to the reference level, if it is not statistically significantly different from the reference level. In some embodiments, a level obtained from a cell or tissue is determined to be substantially similar to a reference level, if it is within the range of 0.75-fold to 1.25-fold of the reference level. In some embodiments, a profile comprising a plurality of levels obtained from a cell or tissue sample is determined to be substantially similar to a reference profile, if the profiles cluster together in a clustering analysis. In some embodiments, a multi-value profile obtained from a cell or tissue is determined to be substantially similar to a reference profile, if the correlation coefficient between the profiles is at least 0.75, at least 0.8, at least 0.85, at least 0.9, at least 0.91, at least 0.92, at least 0.93, at least 0.94, at least 0.95, at least 0.96, at least 0.97, at least 0.98, or at least 0.99.

The term “sample”, as used herein, refers to a biological sample. A biological sample typically comprises a cell or tissue, or biological material derived from a cell or tissue. Examples of biological samples are cell samples and tissue samples obtained from a subject, for example, from a subject having a cancer, cell or tissue cultures, and extracts or preparations obtained from any such samples, for example, protein extracts, isolated proteins or isolated nucleic acids obtained from such samples.

A “proteinaceous” sample is a sample comprising proteins or fragments of proteins. In some embodiments, a proteinaceous sample is a sample derived from a cell that includes proteins or fragments of proteins expressed in the cell. In some embodiments, the sample includes a lysed cell. In some embodiments, the sample includes proteins isolated from a cell. In some embodiments, the sample includes an isolated, enriched, or purified protein fraction from a cell, for example, a protein fraction obtained by methods described herein or known to those of skill in the art to separate nucleic acids, carbohydrates, and/or lipids from proteins or fractions of proteins. In some embodiments, the sample is prepared under conditions suitable for obtaining native proteins from a cell. In some embodiments, the sample is prepared under

conditions that do not significantly affect native protein phosphorylation patterns. In some embodiments, the sample is prepared under conditions that do not significantly affect the antigenic structure of a phosphorylation site identified herein, for example, a phosphorylation site identified herein to be a target of mTOR kinase activity. In some embodiments, the sample is prepared under conditions suitable for obtaining denatured or fragmented proteins.

The term “subject,” as used herein, refers to an individual mammal. In some embodiments, the subject is a human. In some embodiments, the subject is a non-human mammal. In some embodiments, the subject is a non-human primate. In some embodiments, the subject is a rodent. In some embodiments, the subject is a sheep, a goat, a cattle, a cat, or a dog. In some embodiments, the subject is a subject diagnosed to have a cancer. In some embodiments, the subject is a subject diagnosed to have a cancer that exhibits an elevated level of mTOR kinase activity. In some embodiments, the subject is a subject not diagnosed with a cancer.

The term “target,” as used herein in the context of kinases, refers to a substrate of a kinase. The term can, accordingly, refer to a protein (*e.g.*, Grb10 is a target of mTOR kinase), to an amino acid sequence comprising a phosphorylation site (*e.g.*, MNILSS*QS*PLHPSTLNAVIHR (SEQ ID NO: 5) or MNILGS*QS*PLHPSTLSTVIHR (SEQ ID NO: 6) are target sequences of mTOR), or to an amino acid residue (*e.g.* S421 and S423 of mouse Grb10, isoform 3, are targets of mTOR).

The term “tumor,” as used herein, refers to a neoplasm or a solid lesion formed by neoplastic cells. A tumor can be benign, pre-malignant, or malignant. In some embodiments, the tumor is a malignant tumor.

The term “treatment”, interchangeably used herein with the term “therapy,” as used herein, refers to a clinical intervention aimed to prevent or to ameliorate a disease or condition in a subject. In some embodiments, a treatment is aimed to ameliorate an existing condition, for example, a cancer in a subject. In some embodiments, a treatment is aimed to prevent a condition from occurring or from recurring. For example, in some embodiments, an mTOR kinase inhibitor is administered to a subject having a cancer exhibiting an elevated level of mTOR activity in order to inhibit cell proliferation in the malignant cells. For another example, in some embodiments, an mTOR kinase inhibitor is administered to a subject having a cancer exhibiting an elevated level of mTOR activity after a malignant tumor has been removed from the subject, in order to prevent or delay recurrence of the disease. The foregoing examples are non-limiting, and those of skill in the art will readily envision further scenarios of treatment as the invention is not limited in this respect. Some

embodiments include a choice of treatment, referring to a selection of a clinical intervention from a number of alternatives, or to a design of a clinical intervention to meet the specific needs of an individual subject. In some embodiments, a choice of treatment involves the design of a personalized therapeutic approach for a subject having a cancer exhibiting

5 elevated mTOR activity based on the results from diagnostic methods provided herein. For example, in some embodiments, a choice of treatment includes administering to a subject having cancer a specific mTOR inhibitor in combination with an additional kinase inhibitor targeting an mTOR feedback-inhibited pathway based on a determination that cancer cells in the subject exhibit high mTOR activity and elevated levels of a feedback-inhibitor targeted

10 by mTOR in order to avoid feedback relief. In some embodiments, a choice of treatment includes the determination of an appropriate treatment. Some embodiments further include carrying out the selected treatment.

DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS

15 This invention relates to the identification of proteins and sites on those proteins that are phosphorylated by mTOR kinase. Some aspects of this invention relate to the surprising discovery that some proteins that are substrates of mTOR kinase regulate mTOR upstream signaling pathways, thus providing feedback regulatory circuits. Some aspects of this invention relate to methods of classifying cells, for example, neoplastic cells or cancer cells,

20 based on the phosphorylation status of mTOR targets. Some aspects of this invention relate to methods of personalized treatment of subjects having a proliferative disease, for example, a neoplastic disease or a cancer, exhibiting elevated mTOR signaling based on the phosphorylation status of mTOR targets in the diseased cells. Other aspects of this invention relate to methods and materials for the generation of phosphoproteomics profiles that include

25 phosphorylation data for a plurality of mTOR targets. Some aspects of this invention relate to classification of cells or tissues, for example, tumor cells or tissues, based on phosphoproteomic data, for example, based on phosphoproteomic profiles of the cells or tissues. Some aspects of this invention relate to methods of identifying mTOR kinase inhibitors by identifying compounds able to interfere with mTOR kinase activity towards one

30 or more of the mTOR targets provided herein. Some aspects of this invention relate to the identification of Grb10 as a target of mTOR kinase activity, and to methods for determining the level of mTOR activity in a cell based on Grb10 phosphorylation status. Some aspects of this invention relate to the surprising discovery that Grb10 is not only a target of mTOR kinase activity, but also an inhibitor of PI3K kinase activity. Since PI3K is a positive

regulator of mTOR kinase activity, Grb10 has been identified as a mediator of mTOR feedback inhibition herein. Other aspects of this invention relate to the surprising discovery that Grb10 and PTEN mutations are mutually exclusive in certain types of tumor cells. Accordingly, some aspects of this invention relate to the surprising discovery that Grb10 is a tumor suppressor and that Grb10 phosphorylation is a useful biomarker for determining mTOR kinase activity in cells, and particularly in tumor cells. Other aspects of this invention relate to methods and reagents useful for determining the phosphorylation status of a protein or phosphorylation site identified to be an mTOR target herein. For example, some aspects of this invention provide phosphosensitive antibodies or antibody fragments specifically binding an mTOR kinase target site identified herein in either the phosphorylated or the non-phosphorylated state, thus allowing for a determination of the phosphorylation state of such a site in a cell.

mTOR target proteins and sites

Identification of mTOR target sites

Some aspects of this invention relate to the identification of proteins and phosphorylation sites thereon as downstream targets of mTOR kinase activity. Targets of mTOR kinase activity are provided in Tables 1 and 2.

Classification of mTOR targets

Some aspects of this invention relate to the classification of mTOR target phosphorylation sites provided herein as class I (targets of rapamycin-sensitive mTORC1 kinase signaling), class II (targets of rapamycin-insensitive mTORC1 or mTORC2 signaling), and class III (targets of both rapamycin-sensitive and rapamycin-insensitive mTOR signaling) phosphorylation sites.

This classification is useful to determine the type(s) of mTOR signaling exhibited by a cell or tissue and can support a classification of cells that are targeted for therapy, for example, of cancer cells. For example, in some embodiments, the phosphorylation status of an mTOR target is determined in a cancer cell obtained from a subject with a cancer exhibiting elevated mTOR kinase activity. Classification of the type of mTOR signaling can, in some embodiments, be a basis for the selection of an appropriate therapeutic approach. For example, if it is determined that a class I target of mTOR signaling is phosphorylated, then the elevated mTOR kinase activity is rapamycin-sensitive mTORC1 kinase activity. In some such embodiments, a method of treatment is then typically selected that includes

administration of an inhibitor of rapamycin-sensitive mTORC1 signaling, for example, rapamycin or a rapamycin analog.

To give but another example: if it is determined that a class II target of mTOR signaling is phosphorylated, then the elevated mTOR kinase activity is rapamycin-insensitive mTORC1 or mTORC2 kinase activity. In some such embodiments, a method of treatment is then typically selected that includes administration of an mTORC1/2 inhibitor as provided herein. In some embodiments where class I targets of mTOR signaling are found to not be phosphorylated, a method of treatment is typically selected that does not include administration of an mTORC1 inhibitor.

To give a third example: if it is determined that a class III target of mTOR signaling is phosphorylated, then a method of treatment is selected that includes administration of an mTORC1 inhibitor and an mTORC1/2 inhibitor as provided herein. In some embodiments, a method of treatment that includes administering an mTORC1 inhibitor or an mTORC1/2 inhibitor alone may be inappropriate.

Further, some aspects of this invention provide methods to analyze gene ontology distributions in sets of mTOR targets, for example, in order to determine whether a specific signaling pathway is targeted by mTOR in a given cell, or a given therapeutic or experimental scenario.

Exemplary proteins identified in the rapamycin phosphoproteomic screen as targets of mTORC1 signaling.

The phosphoproteomic screen described herein identified numerous proteins as mTOR targets, for example, as mTORC1 targets. As described in more detail elsewhere herein, the expression, expression level, phosphorylation, or phosphorylation level of one or more of such mTOR target proteins, for example, the proteins described in any of tables 1-3, or the level of phosphorylation of their respective phosphorylation sites, is employed, in some embodiments, as a biomarker for monitoring or diagnosing disease. In some embodiments, the mTOR target proteins disclosed herein, for example, the mTORC1 target proteins described in any of tables 1-3, are used in pharmaceutical screens as drug targets for the development of drugs modulating mTOR pathway downstream effects. Some exemplary mTORC1 target proteins identified herein are described in more detail below. These descriptions of exemplary mTOR target proteins are for illustration of some aspects of this disclosure and are not meant to limit the scope of the invention. Grb10, one of the mTORC1 protein targets identified in the phosphoproteomics screen, is described in more detail

elsewhere herein. Briefly, Grb10, also known as growth factor receptor-bound protein 10, is stabilized by mTORC1-mediated phosphorylation, which, in turn, results in feedback inhibition of the PI3K and MAPK pathways. This is consistent with Grb10 expression being frequently downregulated in a variety of cancers. Grb10 is a tumor suppressor with relevance across a broad spectrum of cancer subtypes, and the identification of Grb10 as an mTORC1 substrate links mTORC1 activity to cancers with aberrantly low Grb10 expression or stability. Accordingly, some embodiments provide Grb10 phosphorylation as a biomarker for mTORC1 activity in a cell, tissue, or sample of interest. Methods of using Grb10 expression or phosphorylation assays to monitor mTORC1 activity in a cell, tissue, or sample of interest are also provided. For example, some embodiments provide a method of monitoring the efficacy of a drug on mTORC1 activity in a cell, tissue, or sample, by measuring Grb10 expression or phosphorylation levels. In some embodiments, such assessments are used to diagnose or monitor a disease associated with aberrant levels of mTORC1 activity, for example, cancer, or to adjust a drug dosage, for example, to the minimal dosage necessary to achieve a target mTORC1 activity level, or to choose a suitable drug modulating mTORC1 activity from a plurality of drugs, for example, the drug that shows the highest efficacy at a given dose.

Some of the mTORC1 protein targets identified herein are potential regulators of gene expression. For example, FOXK1 (Forkhead box protein K1), also known to those of skill in the art as MNF, or MNF (myocyte nuclear factor)-beta, is a winged-helix protein expressed selectively and transiently in myogenic precursor cells of the heart and skeletal muscles, and collaborates with proteins of the mammalian Sin3 (mSin3) family to repress transcription. Mutated forms of MNF-beta that fail to bind mSin3 are defective in transcriptional repression and in negative growth regulation, an overexpression phenotype revealed in oncogenic transformation assays. These phenotypic traits associated with MNF-beta dysfunction are consistent with the mTORC1 phenotype.

For another example, ZEB2 (Zinc finger E-box-binding homeobox 2) belongs to the ZEB family of zinc finger transcription factors, which are essential regulators of gene expression during normal embryonic development. ZEB proteins induce epithelial to mesenchymal transition (EMT), a process in which epithelial cells become migratory mesenchymal cells. E-cadherin is a major target gene of ZEB transcriptional repressors, and e-cadherin downregulation is considered a hallmark of EMT. In recent years, the involvement of the ZEB proteins in pathological contexts has been documented as well. For example, ZEB proteins play an important role in mediating Ras-induced EMT in breast

epithelial cells. Mutations in ZEB encoding genes cause severe syndromic malformations, and are implicated in malignant tumor progression. Without wishing to be bound by theory, ZEB2 is believed to be a critical target in lymphangioleiomyomatosis (LAM) that represents the point of convergence of the mTORC1 and ERK-MAP kinase pathways that are critical to this disease.

For another example, NDRG3 is the downstream target of N-Myc. Phosphorylation of NDRG3 links mTOR signaling pathway to Myc activity as an oncogenic transcription factor.

Accordingly, some embodiments provide FOXK1, ZEB2, and/or NDRG3 phosphorylation as a biomarker for mTORC1 activity in a cell, tissue, or sample of interest. Methods of using FOXK1, ZEB2, and/or NDRG3 expression or phosphorylation assays and levels useful for monitoring mTORC1 activity in a cell, tissue, or sample of interest are also provided. For example, some embodiments provide a method of monitoring the efficacy of a drug on mTORC1 activity in a cell, tissue, or sample, by measuring FOXK1, ZEB2, and/or NDRG3 expression or phosphorylation levels. In some embodiments, such assessments are used to monitor or diagnose a disease associated with aberrant mTORC1 activity, as manifest by aberrant FOXK1, ZEB2, and/or NDRG3 phosphorylation level(s), and/or to adjust a drug dosage, for example, to the minimal dosage necessary to achieve a target mTORC1 activity level, or to choose a suitable drug modulating mTORC1 activity from a plurality of drugs, for example, the drug that exhibits the highest efficacy at a given dose.

Some of the mTORC1 protein targets identified herein are regulators of mRNA synthesis, mRNA processing, and protein synthesis. This is consistent with the role mTORC1 activity plays in the control of cell growth, which, if improperly regulated, can contribute to tumor genesis and/or growth. For example, LARP1 binds mRNA *in vitro* via both the La motif and the LARP1 domain. LARP-1 also down-regulates the Ras-MAPK pathway. Accordingly, without wishing to be bound by any particular theory, LARP1 phosphorylation represents an mTORC1-dependent regulation of this feedback loop. The LARP-1 protein colocalizes with P bodies, which function in RNA degradation, and it is believed that the cluster of LARP-1 homologs functions to control the expression of key developmental regulators. Without wishing to be bound by any particular theory, some aspects of this invention provide that LARP-1 functions in P-bodies to attenuate the abundance of Ras-MAPK pathway-regulated mRNAs.

For another example, EDC3 is associated with an mRNA-decapping complex required for removal of the 5'-cap from mRNA prior to its degradation from the 5'-end.

For another example, SRPK2 is involved in SR protein phosphorylation, which influences other aspects of mRNA metabolism, such as splice site selection (alternative splicing), mRNA export, nonsense-mediated decay (NMD), and translation efficiency. Accordingly, some aspects of this disclosure provide that SRPK2 links mTOR/S6K signaling to SR protein activity.

Another example of an mTORC1 target identified herein that regulates mRNA synthesis and processing is CDK12 - (CDC2-related kinase, arginine/serine-rich). CDK12 is involved in the regulation of alternative mRNA splicing. Without wishing to be bound by any particular theory, it is believed that, similar to SRPK2, CDK12 is also involved in regulating mRNA splicing by mTOR signaling. A CDK12-binding partner, cyclin-L1 (CCNL1), is also identified as an mTORC1 target protein herein. Without wishing to be bound by any particular theory, similar to SRPK and CDK12, CCNL1 may contribute to mRNA biogenesis and cell proliferation.

Accordingly, some embodiments provide LARP1, SRPK2, and/or CDK12 phosphorylation as a biomarker for mTORC1 activity in a cell, tissue, or sample of interest. Methods of using LARP1, SRPK2, and/or CDK12 expression or phosphorylation levels to monitor mTORC1 activity in a cell, tissue, or sample of interest are also provided. For example, some embodiments provide a method of monitoring the efficacy of a drug on mTORC1 activity in a cell, tissue, or sample, by measuring LARP1, SRPK2, and/or CDK12 expression or phosphorylation levels. In some embodiments, such assessments are used to monitor or diagnose a disease associated with aberrant mTORC1 activity, as manifest by aberrant LARP1, SRPK2, and/or CDK12 phosphorylation level(s), and/or to adjust a drug dosage, for example, to the minimal dosage necessary to achieve a target mTORC1 activity level, or to choose a suitable drug modulating mTORC1 activity from a plurality of drugs, for example, the drug that exhibits the highest efficacy at a given dose.

Another example of an mTORC1 target protein identified herein is MIB1, an E3 ubiquitin-protein ligase that has been reported to ubiquitinate Notch, which leads to the degradation of Notch. Accordingly, some aspects of this disclosure provide that mTORC1 activity is linked to Notch signaling via phosphorylation of MIB1. Yet another example of an mTORC1 target protein identified herein is IBTK (Isoform 2 of Inhibitor of Bruton tyrosine kinase), which is a protein tyrosine kinase implicated in the primary immunodeficiency disease X-linked agammaglobulinemia (Bruton agammaglobulinemia). IBTK is activated upon binding to PIP3 generated as a result of PI3K activation. Without wishing to be bound by any particular theory, phosphorylation of IBTK affects IBTK's ability to inhibit PI3K

kinase activity. Accordingly, some embodiments of this invention are based on the recognition that there is a link between the mTORC1 signaling system and the regulation of tyrosine phosphorylation.

Accordingly, some embodiments provide MIB1 and/or IBTK phosphorylation as a
 5 biomarker for mTORC1 activity in a cell, tissue, or sample of interest. Methods of using MIB1 and/or IBTK expression or phosphorylation assays to monitor mTORC1 activity in a cell, tissue, or sample of interest are also provided. For example, some embodiments provide a method of monitoring the efficacy of a drug on mTORC1 activity in a cell, tissue, or sample, by measuring MIB1 and/or IBTK expression or phosphorylation levels. In some
 10 embodiments, such assessments are used to monitor or diagnose a disease associated with aberrant mTORC1 activity, as manifested by aberrant MIB1 and/or IBTK phosphorylation level(s), and/or to adjust a drug dosage, for example, to the minimal dosage necessary to achieve a target mTORC1 activity level, or to choose a suitable drug modulating mTORC1 activity from a plurality of drugs, for example, the drug that exhibits the highest efficacy at a
 15 given dose.

Representative protein sequences of Grb10, FOXK1, ZEB2, NDRG3, LARP1, SRPK2, CDK12, MIB1, IBTK, and other proteins identified herein to be mTORC1 substrates, can be found under the respective database entries provided in the tables and the database provided herein, and, for example, in the NCBI database under accession numbers
 20 NP_001171100.1 (growth factor receptor-bound protein 10 (Grb10) isoform 2, *Mus musculus*, SEQ ID NO: 1720), NP_034475.2 (growth factor receptor-bound protein 10 (Grb10) isoform 1, *Mus musculus*, SEQ ID NO: 1721), NP_001001550.1 (growth factor receptor-bound protein 10 (Grb10) isoform c, SEQ ID NO: 7), NP_005302.3 (Grb10 isoform a, SEQ ID NO: 8) and NP_001001549.1 (Grb10 isoform b, SEQ ID NO: 9); NP_001032242.1 (FOXK1, SEQ
 25 ID NO: 10); NP_001165124.1 and NP_055610.1 (ZEB2, SEQ ID NO: 11 and SEQ ID NO: 12, respectively); NP_071922.2 and NP_114402.1 (NDRG3, SEQ ID NO: 13 and SEQ ID NO: 14, respectively); NP_056130.2 (LARP1, SEQ ID NO: 15); NP_872633.1 and NP_872634.1 (SRPK2, SEQ ID NO: 16 and SEQ ID NO: 17, respectively); NP_055898.1 and NP_057591.2 (CDK12, SEQ ID NO: 18 and SEQ ID NO: 19, respectively);
 30 NP_065825.1 (MIB1, SEQ ID NO: 20); and NP_056340.2 (IBTK, SEQ ID NO: 21). These database entries are incorporated herein by reference for disclosure of representative sequences of the respective proteins.

Feedback circuitry involving mTOR targets

Some aspects of this invention relate to the surprising discovery that some mTOR target proteins are involved in feedback loops of mTOR signaling, for example, by inhibiting upstream modulators of mTOR signaling, such as PI3K, Akt, and MAPK, after being phosphorylated as a result of mTOR kinase activity. Some aspects of this invention relate to the surprising discovery that relief of feedback inhibition of cellular pro-survival, pro-proliferation signaling by mTOR downstream targets, for example, by Grb10, can contribute to rapamycin resistance or even clinically detrimental outcome in the treatment of neoplastic disease (*e.g.*, cancer) with mTOR inhibitors. Some aspects of this invention relate to the identification, for the first time, of Grb10 as a target of mTOR kinase activity. Grb10, growth factor receptor-bound protein 10, is a protein well known to those of skill in the art. Representative protein sequences of Grb10 can be found under the respective database entries provided in the tables and the database provided herein, and, for example, in the NCBI database under accession numbers NP_001001550.1 (growth factor receptor-bound protein 10 isoform c), NP_005302.3 (isoform a) and NP_001001549.1 (isoform b). These database entries are incorporated by reference for disclosure of representative Grb10 sequences.

Feedback inhibition of PI3K by Grb10

Some aspects of this invention relate to the surprising discovery that Grb10 is not only a target of mTOR kinase activity, but also a mediator of mTOR feedback inhibition and, thus, a tumor suppressor gene. As described in more detail elsewhere herein, mTOR-mediated phosphorylation of Grb10 results in stabilization and/or prevention of degradation of Grb10. Grb10, in turn, inhibits PI3K kinase activity. PI3K kinase activity targets mTOR and activates mTOR signaling. Accordingly, as provided by some aspects of this invention, treatment of a cancer exhibiting an elevated level of Grb10 phosphorylation can lead to relief of the Grb10-mediated feedback inhibition of PI3K. PI3K signaling, however, promotes proliferation and survival, and aberrant PI3K activity is known to contribute to carcinogenesis. The discovery that some mTOR targets identified herein, for example, Grb10, mediate a feedback inhibition of pro-survival and pro-proliferation signaling (*e.g.* PI3K, Akt, and MAPK signaling) in cancer cells, could explain why some types of cancer exhibiting elevated levels of mTOR activity do not respond favorably to treatment with an mTORC1 inhibitor (*e.g.*, rapamycin) alone. The mTORC1 inhibitor may cause relief of the feedback inhibition which may, in turn result in sustained survival and proliferation, and even an increase or acceleration in disease progression or recurrence, as observed in some clinical trials of cancer treatment with mTOR inhibitors.

Also provided herein are methods of treating a cancer determined to exhibit an elevated level of Grb10 phosphorylation. In some embodiments, the method comprises administering to the subject an mTOR inhibitor and, additionally, an agent that stabilizes Grb10 or that inhibits the degradation of Grb10. In some embodiments, the method comprises effecting an inhibition of Grb10 degradation by administering a compound that inhibits Grb10 degradation. In some embodiments, the compound that inhibits Grb10 degradation is a ubiquitin ligase inhibitor, for example, a ubiquitin E3 ligase inhibitor. In some embodiments, the method comprises administering to the subject an mTOR inhibitor and, additionally, a PI3K inhibitor. PI3K inhibitors are known to those of skill in the art and described in more detail elsewhere herein.

Diagnostic methods

Classification of cancer cells based on Grb10 phosphorylation

Some aspects of this invention provide methods for the classification of a neoplastic disease, for example, a cancer, based on the phosphorylation status of Grb10. In some embodiments, a method is provided that includes obtaining a neoplastic cell from a subject diagnosed to have a cancer, determining the level of Grb10 phosphorylation in the cell, and comparing the level of Grb10 phosphorylation to a reference level. In some embodiments, if the level of Grb10 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity. In some embodiments, the cell is determined to exhibit an elevated level of mTORC1 kinase activity based on an elevated level of Grb10 phosphorylation.

Methods of determining a level of protein phosphorylation, for example, of Grb10 phosphorylation, are well known to those of skill in the art. Exemplary methods as well as materials useful for such methods are described, for example, in Marjo de Graauw (Editor), *Phospho-Proteomics: Methods and Protocols (Methods in Molecular Biology)*, Humana Press; 1 edition (2009), ISBN-10: 1603278338. Phosphosensitive binding agents, for example, phosphosensitive antibodies, are provided herein, are commercially available, or can be obtained by those of skill in the art with no more than routine experimentation.

Such methods include, for example, detection of phosphorylated protein with a phosphosensitive antibody and comparison of the amount of phosphorylated protein detected to the total amount of the protein in a sample. Other methods for quantitative or semi-quantitative detection of phosphorylated protein will be apparent to those of skill in the art and the invention is not limited in this respect.

In some embodiments, a method is provided that includes selecting a method of treatment of a neoplastic disease, for example, a cancer based on a cell from a subject having the disease exhibiting an elevated level of Grb10 phosphorylation. In some embodiments, an elevated level of Grb10 phosphorylation is indicative of an elevated level of rapamycin-sensitive mTORC1 kinase activity in the cell. In some embodiments, a method of treatment is chosen based on the cell exhibiting an elevated level of Grb10 phosphorylation that includes administration of an mTORC1 inhibitor, for example, a rapamycin or a rapamycin analog.

10 ***Classification of cancer cells known to exhibit elevated levels of mTOR activity***

Some aspects of this invention relate to the discovery that the mTOR target Grb10 is an inhibitor of the mTOR upstream regulators, PI3K, Akt, and MAPK, and, thus, can be characterized as a tumor suppressor gene and an mTOR feedback inhibitor. Some aspects of this invention provide a method for selecting a treatment of a cancer known to exhibit an elevated mTOR kinase activity based on the expression level of the mTORC1 target Grb10. In some embodiments, the method comprises obtaining a cancer cell from a subject diagnosed to have a cancer exhibiting an elevated level of mTOR activity, determining the level of Grb10 expression in the cell, and comparing the level of Grb10 expression to a reference level. In some embodiments, if the level of Grb10 expression in the cancer cell is higher than the reference level, then the cell is determined to exhibit a high likelihood of expressing an elevated level of PI3K, Akt, and/or MAPK activity upon being contacted with an mTORC1 inhibitor. In some embodiments, elevated expression of Grb10 supports the conclusion that upon treatment of the cell or a population of cells of the same type, mTORC1-dependent phosphorylation of Grb10 will be decreased or abolished, resulting in rapid ubiquitination and degradation of Grb10 protein, and, subsequently, in a relief of the Grb10-mediated feedback inhibition of PI3K, as described herein. This relief of feedback inhibition may, in some embodiments, result in elevated PI3K signaling. In some embodiments, elevated PI3K in a cancer cell is an undesirable response to treatment of a subject because it can lead to increased cell proliferation and/or survival, thus offsetting or even outweighing the beneficial effect of the administered mTORC1 inhibitor.

Measuring the expression level of an mTOR target protein can be achieved by using methods well known to those of skill in the art, including, but not limited to, protein expression assays, for example, immunostaining methods (*e.g.*, western blot, protein microarray, immunohistochemistry, phosphoproteomic assays using phosphosensitive

binding agents), ELISA, transcript expression assays, for example, RT-PCR, massive parallel sequencing assays, microarray assays, northern blot, or in situ hybridization. Other suitable methods will be apparent to those of skill in the art and the invention is not limited in this respect. See, for example, Sambrook *et al.*, Molecular Cloning, second edition, Cold Spring Harbor Laboratory, Plainview, N.Y.; (1989); Ausubel *et al.*, Current Protocols in Molecular Biology, Current Protocols (1989), and DNA Cloning: A Practical Approach, Volumes I and II (ed. D.N. Glover) IREL Press, Oxford, (1985); and *Current Protocols in Molecular Biology*, Wiley Publishing, accessible at www.currentprotocols.com; each of which is incorporated herein by reference.

In some embodiments, after a cancer cell is classified, a method of treatment of the subject from which the cell was obtained is selected based on the cancer cell exhibiting a high likelihood of expressing an elevated level of PI3K, Akt, and/or MAPK activity upon being contacted with an mTORC1 inhibitor. In some embodiments, the method of treatment comprises administering an effective amount of an mTOR kinase inhibitor and, additionally, an effective amount of an IGF1R, EGFR, PI3K, Akt, MEK, or RSK inhibitor, or a combination thereof. In some embodiments, the method of treatment comprises administering an effective amount of an mTOR kinase inhibitor and, additionally, of a compound stabilizing Grb10 to the subject. In some embodiments, the mTOR kinase inhibitor is an mTORC1 inhibitor, for example, rapamycin or a rapamycin analog. In some embodiments, the selected method of treatment is communicated to the subject, to a physician or other health care professional treating the subject. In some embodiments, the selected method of treatment is carried out.

Determining and classifying mTOR activity in a cell based on phosphoproteomics

Some aspects of this invention provide methods for determining the level of mTOR activity in a cell based on analysis of the phosphorylation state of one or more mTOR targeted phosphorylation sites as provided herein. Some aspects of this invention provide methods to determine a class of mTOR signaling, for example, rapamycin-sensitive mTORC1 signaling, rapamycin-insensitive mTORC1 or mTORC2 signaling, or rapamycin-sensitive and/or rapamycin-insensitive mTOR signaling, in a cell based on an analysis of the phosphorylation state of a phosphorylation site as provided herein.

Methods useful for the determination of the phosphorylation level of a phosphorylation site in a cell are known to those of skill in the art. In some embodiments, such methods comprise obtaining a proteinaceous extract from the cell under conditions that

allow for protein phosphorylation to be preserved with high fidelity. In some embodiments, such methods comprise contacting the cell extract with a phosphosensitive binding agent or with a plurality of phosphosensitive binding agents, for example, phosphosensitive antibodies or antibody fragments.

5 The invention provides phosphosensitive antibodies and antibody fragments to the phosphorylation sites described in the tables and the database. For example, phosphosensitive mTORC1 downstream effector antibodies, including, but not limited to, anti-phospho-NDRG3 (Ser331), anti-phospho-S501/503-Grb10, Anti-CDC2-related Kinase, Arg/Ser-Rich (Ser437), In some embodiments, antibodies provided herein are developed in
10 rabbits. Other phosphosensitive antibodies are described elsewhere herein.

Phosphosensitive antibodies are useful in some embodiments to determine the phosphorylation level of one or more phosphorylation sites disclosed herein. One non-limiting example of such an embodiment is a phosphosensitive protein microarray assay. In some embodiments, the cell extract is contacted with a single phosphosensitive binding agent.

15 In some embodiments, the cell extract is contacted with a plurality of binding agents in parallel. In some such embodiments, the cell is contacted with a microarray comprising a plurality of phosphosensitive binding antibodies or antibody fragments immobilized on a solid surface, for example, a glass surface. Phosphoproteomic assays, arrays, binding agents, and methods for sample preparation and analysis are well known in the art, and exemplary
20 methods are described, for example, in Marjo de Graauw (Editor), *Phospho-Proteomics: Methods and Protocols (Methods in Molecular Biology)*, Humana Press; 1 edition (2009), ISBN-10: 1603278338. The foregoing reference is incorporated herein by reference in its entirety for disclosure of methods and materials useful for the determination of the phosphorylation state of a phosphorylation site on a protein in a cell, tissue, or biological
25 sample.

In some embodiments, the method comprises determining the level of phosphorylation of a phosphorylation site of a protein disclosed in Tables 1 or 2, and comparing the level of phosphorylation to a reference level. If the level of phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated
30 level of mTOR kinase activity. If the level of phosphorylation in the cell is equal or lower than the reference level, then the cell is determined to not exhibit an elevated level of mTOR kinase activity. Methods of determining a level of phosphorylation are provided herein, and additional suitable methods will be apparent to those of skill in the art. The invention is not limited in this respect.

Suitable reference levels and methods of determining a reference level will be apparent to those of skill in the art. For example, if the cell is a neoplastic cell or cancer cell obtained from a subject, for example from a biopsy of a solid tumor in the subject, a suitable reference level may be obtained, in some embodiments, from a cell obtained from healthy or non-malignant tissue adjacent to the solid tumor, or a healthy cell of the same tissue of origin as the tumor cells from the same subject or from a different subject. If the cell is obtained from a healthy subject, a suitable reference level may be obtained from a cell of the same cell type obtained from another healthy subject. In some embodiments, a suitable reference level may be an average level or a range of levels observed or expected in cells obtained from healthy subjects that are of the same cell type of the same tissue of origin as the cell in question. In some embodiments, a reference level is a historical level, based on experience or prior experiments, or a level published or otherwise known in the art. Other suitable reference levels are described elsewhere herein and additional reference levels and methods to obtain such levels will be apparent to those of skill in the art.

In some embodiments, a plurality of phosphorylation sites are assayed including a Grb10 phosphorylation site, a pNDRG3 phosphorylation site, a CDK12 phosphorylation site, a FOXK1 phosphorylation site, a ZEB2 phosphorylation site, a LARP1 phosphorylation site, an MIB1 phosphorylation site, an IBTK phosphorylation site, and/or a SRPK2 phosphorylation site. In some embodiments, a group of phosphorylation sites of proteins involved in a specific biological pathway are assayed, for example, of proteins known to those of skill in the art to be involved in a biological pathway disclosed in Table 10. In some embodiments, the plurality of phosphorylation sites includes mTOR target sites that were previously known. In some embodiments, the plurality of phosphorylation sites comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 1. In some embodiments, the plurality of phosphorylation sites comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 2. In some embodiments, the plurality of phosphorylation sites comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at

least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 3 or in replicate described therein. In some embodiments, the plurality of phosphorylation sites comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 7 or in replicate described therein. In some embodiments, the plurality of phosphorylation sites comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 8. In some embodiments, the plurality of phosphorylation sites comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 11, or in any Rapa or Ku replicate therein

In some embodiments, if a phosphorylation site determined to exhibit a higher level of phosphorylation in a cell in question, for example, a cancer cell obtained from a subject, as compared to a reference level is a class I phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTORC1 activity. In some embodiments, if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class II phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity. In some embodiments, if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class III phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR activity, or an elevated level of rapamycin-insensitive mTOR activity, or both. In some embodiments, if a cell is determined to exhibit a higher level of phosphorylation at phosphorylation sites of more than one class, then the cell is determined to exhibit a combination of elevated levels of mTOR signaling of the respective type.

In some embodiments, a method is provided comprising selecting a method of treatment based on the level of phosphorylation of the phosphorylation site(s) assayed. In

some embodiments, if the cell is determined to exhibit an elevated level of mTOR kinase activity, then a method of treatment is selected that comprises administering an effective amount of an mTOR kinase inhibitor to the subject. In some embodiments, if the cell is determined to not exhibit an elevated level of mTOR kinase activity, then a method of treatment is selected that does not include administering an mTOR kinase inhibitor. In some embodiments, a method is provided that comprises selecting a method of treatment based on the classification of mTOR target sites that are determined to exhibit an elevated level of phosphorylation in the cell. For example, in some embodiments, if the cell is determined to exhibit an elevated level of rapamycin-sensitive mTORC1 activity, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-sensitive mTORC1 kinase activity to the subject. In some embodiments, if the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-insensitive mTORC1 kinase activity to the subject. In some embodiments, if the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR kinase activity, or an elevated level of rapamycin-insensitive mTOR kinase activity, or both, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-sensitive and rapamycin-insensitive mTOR kinase activity or a combination of an inhibitor of rapamycin-sensitive mTOR kinase activity and an inhibitor of rapamycin-insensitive mTOR kinase activity to the subject.

Classification of a cancer based on Grb10 and/or PTEN expression levels

Some aspects of this invention relate to the surprising discovery that mutations leading to loss of function of the tumor suppressor Grb10 and mutations leading to loss of function of the tumor suppressor PTEN, are mutually exclusive. Loss of function of either tumor suppressor leads to elevated PI3K activity, which is thought to significantly contribute to carcinogenesis in certain types of cancer. In some embodiments, a method is provided that allows for the classification of a cancer based on Grb10 or PTEN expression levels. In some embodiments, the method comprises determining the level of expression of Grb10 in a cancer cell. In some embodiments, the method comprises determining the level of expression of PTEN in a cancer cell. In some embodiments, the method comprises determining the level of expression of Grb10 and PTEN in a cancer cell.

Expression levels of Grb10 and PTEN can be determined by various methods known to those of skill in the art including, for example methods for determining a level of protein, methods for determining a level of mRNA. Since phosphorylation affects protein stability, for example, stability of Grb10, methods for determining a level of protein phosphorylation may also be useful in assessing protein expression levels. Some such methods for expression analysis are provided herein, and additional methods will be apparent to those of skill in the art. The invention is not limited in this respect.

In some embodiments, the level of expression determined for Grb10 or PTEN is compared to a reference level, for example, to a level observed or expected in a healthy cell of the same cell type or of the same tissue of origin. In some embodiments, if the level of expression of Grb10 or of PTEN in the cell is lower than the reference level, then the cell is likely to exhibit an elevated level of PI3K activity. In some embodiments, if the cell is a neoplastic cell in a subject, a method of treatment with a combination of an mTOR inhibitor and a PI3K inhibitor or with a dual mTOR/PI3K inhibitor is indicated.

Phosphoproteomics binding agents and arrays

Phosphosensitive binding agents that specifically bind mTOR targets are also provided by the present invention. For example, some aspects of this invention provide antibodies and antibody fragments to each of the mTOR-targeted phosphorylation site disclosed in any of the Tables provided herein, for example, in any of Tables 1, 2, 3, 7, 8, or 11, and each such antibody is within the scope of the present invention. For example, some aspects of this invention provide aptamers and/or adnectins that specifically bind mTOR-targeted phosphorylation sites disclosed in Table 1, 2, 3, 7, 8, or 11, and each such aptamer or adnectin is within the scope of the present invention. In some embodiments, a kit is provided that comprises such phosphosensitive binding agents. A kit may also include a buffer, a container, control samples, or instructions.

Some embodiments provide a phosphoproteomics array that includes a plurality of phosphosensitive binding agents, for example, antibodies or antibody fragments, aptamers or adnectins, each of which specifically bind to a phosphorylation site disclosed in Table 1, 2, 3, 7, 8, or 11. In some embodiments the phosphosensitive binding agents are immobilized on a solid substrate, for example, on the surface of a glass slide, a bead, or a microtiter plate. In some embodiments, the plurality of phosphosensitive binding agents comprises binding agents that specifically bind to at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least

50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 1. In some embodiments, the plurality of phosphosensitive binding agents comprises binding agents that specifically bind to at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 2. In some embodiments, the plurality of phosphosensitive binding agents comprises binding agents that specifically bind to at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 3. In some embodiments, the plurality of phosphosensitive binding agents comprises binding agents that specifically bind to at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 7. In some embodiments, the plurality of phosphosensitive binding agents comprises binding agents that specifically bind to at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 8. In some embodiments, the plurality of phosphosensitive binding agents comprises binding agents that specifically bind to at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 11.

In some embodiments, an anti-phospho-S501/503-Grb10, anti-mTOR, anti-phospho-mTOR (S2481), anti-Grb10 (human), anti-phospho-Akt (Ser473), anti-Akt, anti-S6K, anti-phospho-S6K (T389), anti-IRS2, anti-PARP, anti-caspase 3, anti-4EBP, anti-4EBP (Ser37/46), anti-phospho-ribosomal protein S6 (Ser235/236), anti-ribosomal protein S6, anti-phospho-ERK1/2, anti-phospho-IRS (Y612), anti-p85 and anti-p110 of PI3K, and/or an anti-ERK1/2 antibody or antibody fragment is provided. In some embodiments, phosphosensitive antibodies or antibody fragments are provided for mTOR upstream regulators, including, but not limited to anti-phospho-Akt (Ser473), anti-phospho-ERK1/2, anti-phospho-IRS (Y612), anti-p85, and anti-p110 of PI3K. In some embodiments, phosphosensitive antibodies or antibody fragments are provided for mTOR downstream effectors including, but not limited

to anti-phospho-mTOR (S2481), anti-phospho-Akt (Ser473), anti-phospho-S6K (T389), anti-4EBP (Ser37/46), and anti-phospho-ribosomal protein S6 (Ser235/236).

In some embodiments, antibodies against mTORC1 downstream effectors identified for the first time herein are provided, including, anti-phospho-NDRG3 (Ser331), anti-phospho-S501/503-Grb10, and anti-CDC2-related kinase, Arg/Ser-Rich (Ser437).

Phosphosensitive binding agents, their generation and purification, and their use in assays, arrays, and methods for phosphoproteomics analyses of biological samples are well known in the art, and exemplary methods are described, for example, in Marjo de Graauw (Editor), *Phospho-Proteomics: Methods and Protocols (Methods in Molecular Biology)*, Humana Press; 1 edition (2009), ISBN-10: 1603278338, incorporated herein by reference in its entirety. The foregoing reference is incorporated herein by reference in its entirety for disclosure of phosphosensitive binding agents, their generation and purification, and their use in assays, arrays, and methods for phosphoproteomics analyses of biological samples.

Methods of using a microarray comprising a plurality of phosphosensitive binding agents that specifically bind mTOR targets are also provided. In some embodiments, methods of using a phosphoproteomics array to determine mTOR activity in a cell, for example, in a cancer cell, are provided. In some embodiments, the method comprises contacting a proteinaceous sample derived from the cell with the phosphoproteomics array under conditions suitable for a protein expressed in the cell to bind to an antibody or antibody fragment of the array. Such conditions are well known to those of skill in the art and exemplary protocols for phosphoprotein microarrays are described in Marjo de Graauw (Editor), *Phospho-Proteomics: Methods and Protocols (Methods in Molecular Biology)*, Humana Press; 1 edition (2009), ISBN-10: 1603278338, incorporated herein by reference for the disclosure of such methods and conditions. In some embodiments, the method further comprises determining a level of phosphorylated protein bound to a binding agent, for example, an antibody or antibody fragment of the array. In some embodiments, this step includes quantification, absolute or relative to a reference level, of the amount of protein bound to a specific binding agent. In some embodiments, the method includes comparing the level of phosphorylated protein bound to an antibody or antibody fragment of the array to a reference level, wherein if the level phosphorylated protein in the sample derived from the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

In some embodiments, methods are provided that include generating a phosphoproteomic profile of the cell. In some embodiments, the profile includes

phosphorylation levels of a plurality of proteins, for example, mTOR targets expressed in the cell. In some embodiments, the method further includes comparing the phosphoproteomic profile of the cell with a phosphoproteomic profile of a control cell. In some embodiments, if the phosphoproteomic profile of the cell is similar to that of the control cell, then the cell is

5 determined to exhibit a level of mTOR kinase activity similar to that of the control cell.

Methods for comparing phosphoprotein profiles are well known in the art and include, for example, hierarchical clustering methods, supervised and unsupervised learning methods, classification methods, for example class predictor building methods based on phosphoproteomics profiles from cells of known character, and calculation of correlation

10 parameters, such as distance analysis or correlation coefficient calculations. Useful similarity ranges are also known to those of skill in the art and the invention is not limited in this respect. For non-limiting examples of disclosures of such methods and algorithms, see Lim, Y. (2005) Mining the tumor phosphoproteome for cancer markers. *Clin Cancer Res* 11(9): 3163-3169; Kalume, D. *et al.* (2003) Tackling the phosphoproteome: tools and strategies

15 *Current Opinion in Chemical Biology* 7: 64-69; Schmelzle, K. & White, F. (2006) Phosphoproteomic approaches to elucidate cellular signaling networks. *Current Opinion in Chemical Biology* 17: 406-414; Olsen JV *et al.* Global, in vivo, and site-specific phosphorylation dynamics in signaling networks. *Cell*. 2006 Nov 3;127(3):635-48; Mumby, M. & Brekken, D. (2005) Phosphoproteomics: new insights into cellular signaling. *Genome*

20 *Biology* 6: 230.1-230.7; Zhang *et al.* *J. Proteome Res.* vol. 5 pp. 581-8 2006; Hoffert JD, *et al.* Quantitative phosphoproteomics of vasopressin-sensitive renal cells: regulation of aquaporin-2 phosphorylation at two sites. *Proc Natl Acad Sci U S A.* 2006 May

2;103(18):7159-64; Johnson, S & Hunter, T. (2004) Phosphoproteomics finds its timing. *Nature Biotech* 22(9): 1093-1094; and Marjo de Graauw (Editor), *Phospho-Proteomics: Methods and Protocols (Methods in Molecular Biology)*, Humana Press; 1 edition (2009),

25 ISBN-10: 1603278338; all incorporated herein by reference in their entirety

In some embodiments, the control cell is a healthy cell. In some embodiments, the control cell is a cell exhibiting normal mTOR kinase activity. In some embodiments, the control cell is a cancer cell. In some embodiments, the control cell is a rapamycin-sensitive

30 cancer cell. In some embodiments, the control cell is a rapamycin insensitive cancer cell.

Identification of mTOR kinase inhibitors based on mTOR target analysis

In some aspects, the invention provides methods of identifying an mTOR kinase inhibitors by analyzing the phosphorylation state of an mTOR target as provided herein after

contacting a cell or test sample with a candidate agent. In some embodiments, mTOR phosphorylation efficiency directed towards a target disclosed in Table 1, 2, 3, 7, 8, or 11 is measured in the presence of a candidate agent. In some embodiments, the method includes contacting an mTOR kinase molecule with a polypeptide comprising a phosphorylation site disclosed in Table 1, 2, 3, 7, 8, or 11 under conditions suitable for the mTOR kinase to phosphorylate the phosphorylation site in the presence of a candidate agent. In some embodiments, the level of phosphorylation of the phosphorylation site is then determined and compared to a reference level. In some embodiments, if the level obtained in the presence of the candidate agent is lower than the reference level, then the candidate agent is identified as an mTOR kinase inhibitor.

In some embodiments, the phosphorylation site is a Grb10 phosphorylation site, a pNDRG3 phosphorylation site, a CDK12 phosphorylation site, a FOXK1 phosphorylation site, a ZEB2 phosphorylation site, a LARP1 phosphorylation site, an MIB1 phosphorylation site, an IBTK phosphorylation site, and/or a SRPK2 phosphorylation site. In some embodiments, the candidate agent is a polypeptide, an aptamer, an adnectin, or a small molecule. In some embodiments, the reference level is the level of phosphorylation of the phosphorylation site determined in the absence of the candidate agent. In some embodiments, the level determined in the presence of the candidate agent is lower than the reference level, if the level determined in the presence of the candidate agent is less than 75%, less than 50%, less than 40%, less than 30%, less than 25%, less than 20%, less than 10%, less than 5%, less than 2.5%, or less than 1% of the reference level.

In some embodiments, the contacting is performed *in vitro*. In some embodiments, the contacting is performed *in vivo*. In some embodiments, the reference level is a level observed or expected in the absence of the candidate agent. In some embodiments, the reference level is a level observed or expected in the absence of any candidate agent. In some embodiments, the reference level is a level observed or expected in the presence of a known agent. In some embodiments, the reference level is a level observed or expected in the presence of a control agent.

Subjects and cells

In some embodiments, the subject is an animal. In some embodiments, the subject is a domesticated animal. In some embodiments, the subject is a mammal. In some embodiments, the subject is a non-human mammal. In some embodiments, the subject is a non-human primate. In some embodiments, the subject is a mouse, rat, or rabbit. In some

embodiments, the subject is a sheep, goat, cattle, pig, horse, dog, or cat. In some embodiments, the subject is a human.

In some embodiments, the subject is a healthy subject. In some embodiments, the subject is a subject having a hyperproliferative disease. In some embodiments, the subject is a subject having a neoplastic disease. In some embodiments, the subject is a subject having a cancer. In some embodiments, the subject is a subject having a cancer characterized and/or diagnosed to exhibit an elevated level of mTOR activity. In some embodiments, the subject is a subject who had a tumor removed.

In some embodiments, the cell is a healthy cell. In some embodiments, the cell is any cell. In some embodiments, the cell is a bacterial cell. In some embodiments, the cell is an animal cell. In some embodiments, the cell is a mammalian cell. In some embodiments, the cell is a human cell. In some embodiments, the cell is a cell of a cell line. In some embodiments, the cell is a transformed or immortalized cell. In some embodiments, the cell is a neoplastic cell. In some embodiments, the cell is a tumor cell. In some embodiments, the cell is a cancer cell. In some embodiments, the cell is obtained from a tumor in a subject, for example, by tumor biopsy. In some embodiments, the cell is a cell obtained from a tumor that has been removed from a subject.

In some embodiments, the cell is a cell known to exhibit an elevated level of mTOR activity. In some embodiments, the cell is a cell carrying a mutation in a gene involved in an mTOR signaling pathway. In some embodiments, the gene involved in an mTOR signaling pathway is a gene involved in IGF signaling, EGFR signaling, GF signaling, PI3K signaling, AKT signaling, MAPK signaling, Ras signaling, Raf signaling, or Rb signaling. In some embodiments, the gene is TSC1/2, a receptor tyrosine kinases (RTK), PI3K, PTEN, Akt, Ras, Raf, MEK, LKB, or NF2.

Kinase Inhibitors

Kinase inhibitors useful for some aspects of this invention include, but are not limited to, mTOR inhibitors, PI3K inhibitors, Akt inhibitors, and MAPK inhibitors. Further, inhibitors useful for some methods provided herein include, for example, inhibitors of mTOR target degradation, for example, inhibitors of Grb10 degradation. In some embodiments, a kinase inhibitor, for example, an mTOR inhibitor, as provided herein, is an allosteric mTOR kinase inhibitor or a catalytic mTOR kinase inhibitor. In some embodiments, the allosteric mTOR kinase inhibitor is rapamycin or a rapamycin analog. In some embodiments, the catalytic mTOR kinase inhibitor is an ATP-competitive mTOR kinase inhibitor. Other

allosteric and catalytic mTOR kinase inhibitors are well known to those of skill in the art, and the invention is not limited in this respect.

In some embodiments, an mTOR kinase inhibitor as provided herein is an mTORC1 inhibitor. In some embodiments, an mTOR kinase inhibitor as provided herein is an
5 mTORC1/2 inhibitor. In some embodiments, an mTOR kinase inhibitor as provided herein is rapamycin or a rapamycin analog. In some embodiments, the rapamycin analog is Ridaforolimus, Sirolimus or Everolimus. In some embodiments, an mTOR kinase inhibitor as provided herein is PP242, PP30, AZD8055, OSI-027, WYE354, INK-128, XL388, torin1, rapamycin (sirolimus), FK506 (tacrolimus), CCI779 (temsirolimus), RAD001 (everolimus),
10 AP23573 (deforolimus, ridaforolimus), S-trans,trans-farnesyl thiosalicylic acid (FTS), FKBP38, PX-866, Theophylline, Caffeine, LY303511, PI-103, 2-(morpholin-1-yl)pyrimido[2,1- α]isoquinolin-4-one, or BEZ235 (NVP-BEZ235)

In some embodiments, an mTOR kinase inhibitor as provided herein is a dual PI3K/mTOR kinase inhibitor. In some embodiments, the dual PI3K/mTOR kinase inhibitor
15 is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126. Some of the mTOR kinase inhibitors listed immediately above are in various stages of clinical trials. Additional mTOR inhibitors will be apparent to the skilled artisan as they are well known in the art, and it should be appreciated that the invention is not limited in this respect.

In some embodiments, a PI3K inhibitor is provided that is useful in a therapeutic
20 method provided by aspects of this invention. In some embodiments, a PI3K inhibitor as provided herein is ZSTK474, TGX221, GDC0941, or LY294002, XL147, PX147, BKM120, GSK 615, CAL101, PX-866, Quercetin, Tetrodotoxin citrate, Thioperamide maleate, IC87114, PI-103, BEZ235 (NVP-BEZ235), TGX-115, (-)-Deguelin, NU 7026, Myricetin, Tandutinib, SF1126, XL765, D-87503, D-106669, or GSK615.

25 In some embodiments, a PI3K inhibitor provided herein is a dual PI3K/mTOR kinase inhibitor, for example, NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126. In some embodiments, an Akt inhibitor is provided that is useful in a therapeutic method provided by aspects of this invention. In some embodiments, the Akt inhibitor is perifosine, GSK690693, A443654 or MK2206.

30 In some embodiments, a compound is provided that inhibits the degradation of an mTOR target, for example, of Grb10, NDRG3, CDK12, FOXK1, ZEB2, LARP1, MIB1, IBTK, and/or SRPK2. In some embodiments, the compound that inhibits the degradation of an mTOR target is a ubiquitin ligase inhibitor. In some embodiments, the ubiquitin ligase inhibitor is an E3 ubiquitin ligase inhibitor.

Compositions

In some embodiments, pharmaceutical compositions are provided that comprise an mTOR kinase inhibitor, a PI3K, Akt, or MAPK inhibitor, and/or an agent that inhibits the degradation of an mTOR target, for example, Grb10, NDRG3, CDK12, FOXK1, ZEB2, LARP1, MIB1, IBTK, and/or SRPK2. Pharmaceutical compositions provided herein preferably are sterile and contain an effective amount of one or more therapeutic agents as described herein for producing the desired response in a unit of weight or volume suitable for administration to a patient. If the desired response is amelioration of a hyperproliferative disease, neoplastic disease, or cancer, then the response can, for example, be measured by determining the proliferation of neoplastic or cancer cells in a subject after treatment by, for example, measuring tumor volume, evaluating regression, relapse, or disease symptoms, or by obtaining a cell sample and perform cell counting, flow cytometry, FACS, and other methods well known in the art to be suitable to determine cell proliferation.

In some embodiments, the pharmaceutical compositions as described herein may contain suitable buffering agents, for example, acetic acid in a salt form, citric acid in a salt form, boric acid in a salt form, and/or phosphoric acid in a salt form. The pharmaceutical compositions also may contain, optionally, suitable preservatives, such as ascorbic acid, benzalkonium chloride, benzyl alcohol, m-cresol, chlorobutanol, parabens, EDTA, EGTA, and/or thimerosal. The pharmaceutical compositions may conveniently be presented in unit dosage form and may be prepared by any of the methods well-known in the art of pharmacy.

In some embodiments, a therapeutic method or a method of formulating a kinase inhibitor into a medicament for therapeutic use may include the step of bringing the active agent, for example, a kinase inhibitor as described herein, into association with a carrier which constitutes one or more accessory ingredients. In general, compositions are prepared by uniformly and intimately bringing the active compound(s) into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product.

In some therapeutic embodiments, a composition or pharmaceutical preparation provided herein is administered orally to a subject having a cancer. In some embodiments, compositions as described herein that are suitable for oral administration may be presented as discrete units, such as capsules, tablets, lozenges, each containing a predetermined amount of the active compound. Other examples of compositions include suspensions in aqueous liquids or non-aqueous liquids, such as a syrup, elixir, or an emulsion. Examples of compositions for parenteral administration include, without being limited to, sterile aqueous

or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Examples of aqueous carriers are water, alcoholic/aqueous solutions, emulsions or suspensions, for example, saline and buffered media. Examples of parenteral vehicles are sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, and lactated Ringer's or fixed oils. Examples for intravenous vehicles are fluid and nutrient replenishers, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases, and the like.

In some embodiments, a composition comprising a compound or a combination of compounds, useful in this invention, may further comprise an antioxidant to retard oxidation of one or more component. Additionally, the prevention of the action of microorganisms can be brought about by a preservative such as an antibacterial and antifungal agent, including but not limited to parabens (*e.g.*, methylparabens, propylparabens), chlorobutanol, phenol, sorbic acid, thimerosal or combinations thereof.

The compounds useful in the invention, for example the mTOR, PI3K, Akt or MAPK inhibitors provided herein, may be derivatized in various ways. As used herein "derivatives" of the compounds (*e.g.*, small molecule JAK2 and other kinase inhibitors) include salts (*e.g.*, pharmaceutically acceptable salts), any complexes (*e.g.*, inclusion complexes or clathrates with compounds such as cyclodextrins, or coordination complexes with metal ions such as Mn^{2+} and Zn^{2+}), esters such as *in vivo* hydrolysable esters, free acids or bases, polymorphic forms of the compounds, solvates (*e.g.*, hydrates), prodrugs or lipids, coupling partners and protecting groups. By "prodrugs" is meant for example any compound that is converted *in vivo* into a biologically active compound.

The term "pharmaceutically acceptable salt" in this respect refers to the relatively non-toxic, inorganic or organic acid addition salts of agents of the present invention. These salts can be prepared *in situ* in the administration vehicle or the dosage form manufacturing process, or by separately reacting a purified agent of the invention with a suitable organic or inorganic acid, and isolating the salt thus formed during subsequent purification.

Representative salts include the bromide, chloride, sulfate, bisulfate, phosphate, phosphonate, nitrate, acetate, valerate, oleate, palmitate, stearate, laurate, benzoate, lactate, tosylate, citrate, malate, fumarate, succinate, tartrate, naphthylate, mesylate, glucoheptonate, lactobionate, laurylsulphonate salts, and the like. See, for example, Berge *et al.* (1977) *J. Pharm. Sci.* 66:1-19.

The pharmaceutically acceptable salts of the subject agents include the conventional nontoxic salts or quaternary ammonium salts of the compounds, *e.g.*, from non-toxic organic or inorganic acids. For example, such conventional nontoxic salts include those derived from inorganic acids such as hydrochloride, hydrobromic, sulfuric, sulfamic, phosphoric, nitric, and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, palmitic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isothionic, and the like.

As set out herein, certain compounds may contain a basic functional group, such as amino or alkylamino, and are, thus, capable of forming pharmaceutically acceptable salts with pharmaceutically acceptable acids. The term "pharmaceutically acceptable salts" in this respect refers to the relatively non-toxic, inorganic or organic acid addition salts of compounds of the present invention. These salts can be prepared *in situ* in the administration vehicle or the dosage form manufacturing process, or by separately reacting a purified compound of the invention in its free base form with a suitable organic or inorganic acid, and isolating the salt thus formed during subsequent purification. Representative salts include the hydrobromide, hydrochloride, sulfate, bisulfate, phosphate, phosphonate, nitrate, acetate, valerate, oleate, palmitate, stearate, laurate, benzoate, lactate, tosylate, citrate, maleate, fumarate, succinate, tartrate, naphthylate, mesylate, glucoheptonate, lactobionate, and laurylsulphonate salts and the like. See, for example, *Berge et al. (1977) J. Pharm. Sci.* 66:1-19.

The pharmaceutically acceptable salts of the compounds useful in the present invention include the conventional nontoxic salts or quaternary ammonium salts of the compounds, *e.g.*, from non-toxic organic or inorganic acids. For example, such conventional nontoxic salts include those derived from inorganic acids such as hydrochloride, hydrobromic, sulfuric, sulfamic, phosphoric, nitric, and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, palmitic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isothionic, and the like.

In other cases, the compounds may contain one or more acidic functional groups and, thus, are capable of forming pharmaceutically acceptable salts with pharmaceutically acceptable bases. The term "pharmaceutically acceptable salts" in these instances refers to the relatively non-toxic, inorganic and organic base addition salts of compounds of the

present invention. These salts can likewise be prepared *in situ* in the administration vehicle or the dosage form manufacturing process, or by separately reacting the purified compound in its free acid form with a suitable base, such as the hydroxide, carbonate or bicarbonate of a pharmaceutically acceptable metal cation, with ammonia, or with a pharmaceutically

5 acceptable organic primary, secondary or tertiary amine. Representative alkali or alkaline earth salts include the lithium, sodium, potassium, calcium, magnesium, and aluminum salts and the like. Representative organic amines useful for the formation of base addition salts include ethylamine, diethylamine, ethylenediamine, ethanolamine, diethanolamine, piperazine, and the like. See, for example, *Berge et al. (1977) J. Pharm. Sci.* 66:1-19.

10 In embodiments where the composition is in a liquid form, a carrier can be a solvent or dispersion medium comprising but not limited to, water, ethanol, polyol (*e.g.*, glycerol, propylene glycol, liquid polyethylene glycol, *etc.*), lipids (*e.g.*, triglycerides, vegetable oils, liposomes), and combinations thereof. The proper fluidity can be maintained, for example, by the use of a coating, such as lecithin; by the maintenance of the required particle size by

15 dispersion in carriers such as, for example liquid polyol or lipids; by the use of surfactants such as, for example, hydroxypropylcellulose; or combinations thereof such methods. In many cases, it will be advisable to include isotonic agents, such as, for example, sugars, sodium chloride, or combinations thereof.

20 **Therapeutic methods**

Some aspects of this invention provide therapeutic methods, for example, methods for the treatment of subjects having a hyperproliferative disease, a neoplastic disease, or a cancer. In some embodiments, a method of treatment is personalized to a specific subject by taking into account the phosphorylation level of at least one an mTOR target site in the subject. In

25 some embodiments, therapeutic methods disclosed herein include administration of an mTOR inhibitor, for example, of an mTORC1 or an mTORC1/2 inhibitor. In some embodiments, therapeutic methods described herein include administration of an mTOR inhibitor and an additional kinase inhibitor, for example, a PI3K inhibitor, a MAPK inhibitor, MEK/ERK inhibitor, or an AKT/PKB inhibitor. In some embodiments, therapeutic methods provided

30 herein include administration of a dual mTOR/PI3K inhibitor, or of a combination of an mTOR inhibitor and a PI3K inhibitor.

In some therapeutic embodiments, a composition disclosed herein, for example, a composition comprising an mTOR inhibitor or a composition comprising an mTOR inhibitor and a PI3K inhibitor is administered to a subject having a cancer in an effective amount. An

effective amount, in some embodiments, is an amount sufficient to elicit a desired clinical response in the subject. In some embodiments, the desired response is a slowing or inhibiting of the progression of a disorder, for example, of a malignant neoplastic disorder. In some embodiments, this involves slowing the progression of the disease temporarily, although, in more preferable embodiments, it involves halting the progression of the disease permanently. In some embodiments, the desired response is a permanent reduction of cancer cell proliferation, for example, to a level comparable to a level found in healthy individuals. In some embodiments, a desired response is the induction of cell death in a cancer cell, in a population of cancer cells, or in all cancer cells in a subject. In some embodiments, the desired response is delaying or preventing the manifestation of clinical symptoms characteristic of the disease or condition.

The effect of administering an mTOR inhibitor, either alone or in combination with an additional compound, for example, a PI3K inhibitor, as provided herein, can be monitored by routine methods well known to those of skill in the related medical arts, for example, by methods involving assessment of cancer cell proliferation.

What constitutes an effective amount will depend on the particular condition being treated, the severity of the condition, the individual patient parameters including age, physical condition, size, and weight, the duration of the treatment, the nature of concurrent therapy (if any), the specific route of administration and like factors within the knowledge and expertise of the health care professional treating the subject. These factors are well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. It is generally preferred that a maximum dose of the individual components or combinations thereof be used, that is, the highest safe dose according to sound medical judgment. It will be understood by those of ordinary skill in the art, however, that a lower dose or tolerable dose may be used for medical reasons.

In general, an effective amount of a therapeutic agent, for example, an mTOR inhibitor or a combination of an mTOR inhibitor with a PI3K, Akt, or MAPK inhibitor, as provided herein, for the treatment of a cancer exhibiting an elevated level of mTOR kinase activity is a dose that achieves an alleviation of the specific neoplastic disease or disorder being treated, for example, by prevention, inhibition, amelioration, delay, or elimination of a symptom of such a disease or disorder.

Some embodiments provide a method of inducing cell death and/or inhibiting proliferation in a neoplastic cell exhibiting elevated mTOR kinase activity by contacting the cell with an mTOR kinase inhibitor or a combination of an mTOR kinase inhibitor and

another kinase inhibitor, for example, a PI3K, Akt, or MAPK inhibitor, chosen based on the determination of the type of mTOR kinase signaling active in the cell. In some embodiments, the neoplastic cell is contacted *in vivo* by administering a composition disclosed herein to a subject carrying the cell. In some embodiments, the neoplastic cell is contacted *ex vivo*. In
5 some embodiments, the cell is contacted *in vitro*.

In some embodiments, a neoplastic cell is contacted *in vivo*, *ex vivo*, or *in vitro*, with an effective amount of an mTOR inhibitor or a combination of an mTOR inhibitor and an additional kinase inhibitor, for example, a PI3K, Akt, or MAPK inhibitor, as provided herein. An effective amount, in some embodiments, is an amount sufficient to elicit a desired
10 response in the contacted cell. In some embodiments involving contacting a neoplastic cell exhibiting elevated mTOR activity, for example, because of a mutation in an mTOR upstream pathway, the desired response is a slowing or inhibiting of the proliferation of the cell. In some embodiments, this decreases the proliferation rate and/or cell viability and/or life span, although, in more preferable embodiments, it involves the induction of cell death in
15 the contacted cell or cells.

In some embodiments, the therapeutic methods provided herein further involve the administration of an additional antiproliferative agent to a cancer cell or to a subject carrying a cancer cell, for example, as part of a malignant tumor. Additional antiproliferative agents useful in the methods described herein are well known in the art and include, but are not
20 limited to chemotherapeutic agents (*e.g.*, cytostatic, and cytotoxic agents). Cytotoxic and cytostatic drugs are drugs that kill malignant cells, or inhibit their proliferation, respectively. Examples of cytotoxic and cytostatic drugs include, for example, alkylating agents, antimetabolites, antitumor antibiotics, vinca alkaloids, taxanes, topoisomerase-I compounds, anthracyclines, and epipodophyllotoxins. In addition, angiogenesis inhibiting drugs, including,
25 for example, compounds that block growth promoting receptors (*e.g.*, PDGF-R and VEGF-R) such as sunitinib (Sutent[®]) may be used as additional antiproliferative agents. Non-limiting examples of additional antiproliferative agents include Cytoxan[®] (Cyclophosphamide), Methotrexate, 5-Fluorouracil (5-FU), Adriamycin[®] (Doxorubicin), Prednisone, Nolvadex[®] (Tamoxifen), Taxol[®] (Paclitaxel), Leucovorin, Oncovin[®] (Vincristine), Thioplex[®] (Thiotepa),
30 Arimidex[®] (Anastrozole), Taxotere[®] (Docetaxel), Navelbine[®], (Vinorelbine), Gemzar[®] (Gemcitabine), Ifex[®] (Ifosfamide), Pemetrexed, Topotecan, Melphalan (L-Pam[®]), Cisplatin (Cisplatinum[®], Platinol[®]), Carboplatin (Paraplatin[®]), Carmustine (BCNU; BiCNU[®]), Methotrexate, Edatrexate, Mitomycin C (Mutamycin[®]), Mitoxantrone (Novantrone[®]), Vincristine (Oncovin[®]), Vinblastine (Velban[®]), Vinorelbine (Navelbine[®]), Fenretinide,

Topotecan, Irinotecan, 9-amino-camptothecin (9-AC); Biantrazole, Losoxantrone, Etoposide, and Teniposide.

Administration schedules, formulations, dosages, and administration routes of antiproliferative agents and compositions are well known to those in of skill in the art.

- 5 Exemplary administration routes, schedules, and dosages of commonly used chemotherapeutic drugs are described in Perry, *The Chemotherapy Source Book*, 4th Edition, Lippinkott Williams & Wilkins, 2008, incorporated herein by reference. Such administration schedules may comprise the administration of a single antiproliferative drug or the
- 10 administration of a combination of such drugs, for example, one of the following, commonly administered combinations: CMF (cyclophosphamide, methotrexate, and 5-fluorouracil); classic CMF (oral cyclophosphamide plus methotrexate and 5-fluorouracil); CAF or FAC (cyclophosphamide, Adriamycin[®] (doxorubicin), and 5-fluorouracil); AC (Adriamycin[®] and cyclophosphamide); ACT (Adriamycin[®] plus cyclophosphamide and tamoxifen); AC taxol (Adriamycin[®] plus cyclophosphamide and paclitaxel (Taxol[®])); FACT (5-fluorouracil plus
- 15 adriamycin[®], cyclophosphamide, and tamoxifen); A-CMF or Adria/CMF (4 cycles of adriamycin[®] followed by 8 cycles of CMF); CMFP (CMF plus prednisone); CMFVP (CMF plus vincristine and prednisone); CAFMV (CAF plus methotrexate and vincristine); CMFVATN (CMF plus vincristine, adriamycin[®], thiotepa, and tamoxifen); MF (methotrexate plus 5-fluorouracil and leucovorin). The administration of such combinations of
- 20 antiproliferative drugs and agents in addition to the administration of an mTOR kinase inhibitor with or without an additional kinase inhibitor, for example, a PI3K, Akt, or MAPK inhibitor, is also envisioned to be embraced by some embodiments.

The therapeutic inhibitors and compositions can be administered in a single dose comprising an effective amount of the individual agents. Multiple doses of the compounds of

25 the invention are also contemplated. When a plurality of inhibitors are used together, they may be administered individually or sequentially, either in a single medicament or in separate units to provide therapeutic doses of the individual compounds. Many mTOR inhibitors, PI3K inhibitors, Akt inhibitors and MAPK inhibitors described herein are in clinical studies or even in clinical use. Therapeutic doses of such compounds are, accordingly, well known

30 in the field of medicine. Dosages of compounds in clinical use are described in references such as *Remington's Pharmaceutical Sciences*, 18th ed., 1990; as well as many other medical references relied upon by the medical profession as guidance for the treatment of proliferation disorders.

Administration routes and methods

A variety of administration routes are available for the kinase inhibitors and other therapeutic agents described herein. The particular mode selected will depend, of course, upon the particular compound selected, the particular condition being treated and the dosage required for therapeutic efficacy. The methods of this invention may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of compounds without causing clinically unacceptable adverse effects. Examples of modes of administration are parenteral routes. The term "parenteral" includes subcutaneous, intravenous, intramuscular, intraperitoneal, and intrasternal injection, or infusion techniques. Other routes include, but are not limited to, oral, nasal, dermal, sublingual, and local.

The formulations of the invention are administered in pharmaceutically acceptable solutions, which may routinely contain pharmaceutically acceptable concentrations of salts, buffering agents, preservatives, compatible carriers, adjuvants, and optionally other therapeutic ingredients.

According to the methods provided by aspects of the invention, the compounds described herein may be administered in a pharmaceutical composition. In some embodiments, a pharmaceutical composition comprises a compound provided by aspects of the invention and a pharmaceutically acceptable carrier. As used herein, a pharmaceutically acceptable carrier refers to a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients.

Pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials which are well known in the art. Such preparations may routinely contain salt, buffering agents, preservatives, compatible carriers, and optionally other therapeutic agents. When used in medicine, the salts should be pharmaceutically acceptable, but non-pharmaceutically acceptable salts may conveniently be used to prepare pharmaceutically acceptable salts thereof and are not excluded from the scope of the invention. Such pharmacologically and pharmaceutically acceptable salts include, but are not limited to, those prepared from the following acids: hydrochloric, hydrobromic, sulfuric, nitric, phosphoric, maleic, acetic, salicylic, citric, formic, malonic, succinic, and the like. Also, pharmaceutically acceptable salts can be prepared as alkaline metal or alkaline earth salts, such as sodium, potassium or calcium salts.

The compounds used in the invention may be formulated into preparations in solid, semi-solid, liquid or gaseous forms such as tablets, capsules, powders, granules, ointments,

solutions, depositories, inhalants and injections, and usual ways for oral, parenteral or surgical administration. Some aspects of the invention also embrace pharmaceutical compositions which are formulated for local administration, such as by implants.

Compositions suitable for oral administration may be presented as discrete units, such as capsules, tablets, lozenges, each containing a predetermined amount of the active compound. Other compositions include suspensions in aqueous liquids or non-aqueous liquids such as a syrup, elixir or an emulsion. When the compounds described herein are used therapeutically, in certain embodiments a desirable route of administration may be by pulmonary aerosol.

In some embodiments, a compound provided by some aspects of the invention may be administered directly to a tissue. Direct tissue administration may be achieved by direct injection. A compound may be administered once or alternatively may be administered in a plurality of administrations. If administered multiple times, a compound may be administered via different routes. For example, the first (or the first few) administrations may be made directly into the affected tissue while later administrations may be systemic.

For oral administration, the compounds can be formulated readily by combining the active compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a subject to be treated. Pharmaceutical preparations for oral use can be obtained as solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Optionally the oral formulations may also be formulated in saline or buffers for neutralizing internal acid conditions or may be administered without any carriers.

Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the

tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. Microspheres formulated for oral administration may also be used. Such microspheres have been well defined in the art. All formulations for oral administration should be in dosages suitable for such administration.

For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention may be conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebulizer, with the use of a suitable propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, *e.g.*, gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

The compounds, when it is desirable to deliver them systemically, may be formulated for parenteral administration by injection, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampoules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing, and/or dispersing agents.

Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers

(such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases and the like. Lower doses will result from other forms of administration, such as intravenous administration. In the event that a response in a subject is insufficient at the
5 initial doses applied, higher doses (or effectively higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits. Multiple doses per day are contemplated to achieve appropriate systemic levels of compounds.

Other delivery systems can include time-release, delayed release or sustained release delivery systems. Such systems can avoid repeated administrations of the compound,
10 increasing convenience to the subject and the physician. Many types of release delivery systems are available and known to those of ordinary skill in the art. They include polymer base systems such as poly(lactide-glycolide), copolyoxalates, polycaprolactones, polyesteramides, polyorthoesters, polyhydroxybutyric acid, and polyanhydrides.

Microcapsules of the foregoing polymers containing drugs are described in, for example, U.S.

15 Patent 5,075,109. Delivery systems also include non-polymer systems that are: lipids including sterols such as cholesterol, cholesterol esters and fatty acids or neutral fats such as mono- di- and tri-glycerides; hydrogel release systems; silastic systems; peptide based systems; wax coatings; compressed tablets using conventional binders and excipients; partially fused implants; and the like. Specific examples include, but are not limited to: (a)
20 erosional systems in which the platelet reducing agent is contained in a form within a matrix such as those described in U.S. Patents 4,452,775, 4,675,189, and 5,736,152 and (b)
• diffusional systems in which an active component permeates at a controlled rate from a polymer such as described in U.S. Patents 3,854,480, 5,133,974 and 5,407,686. In addition, pump-based hardware delivery systems can be used, some of which are adapted for
25 implantation.

Therapeutic formulations useful in the invention may be prepared for storage by mixing a kinase inhibitor having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizers (*Remington's Pharmaceutical Sciences* 16th
edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions.

30 Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as

methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as TWEENTM, PLURONICSTM or polyethylene glycol (PEG).

EXAMPLES

Two sets of large-scale, quantitative phospho-proteomics experiments were performed to fully define how mTOR-containing complexes signal to downstream effectors (Figure 1A). The first SILAC experiment (rapamycin screen) was performed using growth factor-deprived *TSC2* ^{-/-} mouse embryonic fibroblasts (MEFs). Deletion of the *TSC2* tumor suppressor gene decouples mTORC1 from many upstream inputs, leading to constitutive hyper-activation of mTORC1 signaling (7). mTORC1 is still potently and specifically inhibited by rapamycin in these cells, which provides a sensitized genetic background for the study of mTORC1 signaling in the absence of other mitogen-regulated phosphorylation cascades.

Global quantitative phosphoproteomics defines the signaling networks downstream of both mTORC1 and mTORC2

Two populations of *TSC2* ^{-/-} cells were grown in parallel, one in conventional media ("light") and the other in media containing [¹³C₆¹⁵N₂]lysine and [¹³C₆¹⁵N₄]arginine ("heavy") (Figure 1A and Table 5). As shown in Figure 5A, phosphopeptides were successfully enriched using a two-step SCX-IMAC procedure with the phosphopeptides representing 67.8% of the peptides identified. We performed two biological replicates of this experimental design with cross-labeling (swapping the labeled state of the rapamycin-treated cells, Table 5), from which a total of 14,635 (FDR=0.25%) and 32,500 (FDR=0.28%) phosphopeptides were identified, respectively. These corresponded to identification of at least 4,484 and 6,832 unique phosphorylation sites on 1,615 and 1,866 proteins, respectively. The quantitation was highly accurate (Table 5) with 93.7% of the phosphoproteome changing less than 50% in abundance between the rapamycin-treated (light) and control (heavy) cells (second biological replicate experiment, Median Log₂(H/L) = -0.02 and standard deviation

Log₂(H/L) = 0.53, Figure 1A). Gene names and sequences of the phosphopeptides whose intensities decrease after rapamycin treatment (Rapamycin screen) are identified in Table 7. Note that the Rapamycin screen includes two biological replicates. For the first replicate (Table 7 Rapa Replicate 1), the light cells were controls whereas the heavy cells were treated with rapamycin. For the second replicate experiment (Table 7 Rapa Replicate 2), the light cells were treated with rapamycin and heavy cells were controls.

Based on the tight distribution of the quantified phosphopeptides, we considered phosphorylated peptides whose relative abundance decreased ≥ 2 -fold as regulated in a rapamycin-sensitive fashion. Using this criteria, several hundred peptides (corresponding to 148 and 85 proteins respectively, in the two biological replicates, Table 11) were determined to contain rapamycin-sensitive phosphorylation sites. Table 11 identifies proteins with downregulated phosphorylation identified in the rapamycin and Ku-0063794 screen. Note that there are two biological replicate experiments for the rapamycin screen ("Table 11 Rapa Replicate 1," and "Table 11 Rapa Replicate 2," respectively) and one Ku-0063794 replicate ("Table 11 Ku"). Treatment for the light and heavy cells in each experiment is described in Figure 1C. We observed a similar distribution for the phosphopeptides in the first biological replicate experiment and found 85 proteins (Table 11) that carried rapamycin-sensitive phosphorylation sites. In addition, there was a substantial overlap in the downregulated proteins between replicates and 40 of these proteins were found in both experiments (Figure 5B).

For the Ku-screen, wild-type MEFs were grown in light and heavy SILAC media and starved overnight for serum. The light cells were treated with 20 nM rapamycin for 2 hrs, while the heavy cells were treated in parallel with a combination of 20 nM rapamycin and 2 μ M of Ku-0063794 for 2 hrs. Both the light and heavy cell were subsequently stimulated with insulin for 15 minutes and samples were pooled and analyzed by quantitative mass spectrometry. Ku-0063794 is a recently identified compound that competitively inhibits mTOR kinase activity by occupying the ATP-binding pocket (Figure 5C) (4, 11). For the Ku-screen, a total of 34,642 phosphopeptides were identified with a false discovery rate of 0.28%, which corresponded to identification of 6,220 unique phosphorylation sites on 1,867 proteins (Table 5). Gene names and sequences of the phosphopeptides whose intensities decrease after Ku-0063794 treatment are identified in Table 8. Note that the light cells were treated with rapamycin and serve as controls whereas the heavy cells were treated with a combination of rapamycin and Ku-0063794. A very tight distribution of phosphopeptides

was observed (Median $\text{Log}_2(\text{H/L}) = -0.03$ and standard deviation $\text{Log}_2(\text{H/L}) = 0.34$) and phosphorylated peptides whose relative abundance decreased ≥ 2 -fold were considered regulated by Ku-sensitive, but rapamycin-insensitive mTOR signaling (Figure 1A). Using these criteria, 100 proteins were determined to contain downregulated phosphorylation after Ku-0063794 treatment (Table 11). The identified phospho-proteins included many known downstream targets of mTORC2 (Table 6), including GSK3 β , Braf, Akt1s1 (Akt substrate) and NDRG1 (SGK substrate). Combining the data from both the Rapa-screen and the Ku-screen, we identified a total of 81,777 phosphopeptides, and more than 11,271 unique phosphorylation sites on 2,778 proteins, with 9,694 of the sites confidently localized (Ascore ≥ 13) (Table 5).

Phosphorylation specificity of the downstream effectors in the mTORC1 and mTORC2 signaling networks

Table 9 describes the classification of mTOR targets identified in the rapamycin and Ku-0063794 screens. Class I includes downstream effectors of rapamycin-sensitive mTORC1. Class II includes downstream effectors of rapamycin-insensitive mTORC1 or mTORC2. Class II includes the proteins downstream of both mTORC1 and mTORC2. Names of the genes and the sequences of the phosphopeptides are shown.

Class I sites represent phosphorylation events that are mediated by rapamycin-sensitive mTORC1/S6K signaling, (e.g. phospho-rpS6 S235/S236 phosphorylation).

Class II sites represent phosphorylation events mediated by rapamycin-insensitive mTORC1 or mTORC2 function. For example, 4EBP1 T36/T45 phosphorylation, previously characterized as a rapamycin insensitive mTORC1 substrate (12), only decreased slightly (20%) after rapamycin treatment, while phosphorylation at these sites decreased dramatically (7.2-fold) in the Ku-0063794 screen (Figures 1C, 5C and 6A). As another example, NDRG1 was also identified to contain Class II phosphorylation sites at S330/S333 (Figures 1C and 6B) and was recently shown to be a substrate of SGK (8), whose activation is under the control of mTORC2.

Class III represents phosphorylation sites that are both the rapamycin-sensitive and Ku-sensitive mTOR substrates. For example, GSK3 β S9 phosphorylation is downregulated by approximately 3.3-fold and 2.2-fold in the rapamycin and Ku-0063794 screens, respectively (Figures 1C and 6C), consistent with the previous observation that it can be a substrate of both Akt and S6K (9). As another example for the Class III phosphorylation, the

abundance of mTOR autophosphorylation at S2478/S2481 decreased 3.6-fold in the rapamycin screen (Figure 7A). Surprisingly, it was previously shown that S2481 is a conserved, rapamycin-insensitive, autophosphorylation site of mTOR (Figure 7B) (20). Immunoblot analysis confirmed that site was indeed rapamycin-sensitive (Figures 5C and 7C). Intriguingly, acute rapamycin treatment only led to partial dephosphorylation of this site. In contrast, mTOR S2481 phosphorylation was completely abolished as a result of mTOR kinase inhibitor treatment (Figures 5C and 7D). Taken together, the data demonstrate that mTOR S2481 phosphorylation is regulated in both a rapamycin sensitive- and insensitive-manner.

There were several surprising examples of phosphopeptides that are insensitive to both rapamycin and Ku-0063794 as identified by the two phosphoproteomics screens. The intensity of a T70 singly phosphorylated 4EBP1 peptide did not change in either the rapamycin or the Ku-0063794 screen (Figures 1C and 6A), indicating the 4EBP T70 is not phosphorylated by mTOR in this context. Indeed, several reports suggested that this site might be targeted by ERK2, another proline-directed kinase (21). In addition, we found that the 4EBP-1 S85/S100 phosphorylation was also mTOR-independent (Figure 1C).

Linking phosphorylation events to the biological processes regulated by mTORC1 and mTORC2

To assess the predicated effects of mTOR inhibition in cells as a result of either rapamycin or Ku-0063794 treatment, we mapped the downregulated proteins in the two screens to Gene Ontology (GO) terms with respect to Biological Process (BP) and also performed gene functional classification analysis of these proteins. Table 10 describes the results of GO analysis of the hits identified in the rapamycin and Ku-0063794 screens.

Pathways that the rapamycin-sensitive and Ku-0063794-sensitive hits overrepresented are shown in “Table 10 Rapa pathways” and “Table 10 Ku pathways”, respectively. Also shown is the biological process that the rapamycin-sensitive and Ku-0063794-sensitive hits overrepresented (Table 10 Rapa BP GO, and Table 10 Ku BP GO, respectively).

Interestingly, for the rapamycin screen, the top enriched BPs included negative regulation of macromolecule metabolic process ($P = 4.2 \times 10^{-7}$), negative regulation of cellular biosynthetic process ($P = 4.2 \times 10^{-6}$), response to insulin stimulus ($P = 2.6 \times 10^{-4}$), negative regulation of transcription ($P = 2.7 \times 10^{-4}$) and vesicle-mediated transport ($P = 6.0 \times 10^{-4}$). By grouping the hits based on functional similarities, we also found that the downregulated proteins in the rapamycin screen were enriched for kinases ($P = 2.1 \times 10^{-20}$), WD40-repeat containing

proteins ($P = 8.9 \times 10^{-12}$), proteins involved in transcription regulation ($P = 3.1 \times 10^{-9}$) and proteins involved in RNA processing ($P = 3.3 \times 10^{-5}$). The identification of many kinases in the downregulated proteins provides interesting points for potential signal integration and crosstalk. One example is the Ser/Thr kinase, unc-51-like kinase 1 (ULK1). Previously
 5 published research has demonstrated that ULK1 is positively involved in autophagy response (22). ULK1 has also been shown to interact with mTORC1 through binding to raptor (23). We identified three phosphorylation sites on ULK1 (S747/S757/T763) that showed a 4-fold downregulation after rapamycin treatment (Table 1), suggesting that ULK1 is likely a *bona fide* mTORC1 substrate. As mTORC1 is known to antagonize macroautophagy, it is
 10 tempting to speculate that mTORC1 negative regulates ULK1 either directly or indirectly via inhibitory phosphorylation events. Interestingly, in mammalian cells, knockdown of the related kinase ULK2 had no effect on the autophagic response (22). Interestingly, all three of the rapamycin-sensitive ULK1 phosphorylation sites are proline-directed (SP or TP), whereas two of the three comparable sites in ULK2 possess a C-terminal alanine, making it unlikely
 15 that these residues are similarly phosphorylated by mTORC1 (Figure 7E).

For the downregulated proteins identified in the Ku-0063794 screen, the top enriched BPs included lamellipodium assembly ($P = 0.003$), protein amino acid phosphorylation ($P = 0.007$), the insulin receptor signaling pathway ($P = 0.01$), actin filament-based process ($P = 0.015$) and nucleocytoplasmic transport ($P = 0.015$). Gene functional classification analysis
 20 revealed that the downregulated proteins were enriched for ATP-binding proteins ($P = 2.4 \times 10^{-11}$) and zinc-finger domain containing proteins ($P = 2.1 \times 10^{-4}$). Intriguingly, it has been suggested that mTORC2 promotes organization of the actin cytoskeleton upon growth factor stimulation through a mechanism that is poorly defined. The identification of a total of 10 proteins (CCDC88A, ARHGEF17, NCK1, myo9b, Mtap1b, Epb4.113, vcl, Spnb2, FLNC,
 25 Npm1) in the Ku-0063794 screen that are related to cytoskeleton regulation provides an opportunity for the discovery of novel points of regulation. For example, we identified a peptide from filamin-C (FLNC) in the Ku-0063794 screen that was singly phosphorylated at S2234 (Figure 2). S2234 is localized in an AGC kinase substrate motif (RERLGS*F, SEQ ID NO: 22) and has previously been shown to be phosphorylated by Akt *in vitro* (24). We
 30 found S2234 could be categorized as a Class II phosphorylation site (rapamycin-insensitive and Ku0063794-sensitive, Figure 2 and Table 1), suggesting that it is not an S6K substrate but rather the substrate of Akt or SGK. FLNC crosslinks actin filaments into a three-dimensional network and is involved in assembling signaling complexes near the cell membrane (25). Interestingly, filamin-A (FLNA) has been shown to be phosphorylated at a

similar site (S2152, RRRAPS*V, SEQ ID NO: 23) by RSK and Pak protein kinases which regulates FLNA function in cell migration (26). It will clearly be of great interest to investigate whether mTORC2 regulates actin assembly and cell migration through Akt- or SGK-mediated phosphorylation of FLNC and whether this phosphorylation coordinates regulation of these processes with Ras-, Cdc42- and Rac-mediated phosphorylation of FLNA.

The analysis identified 4,484 and 6,832 unique phosphorylation sites on 1,615 and 1,866 proteins from two biological replicate experiments, respectively, and achieved a high level of accuracy in quantitation (Table 5). Several hundred peptides corresponding to 148 and 85 proteins in the two replicates (Table 11) were determined to contain rapamycin-sensitive phosphorylation sites (defined as phosphorylated peptides whose relative abundance decreased ≥ 2 -fold in response to rapamycin treatment). There was a substantial overlap in the downregulated proteins between the replicates, as 40 proteins were found in both experiments (Figure 5B). Supporting the validity of the approach, many known effectors of the mTORC1 signaling pathway were identified in the downregulated population (Table 6), including p70S6K, 4EBP1/2, Akt1s1 (PRAS40), rpS6, eIF4B, eIF4G1 and GSK3 β . A representative identification of the known rapamycin-sensitive phosphorylation sites on ribosomal protein S6 is shown in Figure 1B.

Rapamycin is an allosteric inhibitor that only partially inhibits mTORC1 signaling and has no effect on the activity of mTORC2 under short-term treatment conditions (3). In contrast, newly discovered ATP-competitive mTOR inhibitors block the activity of both mTORC1 and mTORC2 (2). To identify rapamycin-insensitive mTORC1, and mTORC2 substrates, we used the mTOR kinase inhibitor Ku-0063794 and performed a second SILAC experiment (Ku-0063794 screen) (Figure 1A). The light cells were treated with 20 nM rapamycin for 2 hrs, while the heavy cells were treated in parallel with a combination of 20 nM rapamycin and 2 μ M of Ku-0063794 for 2 hrs. Both the light and heavy cells were subsequently stimulated with insulin for 15 minutes and samples were pooled and analyzed by quantitative mass spectrometry. By creating a rapamycin-inhibited background in both the light and heavy cells, the combination of insulin stimulation and treatment with the mTOR kinase inhibitor leads to the identification of proteins specifically phosphorylated by rapamycin-insensitive mTOR signaling and kinases activated downstream of mTORC2 such as Akt and SGK.

In this experiment, one hundred proteins were determined to contain downregulated phosphorylation after Ku-0063794 treatment (Table 11). The identified phospho-proteins included many known downstream targets of mTORC2 (Table 6), including GSK3 β , Braf, Akt1s1 (Akt substrates) and NDRG1 (SGK substrate).

To identify the specific downstream effectors of the two mTOR complexes, we compared the fold-change in phospho-peptides identified in both the rapamycin and Ku-0063794 screens (Figure 1C). As expected, the majority of phospho-peptides in the cell are not affected by either rapamycin or Ku-0063794 treatment and show a heavy:light ratio close to 1:1 in both screens. However, there are clearly phosphopeptides that are mediated by mTORC1 and/or mTORC2 signaling, which can further be divided into three categories. Class I sites include rapamycin-sensitive events that are not further decreased by Ku-0063794 treatment, and represent canonical mTORC1 downstream effectors, such as rpS6 S235/236 phosphorylation (Figure 1C). Class II sites include Ku-0063794-sensitive events that are not affected by rapamycin treatment and represent either rapamycin-resistant mTORC1 downstream effectors, such as 4EBP1 T36/T45 (Figures 1C, 5C and 6A), or sites downstream of the mTORC2 signaling, such as the recently described SGK-mediated NDRG1 S330/S333 phosphorylation events (Figures 1C and 6B) (8). Finally, Class III sites are sensitive to both compounds. For example, GSK3 β S9 phosphorylation is downregulated in both the rapamycin and Ku-0063794 screens (Figures 1C and 6C), consistent with the previous observation that GSK3 β can be a substrate of both Akt and S6K (9). In addition, we identified mTOR autophosphorylation at S2481 as a Class III site that is regulated in both a rapamycin sensitive- and insensitive-manner (Figure 7) (these target classes are discussed in more detail elsewhere herein).

We performed pathway analysis using DAVID (10), to determine the signaling networks that are statistically overrepresented by the hits in the rapamycin and Ku-0063794 screens (Figures 1D and 5D). Not surprisingly, proteins with downregulated phosphorylation in both screens were highly enriched for the canonical mTOR pathway ($P = 1.6 \times 10^{-6}$, ranked first, for the rapamycin screen and $P = 0.0014$, ranked second, for the Ku-0063794 screen).

Interestingly, one of the enriched GO classes in the rapamycin screen is the transmembrane receptor protein tyrosine kinase (RTK) signaling pathway ($P = 0.01$), suggesting that mTORC1 might inhibit proteins in the upstream PI3K and MAPK pathways through modulating the activities of these RTKs. In particular, we observed that phosphorylation of two sites on the growth factor receptor-bound protein 10 (Grb10,

S501/S503, ⁴⁹⁶MNILLSS*QS*PLHPSTLNAVIHR⁵¹⁶ (SEQ ID NO: 24), mass error = 2.32 ppm, Xcorr = 4.39) was strongly inhibited by rapamycin (Figures 2A and 8A). The level of phosphorylation decreased by more than 27-fold after a 2h rapamycin treatment (Table 6). The intensity of a triply phosphorylated Grb10 peptide (T76/S96/S104, insufficient MS/MS
5 fragment ions to localize T76) also decreased by about five-fold after rapamycin treatment (Table 6). In contrast, phosphorylation of two other Grb10 sites, S455 and S458, did not change after a 2-hr rapamycin treatment (Figure 8B), suggesting that decreased S501/S503 phosphorylation was not the result of a change in Grb10 protein abundance.

Grb10 belongs to the growth factor receptor-bound (Grb) protein family, which contains
10 Grb7, Grb10 and Grb14. Members of this protein family serve as cellular adaptor proteins that bind to activated receptor tyrosine kinases (11). Grb10 has an N-terminal Ras-associating (RA) domain, a PH domain, a C-terminal SH2 domain and a BPS (between PH and SH2) domain, in which the two rapamycin-sensitive phosphorylation sites reside (Figure 2B). The S501/S503 sites, and their flanking sequences, are highly conserved in vertebrates (Figure
15 2B), suggesting that they could be functionally relevant and phosphorylated by a common evolutionarily conserved kinase, such as mTOR.

We developed a phosphospecific antibody (Figures 9A and 9B) to further characterize these two Grb10 phosphorylation sites. Treatment of *TSC2*^{-/-} MEFs with 20 nM rapamycin induced rapid dephosphorylation of Grb10, within 15 min, and remained completely inhibited
20 for the remainder of the time course examined (Figure 2C). The dephosphorylation kinetics correlated well with that of S6K. We also found that Grb10 phosphorylation at S501/S503 is sensitive to amino acid availability in *TSC2*^{-/-} MEFs (Figure 2D).

To determine whether the Grb10 S501/S503 sites can be phosphorylated by other kinases, we treated *TSC2*^{-/-} cells with staurosporine, a broad-spectrum kinase inhibitor that does not
25 suppress mTOR activity (12). No change in the phosphorylation level of Grb10 S501/S503 phosphorylation was observed in response to staurosporine treatment (Figure 2E). In contrast, treatment of Ku-0063794 led to a dose-dependent dephosphorylation of Grb10, correlating with the dephosphorylation of mTOR, 4EBP and rpS6. Interestingly, S6K activity was inhibited by staurosporine treatment, as shown by a complete loss of rpS6 phosphorylation,
30 suggesting that Grb10 S501/S503 was directly phosphorylated by mTORC1 rather than by S6K.

We further investigated the effects of growth factor stimulation and rapamycin-mediated inhibition on Grb10 phosphorylation in other cell types. Wild-type MEFs were serum-starved and then stimulated with either insulin or 10% serum, both of which led to a robust

increase in Grb10 phosphorylation (Figure 2F). The insulin- or serum-induced increase in Grb10 phosphorylation was completely blocked by rapamycin pre-treatment. It was previously reported that Grb10 S503 (S476 in human Grb10 isoform 3) was phosphorylated by ERK1/2 *in vitro* (13). We found that inhibiting MEK by using AZD6244 completely

5 abolished the activities of ERK but had no effect on Grb10 S501/S503 phosphorylation (Figure 2F), indicating that phosphorylation at these two sites on Grb10 is not mediated by ERK *in vivo*. We also tested other mTOR catalytic site inhibitors, including LY294002, NVP-BEZ235, torin and pp242 (14), all of which completely abolished Grb10 S501/S503 phosphorylation (Figure 2G).

10 We next examined the *in vivo* interaction between Grb10 and the components of the mTOR complexes. We co-overexpressed HA-tagged Grb10 with Myc-tagged raptor or rictor in HEK293T cells. Grb10 was found to interact with raptor, but not rictor, suggesting Grb10 is a binding partner of mTORC1, but not mTORC2 (Figure 3A). To further evaluate the possibility that Grb10 is a substrate of mTORC1, we prepared recombinant Grb10 from

15 bacteria and subjected it to an *in vitro* kinase assay using recombinant mTOR. As shown in Figure 3B, Grb10 was robustly phosphorylated by recombinant mTOR at S501/S503.

We found long-term inhibition of mTORC1 by rapamycin led to a significant decrease in Grb10 protein levels (Figure 3C) while Grb10 mRNA levels showed a modest (approximately 2-fold) decrease, suggesting mTORC1 activity positively regulates Grb10

20 expression at both the transcriptional and post-translational levels. Similarly, knockdown of the mTORC1 component raptor led to a decreased level of Grb10 protein, correlating with diminished mTORC1 activity, as shown by phospho-4EBP levels (Figure 3D). In addition, long-term treatment with mTOR kinase inhibitors, including LY-294002, NVP-BEZ235, torin and pp242 all led to reduced Grb10 protein expression (Figure 9C). Similar results were

25 obtained in *TSC1*^{-/-} MEFs (Figure 9D). In contrast, we found Grb10 was highly overexpressed in *TSC2*^{-/-} and *TSC1*^{-/-} MEFs compared with their wild-type counterparts (Figures 3E and 9E), correlating with elevated mTORC1 activity in these cells.

To explore whether mTORC1-mediated Grb10 stabilization depends on phosphorylation on S501/S503, we transfected WT-Grb10, Grb10-S501A/S503A (AA) mutant and Grb10-S501D/S503D (DD) mutant into HEK293T cells. Exogenous wild type

30 (WT) and DD mutant Grb10 proteins were expressed at equal levels, while expression of the AA mutant was markedly reduced, suggesting lower protein stability for the unphosphorylated form of Grb10 (Figure 3F). To confirm this result, we generated *TSC2*^{-/-} MEFs stably expressing the HA-tagged Grb10-DD mutant and treated these cells with rapamycin. Long-

term rapamycin treatment decreased endogenous, wild-type Grb10 levels but had no effect on the DD mutant protein levels (Figure 3G). To rule out the possibility that this result was an artifact based on protein overexpression, we repeated the experiment on *TSC2*^{-/-} cells expressing HA-tagged wild-type Grb10, in which rapamycin treatment decreased both the endogenous and ectopically expressed Grb10 (Figure 9F). These data support a critical role for mTORC1 in stabilizing Grb10 through phosphorylation of the S501/S503 residues.

Grb10 has been suggested to function as a negative regulator of the insulin signaling pathway. In mice with genetically disrupted Grb10 function, overgrowth of both the embryo and placenta was observed, and these mice are approximately 30% larger than normal at birth (15). In addition, enhanced activity of the insulin-stimulated PI3K/Akt pathway was observed in insulin target tissues, including skeletal muscle and adipose tissue (16). We examined the role of mTORC1-mediated Grb10 protein stabilization and accumulation in mTORC1 mediated negative feedback on the PI3K/Akt pathway.

As expected from previous reports (5, 6), both the PI3K/Akt and MAPK pathways were highly suppressed in *TSC2*^{-/-} cells due to constitutively elevated mTORC1 activity. In contrast, Akt was strongly activated in Grb10 knockdown cells under both serum-starved and insulin/IGF stimulation conditions (Figure 4A). In addition, Grb10 knockdown also led to ERK hyperactivation upon insulin/IGF stimulation. Conversely, overexpression of Grb10 in HEK293 cells substantially interfered with activation of PI3K, as judged by decreased Akt T308 phosphorylation (Figure 10A). The observed inhibition was not affected by the phosphorylation status of S501/S503. Previous work demonstrated that Grb10 interferes with insulin-mediated PI3K activation by binding to, and inhibiting, the insulin receptor (11). We confirmed this observation and demonstrated that Grb10 overexpression interferes with insulin receptor-dependent IRS phosphorylation and subsequent PI3K recruitment (Figures 10B, 10C and 10D).

The current model of the negative feedback loop from mTORC1 to PI3K involves S6K-mediated phosphorylation and subsequent degradation of IRS1/2 (6). However, it has also been shown that overexpression of a dominant-negative, kinase-deficient S6K1 failed to completely recapitulate the hyperactivation of Akt induced by overexpression of kinase-dead mTOR, suggesting mTORC1 is directly involved in modulating this feedback inhibition loop (17). Our data clearly show that hyperactivation of mTORC1/S6K promotes feedback loop inhibition of PI3K through a two-prong mechanism: (1) mTORC1/S6K-mediated phosphorylation and degradation of a positive regulator of PI3K signaling, IRS, and (2)

mTORC1-mediated phosphorylation and accumulation of a negative regulator of PI3K signaling, Grb10.

Numerous genetic alterations in cancers result in hyperactivation of the mTOR complexes. Based on these observations, rapamycin analogues are currently approved, or
5 being assessed in various clinical trials, as targeted therapeutics against several cancer subtypes. However, with a few exceptions, the current results have been disappointing, as the clinical outcome of rapamycin treatment is unpredictable and rapamycin is largely ineffective as a monotherapy (3). In particular, it has been shown that post-surgical, maintenance rapamycin treatment led to PI3K/Akt activation in glioblastoma patients, and this activation
10 was associated with shorter time-to-progression(4). We asked whether PI3K hyperactivation induced by Grb10 knockdown (which phenotypically mimics rapamycin-induced Grb10 depletion) would contribute to the survival of cells undergoing stress-induced apoptosis. In response to either staurosporine or etoposide, reduced caspase 3 cleavage was observed in Grb10 knockdown cells compared to control cells. These results indicate that Grb10
15 depletion is sufficient to protect cells from apoptosis (Figures 4B and 10E). Combined with the recent finding that rapamycin can protect cells from energy stress-induced death (18), these results provide a plausible mechanism as to why the effect of rapamycin therapy is cytostatic rather than cytotoxic in some types of cancers and suggest a complete understanding of the feedback inhibition control will be critical in designing combination
20 therapy involving rapamycin and DNA-damaging reagents or reagents targeting metabolic pathways.

To explore the role of Grb10 in cancer progression, we performed a comprehensive meta-analysis of *GRB10* expression based on published microarray data. *GRB10* expression is significantly down-regulated in many tumor types compared to their normal tissue
25 counterparts (Figure 4C). The most profound down-regulation was observed in infiltrating bladder urothelial carcinoma, glioblastoma, breast, myeloma, prostate and pancreatic cancers. Given that loss of Grb10 results in a dramatic activation of the PI3K/Akt pathway (Figure 4A), we performed correlation analysis between variations in the expression of *GRB10* and *PTEN*, a known negative regulator of the PI3K/Akt pathway and tumor suppressor gene.
30 While both *GRB10* and *PTEN* are ubiquitously down-regulated, in all cases there was a significantly ($p < 0.05$) negative correlation between *GRB10* and *PTEN* expression. The most striking differences were observed in breast carcinoma (Pearson correlation coefficient = -0.7, $p = 0.02$) and myeloma (Pearson correlation coefficient = -0.82, $p = 0.001$) (Figure 4D). The data suggest that *GRB10* loss provides an alternative mechanism of PI3K/Akt activation

when *PTEN* expression is retained. It is particularly compelling that this correlation is only observed in tumor samples but not the normal tissue controls (Figure 4E). It has been previously reported that *PIK3CA* mutations and *PTEN* loss are mutually exclusive in breast cancer (19), suggesting that an increased level of PIP₃ resulting from of genetic alteration of either *PIK3CA* or *PTEN* relieves selective pressure targeting the other gene. Similarly, Grb10 loss, which results in PI3K hyperactivation, might provide the cells with growth and survival advantages that are redundant with respect to *PTEN* loss-of-function, suggesting that Grb10 might be a novel tumor suppressor that is regulated by mTORC1. These data point to the exciting therapeutic prospects of targeting Grb10 stability in cancer therapy.

Materials and Methods

Cells and Reagents

Human embryonic kidney (HEK) 293E cells, immortalized wild-type mouse embryonic fibroblast (MEF) cells and *TSC2*^{-/-} MEFs (a kind gift from David Kwiatkowski, Brigham and Women's Hospital) were maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum. In collaboration with Millipore Inc., we generated anti-phospho-S501/S503-Grb10 antibodies. Anti-mTOR, anti-phospho-mTOR (S2481), anti-Grb10 (human), anti-phospho-Akt (S473), anti-phospho-Akt (T308), anti-Akt, anti-S6K, anti-phospho-S6K (T389), anti-IRS2, anti-PARP, anti-caspase 3, anti-4EBP, anti-4EBP (T37/T46), anti-phospho-ribosomal protein S6 (S235/S236), and anti-ribosomal protein S6 antibodies were obtained from Cell Signaling Technology. Anti-phospho-ERK1/2 antibody, insulin, Phorbol Myristate Acetate (PMA), Epidermal Growth Factor (EGF) and polybrene were purchased from Sigma. Anti-Grb10 (mouse), anti-phospho-IRS (Y612), anti-p85 and anti-p110 of PI3K antibodies were purchased from Santa Cruz, Invitrogen, Millipore and BD, respectively. ERK1/2 antibody and anti-HA antibody were prepared in the lab. LY294002 and AktVIII inhibitor were purchased from Calbiochem. Lipofectamine 2000 was purchased from Invitrogen. Torin was kindly provided by Nathanael Gray (Dana Farber Cancer Institute).

SILAC cell culture

TSC2^{-/-} MEFs were used in the rapamycin screen due to constitutive hyperactivation of mTORC1 signaling in this cell line. Cells were grown in light ([¹²C₆¹⁴N₂]Lys, [¹²C₆¹⁴N₄]Arg) and heavy ([¹³C₆¹⁵N₂]Lys, [¹³C₆¹⁵N₄]Arg) DMEM (Cambridge Isotope Labs), respectively. Both light and heavy DMEM were supplemented with 10% dialyzed FBS

(Invitrogen). Cells were serum-deprived for 17 hours and cells were cultured in heavy media were treated with 20 nM rapamycin for two hours. We performed two biological replicates of this experimental design with cross-labeling (swapping the labeled state of the rapamycin-treated cells). For the purposes of illustration, the data for biological replicate #2 is presented in Figure 1A and 1D.

The Ku-0063794 screen was performed using wild-type (WT) MEFs. Cells were grown in the aforementioned SILAC media. Both the light and heavy cells were starved of serum for 17 hrs. The light cells were treated with 20 nM rapamycin for 2 hrs, while the heavy cells were treated with a combination of 20 nM rapamycin and 2 μ M Ku-0063794 for 2 hrs. Both the light and heavy cells were then stimulated with 100 nM insulin for 15 min.

Sample preparation for mass spectrometric analysis

The heavy and light cells were lysed in urea buffer (8 M urea, 20 mM HEPES pH 7.0, 75 mM β -glycerolphosphate, 1 mM sodium vanadate, 1 mM DTT and 1.5 mM EGTA) and the lysates were combined at a 1:1 ratio. Lysates were reduced by adding DTT to a final concentration of 3 mM, followed by incubation at room temperature for 20 min. Cysteines were alkylated by adding iodoacetamide to a final concentration of 50 mM, followed by incubation in the dark for 20 min. The lysates were diluted to a final concentration of 2 M urea by addition of 100 mM NH_4OAc and were digested overnight with sequencing-grade trypsin (Promega) at a 1:100 (enzyme:substrate) ratio. Digestion was quenched by addition of trifluoroacetic acid to a final concentration of 0.1% and precipitates were removed by centrifugation at 4,000 rpm for 30 min. Peptides were desalted on SepPak C18 columns (Waters) according to manufacturer's instructions.

Phosphopeptides were enriched by SCX-IMAC (27). Briefly, lyophilized peptides were resuspended in 500 μ l SCX buffer A (5 mM KH_2PO_4 , pH 2.65, 30% acetonitrile) and injected onto a SCX column (Polysulfoethyl aspartamide, 9.4 mm $\times$ 200mm, 5 μ M particle size, 200 Å pore size, PolyLC). Gradient was developed over 35 min ranging from 0% to 21% buffer B (5 mM KH_2PO_4 , pH 2.65, 30% acetonitrile, 350 mM KCl) at a flow rate of 2 ml/min. Twelve fractions were collected and lyophilized. Peptides were then desalted using SepPak C18 columns and were subjected to IMAC (Sigma) for phosphopeptide enrichment. The eluate was further desalted using STAGE tips (28) and lyophilized.

Mass spectrometry analysis and data processing

The rapamycin screen samples were analyzed by LC-MS/MS on an LTQ-Orbitrap mass spectrometer (Thermo, San Jose, CA) using the top ten method. The Ku-0063794 screen samples were analyzed on an LTQ-Velos mass spectrometer (Thermo Fischer Scientific, San Jose, CA) using the top twenty method. MS/MS spectra were searched against a composite database of the mouse IPI protein database (Version 3.60) and its reversed complement using the Sequest algorithm. Search parameters allowed for a static modification of 57.02146 Da for Cys and a dynamic modification of phosphorylation (79.96633 Da) on Ser, Thr and Tyr, oxidation (15.99491 Da) on Met, stable isotope (10.00827 Da) and (8.01420 Da) on Arg and Lys, respectively. Search results were filtered to include <1% matches to the reverse data base by the linear discriminator function (Huttlin *et al.*, manuscript in preparation) using parameters including Xcorr, dCN, missed cleavage, charge state (exclude 1+ peptides), mass accuracy, peptide length and fraction of ions matched to MS/MS spectra. Phosphorylation site localization was assessed by the Ascore algorithm (29) based on the observation of phosphorylation-specific fragment ions and peptide quantification was performed by using the Vista algorithm (30, 31).

We further filter the peptides according to the following criteria for quantitation of the peptide abundance changes: (1) Vista confidence score must be at least 85, (2) signal to noise ratio ($S/N \geq 3$ for both the heavy and light peptides, (3) in the cases where one of the isotopic species has an S/N of ≤ 3 , S/N of the other was required to be ≥ 5 , and (4) in the cases where only the heavy or light version of a peptide was found, we reported the peak S/N ratio, or its inverse, as a proxy for relative abundance measurement. For such peptides, we also required S/N of at ≥ 5 for the observed species.

Plasmids

The cDNA for human Grb10 (NCBI gene symbol GRB10; Gene ID: 2887) was obtained from Invitrogen and amplified by PCR. The product was subcloned into (1) the BamH I and EcoR I sites of pKH3, (2) the BamH I and EcoR I sites of pGEX-4T-3 or (3) the Hind III and EcoR I sites of pLPCX. The Grb10 point mutant constructs were generated using the QuickChange site-directed mutagenesis kit (Stratagene). pRK5-Myc-raptor and pRK5-Myc-Rictor were kindly provided by David Sabatini (MIT). Lentiviral plasmids ($\Delta 8.9$ and VSVG) were kind gifts from Andrew Kung (Dana Farber Cancer Institute) and David Baltimore (California Institute of Technology).

Immunoprecipitation

Cells were extracted with lysis buffer A (40 mM HEPES, pH 7.5, 120 mM NaCl, 1 mM EDTA, 10 mM β -glycerophosphate, 50 mM NaF, 2 mM phenylmethylsulfonyl fluoride, 2 mg/ml aprotinin, 2 mg/ml leupeptin, and 1mg/ml pepstatin, 1mM DTT) containing 1% Triton X-100, 1% NP-40, or 0.2% CHAPS. After centrifugation, supernatants were collected and pre-cleared for 1 h with protein A- and G-Sepharose beads (GE Healthcare Biosciences). After centrifugation at 3,000 rpm for 5 min, the supernatants were incubated with the antibody at 4°C for 2 h, and then incubated with protein A- and G-Sepharose for an additional hour. Beads were washed four times with the lysis buffer and eluted in 2x reducing sample buffer.

Mammalian lentiviral shRNAs

Lentiviral short hairpin RNA (shRNA) expression vectors were a kind gift from William Hahn (Dana Farber Cancer Institute). To generate the lentiviruses, shRNA plasmids were co-transfected into HEK293TD cells along with packaging (Δ 8.9) and envelope (VSVG) expression plasmids using lipofectamine 2000 (Invitrogen). Two days after transfection, viral supernatants were harvested and filtered. Recipient cells were infected in the presence of a serum-containing medium supplemented with 8 μ g/ml polybrene. Following infection for 36 h, cells were treated with 2.0 μ g/ml puromycin (Sigma) and cell lines that stably expressed the shRNAs were selected. Knockdown efficiencies were examined by immunoblot assay using antibodies against the target protein.

Immunoblot analysis

For immunoblot analysis, the cells were extracted in lysis buffer (20 mM HEPES (pH 7.5), 1% Triton X-100, 150 mM NaCl, 10 mM EDTA, 1 mM EGTA, 1 mM sodium orthovanadate, 1 mM NaF, 2 mM phenylmethylsulfonyl fluoride, 2 mg/ml aprotinin, 2 mg/ml leupeptin, and 1mg/ml pepstatin), and extracts were mixed with the 5X reducing buffer (60 mM Tris-HCl, pH 6.8, 25% glycerol, 2% SDS, 14.4 mM 2-mercaptoethanol, 0.1% bromophenol blue). Samples were boiled for 5 min and subject to electrophoresis using the standard SDS-PAGE method. Proteins were then transferred to a nitrocellulose membrane (Whatman). The membranes were blocked with a TBST buffer (25 mM Tris-HCl, pH 7.5, 150 mM NaCl, 0.05% Tween 20) containing 3% nonfat dried milk, and probed overnight with primary antibodies at 4 °C and for 1h at RT with peroxidase-conjugated secondary

antibodies. Blots were developed using enhanced chemiluminescence, exposed on autoradiograph film and developed using standard methods.

Recombinant protein purification

5 For the purification of GST-tagged proteins, plasmids were transformed into *Escherichia coli* strain BL21 (DE3), and purified to homogeneity from crude lysates using glutathione-sepharose beads (GE Healthcare) according to the manufacture's protocol. Briefly, protein production was initiated by adding isopropyl-D-thiogalactopyranoside (Sigma) to the cultures. Bacteria were collected by centrifugation, resuspended in PBS and
10 lysed by sonication. After centrifugation at 13,000 rpm for 15 min, the supernatant was incubated with glutathione-sepharose beads for 1 h. The beads were washed with PBS three times and the recombinant protein was eluted with PBS containing 20 mM reduced glutathione. Proteins were dialyzed against PBS and stored at -80 °C until use.

Quantitative RT-PCR analysis

Total cellular RNA was purified from cultured cells using the RNeasy mini kit (Qiagen) following the manufacturer's protocol. For quantitative real-time PCR (qRT-PCR), RNA was reverse-transcribed using the High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems) according to the manufacturer's instructions. The resulting cDNA was analyzed
20 by qRT-PCR using the QuantiTect SYBR Green qPCR System (Qiagen). A QuantiTect Primer Assay for mouse Grb10 was used to amplify the target gene, while the β -actin primers (β -actin forward, ACCCAGATCATGTTTGAGACCT (SEQ ID NO: 25); and β -actin reverse, GCAGTAATCTCCTTCTGCATCC (SEQ ID NO: 26)) were used as a normalization control. All reactions were run on an ABI 7900HT Fast Real-Time PCR
25 instrument with a 15 min hot start at 95°C followed by 40 cycles of a 3-step thermocycling program: denaturation: 15 s at 94°C, annealing: 30 s at 55°C and extension: 30 s at 70°C. Melting curve analysis was performed at the end of every run to ensure that a single PCR product of the expected melting temperature was produced in a given well. A total of 3 biological replicates x 4 technical replicates/biological replicate were performed for each
30 treatment group. Data analysis utilized the comparative C_t method ($\Delta\Delta C_t$ method).

Analysis of *GRB10* and *PTEN* expression in human samples.

Microarray expression data from six independent data sets corresponding to patient samples from bladder (GSE3167), glioblastoma (GSE4536), breast (GSE5764), myeloma (GSE5900), pancreatic (GSE1542) carcinoma and matching normal tissues were downloaded from Gene Expression Omnibus (www.ncbi.nlm.nih.gov/geo/) and for prostate carcinoma from the Broad Institute cancer program datasets (www.broadinstitute.org/cgi-bin/cancer/datasets.cgi). The correlation in the gene expression between *GRB10* and *PTEN* was performed using Pearson's correlation coefficient analysis and the samples were clustered using the Euclidean distance metric and Ward's linkage algorithm.

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REFERENCES

1. X. M. Ma, J. Blenis, *Nat Rev Mol Cell Biol* **10**, 307 (2009).
2. D. R. Alessi, L. R. Pearce, J. M. Garcia-Martinez, *Sci Signal* **2**, pe27 (2009).
3. A. Y. Choo, J. Blenis, *Cell Cycle* **8**, 567 (2009).
- 15 4. T. F. Cloughesy *et al.*, *PLoS Med* **5**, e8 (2008).
5. A. Carracedo *et al.*, *J Clin Invest* **118**, 3065 (2008).
6. O. J. Shah, Z. Wang, T. Hunter, *Curr Biol* **14**, 1650 (2004).
7. D. J. Kwiatkowski, B. D. Manning, *Hum Mol Genet* **14 Spec No. 2**, R251 (2005).
8. J. T. Murray *et al.*, *Biochem J* **384**, 477 (2004).
- 20 9. H. H. Zhang, A. I. Lipovsky, C. C. Dibble, M. Sahin, B. D. Manning, *Mol Cell* **24**, 185 (2006).
10. W. Huang da, B. T. Sherman, R. A. Lempicki, *Nat Protoc* **4**, 44 (2009).
11. M. A. Lim, H. Riedel, F. Liu, *Front Biosci* **9**, 387 (2004).
12. A. Y. Choo, S. O. Yoon, S. G. Kim, P. P. Roux, J. Blenis, *Proc Natl Acad Sci U S A*
- 25 **105**, 17414 (2008).
13. P. Langlais *et al.*, *Biochemistry* **44**, 8890 (2005).
14. D. A. Guertin, D. M. Sabatini, *Sci Signal* **2**, pe24 (2009).
15. M. Charalambous *et al.*, *Proc Natl Acad Sci U S A* **100**, 8292 (2003).
16. L. Wang *et al.*, *Mol Cell Biol* **27**, 6497 (2007).
- 30 17. A. Tzatsos, K. V. Kandror, *Mol Cell Biol* **26**, 63 (2006).
18. A. Y. Choo *et al.*, *Mol Cell* **38**, 487 (2010).
19. L. H. Saal *et al.*, *Cancer Res* **65**, 2554 (2005).
20. R.T. Peterson, P.A. Beal, M. J. Comb, S. L. Schreiber, *J Biol Chem* **275**, 7416 (2000).
21. T. P. Herbert, A. R. Tee, C. G. Proud, *J Biol Chem* **277**, 11591 (2002).

22. E. Y. Chan, S. Kir, S. A. Tooze, *J Biol Chem* **282**, 25464 (2007).
23. N. Hosokawa *et al.*, *Mol Biol Cell* **20**, 1981 (2009).
24. J. T. Murray, D. G. Campbell, M. Pegg, A. Mora, P. Cohen, *Biochem J* **384**, 489 (2004).
- 5 25. J. M. Dyson *et al.*, *J Cell Biol* **155**, 1065 (2001).
26. M. S. Woo, Y. Ohta, I. Rabinovitz, T. P. Stossel, J. Blenis, *Mol Cell Biol* **24**, 3025 (2004).
27. J. Villen, S. A. Beausoleil, S. A. Gerber, S. P. Gygi, *Proc Natl Acad Sci U S A* **104**, 1488 (2007).
- 10 28. J. Rappsilber, Y. Ishihama, M. Mann, *Anal Chem* **75**, 663 (2003).
29. S. A. Beausoleil, J. Villen, S. A. Gerber, J. Rush, S. P. Gygi, *Nat Biotechnol* **24**, 1285 (2006).
30. N. Dephoure *et al.*, *Proc Natl Acad Sci U S A* **105**, 10762 (2008).
31. C. E. Bakalarski *et al.*, *J Proteome Res* **7**, 4756 (2008).

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INCORPORATION BY REFERENCE

All publications, patents and sequence database entries mentioned herein, including those items listed below and in the databases and tables provided or referred to herein, are hereby incorporated by reference in their entirety for disclosure of the relevant subject matter indicated, as if each individual database entry, publication, or patent was specifically and individually indicated to be incorporated by reference. The specification provides a number of International Protein Index (IPI) accession numbers, starting with IPI followed by a number. International Protein Index database entries identified by IPI accession number in the specification are incorporated by reference for disclosure of the respective protein sequence and accompanying protein information. The IPI database can be accessed at the European Bioinformatics Institute homepage (www.ebi.ac.uk/), for example, at (www.ebi.ac.uk/IPI/IPIhelp.html). In case of conflict, the present application, including any definitions herein, will control.

30

EQUIVALENTS AND SCOPE

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention

described herein. The scope of the present invention is not intended to be limited to the above description, but rather is as set forth in the appended claims.

In the claims articles such as “a,” “an,” and “the” may mean one or more than one unless indicated to the contrary or otherwise evident from the context. Claims or descriptions that include “or” between one or more members of a group are considered satisfied if one, more than one, or all of the group members are present in, employed in, or otherwise relevant to a given product or process unless indicated to the contrary or otherwise evident from the context. The invention includes embodiments in which exactly one member of the group is present in, employed in, or otherwise relevant to a given product or process. The invention also includes embodiments in which more than one, or all of the group members are present in, employed in, or otherwise relevant to a given product or process. Furthermore, it is to be understood that the invention encompasses all variations, combinations, and permutations in which one or more limitations, elements, clauses, descriptive terms, *etc.*, from one or more of the claims or from relevant portions of the description is introduced into another claim. For example, any claim that is dependent on another claim can be modified to include one or more limitations found in any other claim that is dependent on the same base claim.

Furthermore, where the claims recite a composition, it is to be understood that methods of using the composition for any of the purposes disclosed herein are included, and methods of making the composition according to any of the methods of making disclosed herein or other methods known in the art are included, unless otherwise indicated or unless it would be evident to one of ordinary skill in the art that a contradiction or inconsistency would arise. For example, it is to be understood that any of the compositions of the invention can be used for vocal cord repair or other soft tissue repair or augmentation. It is also to be understood that any of the compositions made according to the methods for preparing compositions disclosed herein can be used for vocal cord repair or other soft tissue repair or augmentation. In addition, the invention encompasses compositions made according to any of the methods for preparing compositions disclosed herein.

Where elements are presented as lists, *e.g.*, in Markush group format, it is to be understood that each subgroup of the elements is also disclosed, and any element(s) can be removed from the group. It is also noted that the term “comprising” is intended to be open and permits the inclusion of additional elements or steps. It should be understood that, in general, where the invention, or aspects of the invention, is/are referred to as comprising particular elements, features, steps, *etc.*, certain embodiments of the invention or aspects of the invention consist, or consist essentially of, such elements, features, steps, *etc.* For

purposes of simplicity those embodiments have not been specifically set forth *in haec verba* herein . Thus for each embodiment of the invention that comprises one or more elements, features, steps, *etc.*, the invention also provides embodiments that consist or consist essentially of those elements, features, steps, *etc.*

- 5 Where ranges are given, endpoints are included. Furthermore, it is to be understood that unless otherwise indicated or otherwise evident from the context and/or the understanding of one of ordinary skill in the art, values that are expressed as ranges can assume any specific value within the stated ranges in different embodiments of the invention, to the tenth of the unit of the lower limit of the range, unless the context clearly dictates otherwise. It is also to be understood that unless otherwise indicated or otherwise evident from the context and/or the understanding of one of ordinary skill in the art, values expressed as ranges can assume any subrange within the given range, wherein the endpoints of the subrange are expressed to the same degree of accuracy as the tenth of the unit of the lower limit of the range.
- 10
- 15 In addition, it is to be understood that any particular embodiment of the present invention may be explicitly excluded from any one or more of the claims. Any embodiment, element, feature, application, or aspect of the compositions and/or methods of the invention, can be excluded from any one or more claims. For purposes of brevity, all of the embodiments in which one or more element, feature, purpose, or aspect is excluded are not set forth explicitly herein.
- 20

TABLES

The Tables provided below are referred to in the specification and the claims. Because some of the tables are lengthy, they are provided in this subsection.

25

Table1:

Gene Symbol	Annotation
1110013L07Rik	Putative uncharacterized protein
1600027N09Rik	RIKEN cDNA 1600027N09 gene
2610110G12Rik	Isoform 1 of UPF0635 protein C6orf134 homolog
Aak1	Isoform 2 of AP2-associated protein kinase 1
Adamts2	A disintegrin and metalloproteinase with thrombospondin motifs 2
Ahctf1	AT-hook-containing transcription factor 1
Ahnak	AHNAK nucleoprotein isoform 1
Aim1l	Absent in melanoma 1-like
Akt1s1	Proline-rich AKT1 substrate 1

Gene Symbol	Annotation
Alkbh6	24 kDa protein
Arhgap17	Isoform 1 of Rho GTPase-activating protein 17
Atg2a	Autophagy-related protein 2 homolog A
B230208H17Rik	Putative GTP-binding protein Parf
Bat2l	Isoform 1 of Protein BAT2-like
Bcas3	Isoform 1 of Breast carcinoma-amplified sequence 3 homolog
Bclaf1	Isoform 2 of Bcl-2-associated transcription factor 1
Bcr	Breakpoint cluster region protein
Bmp2k	Isoform 1 of BMP-2-inducible protein kinase
Bod1l	biorientation of chromosomes in cell division 1-like
C130092O11Rik	Isoform 1 of Uncharacterized protein KIAA1680
Cabin1	calcineurin binding protein 1
Carhsp1	Calcium-regulated heat stable protein 1
Ccdc6	coiled-coil domain containing 6
Ccnl1	Isoform 1 of Cyclin-L1
Cd2ap	CD2-associated protein
Cdgap	Cdc42 GTPase-activating protein
Chd1	Chromodomain-helicase-DNA-binding protein 1
Crks	Isoform 2 of Cell division cycle 2-related protein kinase 7
Cttn	Src substrate cortactin
Cux1	cut-like homeobox 1 isoform a
D6Wsu116e	Isoform 1 of Protein FAM21
D830015G02Rik	Putative uncharacterized protein
Dab2	Isoform p93 of Disabled homolog 2
Ddx21	Nucleolar RNA helicase 2
Dennd4a	hypothetical protein LOC102442
Dhx15	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15
Dnajc2	DnaJ homolog subfamily C member 2
Dock11	Dedicator of cytokinesis protein 11
Edc3	Enhancer of mRNA-decapping protein 3
Edc4	Isoform 1 of Enhancer of mRNA-decapping protein 4
Eef2k	Elongation factor 2 kinase
Ehbp1	Isoform 2 of EH domain-binding protein 1
Ehmt2	Isoform 1 of Histone-lysine N-methyltransferase H3 lysine-9 specific 3
Eif3a	Eukaryotic translation initiation factor 3 subunit A
Eif4b	Eukaryotic translation initiation factor 4B
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2
Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1
Eif5;LOC100047658	Eukaryotic translation initiation factor 5
Emg1	Probable ribosome biogenesis protein NEP1
Eps8l2	Isoform 1 of Epidermal growth factor receptor kinase substrate 8-like protein 2
Epyc	Epiphycan

Gene Symbol	Annotation
Erc1;LOC100048600	Isoform 1 of ELKS/RAB6-interacting/CAST family member 1
Ext1	Exostosin-1
Fbxw9	F-box and WD-40 domain protein 9
Fkbp15	Isoform B of FK506-binding protein 15
FLNA	Filamin-A
Fmn13	Isoform 1 of Formin-like protein 3
Foxk1	Forkhead box protein K1
Foxk2	Isoform 1 of Forkhead box protein K2
Fxr1	Isoform E of Fragile X mental retardation syndrome-related protein 1
Gbf1	Golgi-specific brefeldin A-resistance factor 1
Gm13099	Novel protein similar to preferentially expressed antigen in melanoma-like family
Gm13697	Novel protein containing MIF4G and MA3 domains
Gm14085	Novel protein similar to solute carrier family 28 (Sodium-coupled nucleoside transporter) member 2
Gm6988	similar to hCG1640785
Gm9757	Putative uncharacterized protein
Gon4l	RIKEN cDNA 5830417I10 gene
Grb10	Isoform 3 of Growth factor receptor-bound protein 10
Gsk3b	Glycogen synthase kinase-3 beta
Gtf2f1	General transcription factor IIF subunit 1
Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2
Herc1	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1
Hisppd1	140 kDa protein
Hn1l	Hematological and neurological expressed 1-like protein
Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase
Inf2	Isoform 1 of Inverted formin-2
Iqsec1	IQ motif and Sec7 domain 1 isoform b
Irs2	Insulin receptor substrate 2
Iws1	Isoform 1 of Protein IWS1 homolog
Junb	Transcription factor jun-B
Kdm3b	Isoform 2 of Lysine-specific demethylase 3B
Kdm6a	Isoform 1 of Lysine-specific demethylase 6A
Ktn1	Isoform 1 of Kinectin
Larp1	Isoform 1 of La-related protein 1
Larp4	Putative uncharacterized protein
Larp7	Isoform 1 of La-related protein 7
Ldhd	22 kDa protein
Lin9	Isoform 2 of Lin-9 homolog
Llg1	lethal giant larvae homolog 1 isoform 1
LOC100048123;Akt2	RAC-beta serine/threonine-protein kinase
LOC100048559;Sfrs1	Isoform 1 of Splicing factor arginine/serine-rich 1
Luc7l2	Isoform 1 of Putative RNA-binding protein Luc7-like 2
Macf1	Isoform 3 of Microtubule-actin cross-linking factor 1

Gene Symbol	Annotation
Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1
Megf11	Isoform 4 of Multiple epidermal growth factor-like domains 11
Mett10d	Isoform 1 of Putative methyltransferase METT10D
Mib1	E3 ubiquitin-protein ligase MIB1
Micall1	Isoform 1 of MICAL-like protein 1
Mll2	similar to myeloid/lymphoid or mixed-lineage leukemia 2
Mllt4	Isoform 3 of Afadin
Mogat1	2-acylglycerol O-acyltransferase 1
Mtap1b	Microtubule-associated protein 1B
Mtor	Isoform 1 of FKBP12-rapamycin complex-associated protein
Myef2	Isoform 2 of Myelin expression factor 2
Myo5a	Myosin-Va
Nacc1	Nucleus accumbens-associated protein 1
Ndr3	Protein NDRG3
Nfic	Isoform 1 of Nuclear factor 1 C-type
Npm1	Nucleophosmin
Numa1	Nuclear mitotic apparatus protein 1
Palm	Isoform 1 of Paralemmmin
Pat1	Protein PAT1 homolog 1
Pbx2	Pre-B-cell leukemia transcription factor 2
Pcbp1	Poly(rC)-binding protein 1
Pcbp2	Isoform 1 of Poly(rC)-binding protein 2
Pcm1	Isoform 1 of Pericentriolar material 1 protein
Pcd11	Protein RRP5 homolog
Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B
Peg3	Isoform 1 of Paternally-expressed gene 3 protein
Pgrmc2	Membrane-associated progesterone receptor component 2
Phf3	PHD finger protein 3
Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1
Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2
Pi4k2a	Phosphatidylinositol 4-kinase type 2-alpha
Pkn2	Isoform 1 of Serine/threonine-protein kinase N2
Pla2g4a	Cytosolic phospholipase A2
Plekhm1	Pleckstrin homology domain-containing family M member 1
Pom121	Nuclear envelope pore membrane protein POM 121
Ppfibp2	Isoform 4 of Liprin-beta-2
Ppp1r12a	MCG122391 isoform CRA_e
Prkd2	Serine/threonine-protein kinase D2
Ptk2	Isoform 1 of Focal adhesion kinase 1
Qsox2	Isoform 3 of Sulfhydryl oxidase 2
Rab1	Ras-related protein Rab-1A
Ranbp10	Ran-binding protein 10
Ranbp9	RAN binding protein 9

Gene Symbol	Annotation
Rb1	Retinoblastoma-associated protein
Rfc1	Rfc1 protein
Rictor	Isoform 1 of rapamycin-insensitive companion of mTOR
Rnf19b	IBR domain containing 3
Rps6	29 kDa protein
Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1
Rsl1d1	Putative uncharacterized protein
rsp6	29 kDa protein
Sap30	Histone deacetylase complex subunit SAP30
Sbno1	Isoform 2 of Protein strawberry notch homolog 1
Scrib	Isoform 1 of Protein LAP4
Serbp1	Isoform 1 of Plasminogen activator inhibitor 1 RNA-binding protein
Setd1a	SET domain containing 1A
Sfrs18	splicing factor arginine/serine-rich 18
Sfrs8	splicing factor arginine/serine-rich 8
Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha
Slc4a1ap	solute carrier family 4 (anion exchanger) member 1 adaptor protein
Smarca4	Putative uncharacterized protein
Smarcad1	Isoform 1 of SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A containing DEAD/H box 1
Smarcc2	Isoform 2 of SWI/SNF complex subunit SMARCC2
Snx17	Sorting nexin-17
Snx30	Sorting nexin-30
Sorbs3	Vinexin
Spna2	Isoform 2 of Spectrin alpha chain brain
Sqstm1	Isoform 1 of Sequestosome-1
Srpk2	serine/arginine-rich protein-specific kinase 2
Srrm1	Isoform 2 of Serine/arginine repetitive matrix protein 1
Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2
St5	Isoform 1 of Suppression of tumorigenicity 5
Strn3	Striatin-3
Syap1	Synapse-associated protein 1
Tbc1d4	140 kDa protein
Tcfef	Transcription factor EB
Tinf2	Putative uncharacterized protein
Tjp2	Tight junction protein ZO-2
Tmem106b	Transmembrane protein 106B isoform CRA_b
Tmpo	Isoform Beta of Lamina-associated polypeptide 2 isoforms beta/delta/epsilon/gamma
Tnc	Isoform 1 of Tenascin
Tns1	tensin 1
Tox4	TOX high mobility group box family member 4
Trim28	Isoform 1 of Transcription intermediary factor 1-beta
Trip10	Isoform 3 of Cdc42-interacting protein 4
Ubxn7	UBX domain-containing protein 7

Gene Symbol	Annotation
Ulk1	Putative uncharacterized protein
Usp24	Isoform 1 of Ubiquitin carboxyl-terminal hydrolase 24
Usp36	Ubiquitin specific peptidase 36
Uvrag	UV radiation resistance associated
Vwa5b1	von Willebrand factor A domain-containing protein 5B1
Wdr91	WD repeat-containing protein 91
Wnk1	Serine/threonine-protein kinase WNK1
Zc3h4	Isoform 2 of Zinc finger CCCH domain-containing protein 4
Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK
Zeb2	Zinc finger E-box-binding homeobox 2
Zfp106	Isoform 1 of Zinc finger protein 106
Zfp516	Zinc finger protein 516
Znrf2	E3 ubiquitin-protein ligase ZNRF2

Table 1. Names and annotations of proteins identified to harbor phosphopeptides whose intensities decrease after rapamycin treatment (rapamycin screen). Note that the rapamycin screen included two biological replicates. For the first replicate, the light cells were controls whereas the heavy cells were treated with rapamycin. For the second replicate experiment, the light cells were treated with rapamycin, and the heavy cells were controls. Table 1 includes all unique proteins identified in both replicates. Protein sequences and phosphorylation sites can be identified from the identifiers provided in the tables and database provided herein.

Table 2:

Gene Symbol	Annotation
Myo18a	Isoform 4 of Myosin-XVIIIa
Brd2	Isoform 2 of Bromodomain-containing protein 2
6330577E15Rik	Uncharacterized protein C10orf78 homolog
Best3	Bestrophin-3
Larp1	Isoform 1 of La-related protein 1
Fam62c	Isoform 1 of Extended synaptotagmin-3
Mdn1	Midasin homolog
Rtn4	Isoform 2 of Reticulon-4
Pcdh24	Pcdh24 protein
Synj1	similar to mKIAA0910 protein
Zfp318	zinc finger protein 318 isoform 1
Akt1s1	Proline-rich AKT1 substrate 1
Alpk3	myocyte induction differentiation originator
Zc3h14	Isoform 2 of Zinc finger CCCH domain-containing protein 14
Edc4	Isoform 1 of Enhancer of mRNA-decapping protein 4
Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2
Kif20b	Isoform 1 of M-phase phosphoprotein 1
1110007A13Rik	UPF0557 protein C10orf119 homolog
Pi4k2a	Phosphatidylinositol 4-kinase type 2-alpha
Top2b	DNA topoisomerase 2-beta
BC021381	Isoform 2 of Uncharacterized protein KIAA1931
Bbx	Isoform 1 of HMG box transcription factor BBX
Vcl	Vinculin
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1
Rrp15	RRP15-like protein
D10Wsu102e	Uncharacterized protein C12orf45 homolog
Braf	Isoform 1 of B-Raf proto-oncogene serine/threonine-protein kinase
Atg2b	Isoform 1 of Autophagy-related protein 2 homolog B
Npm1	Nucleophosmin
Pcsk5	proprotein convertase subtilisin/kexin type 5
Mtap1b	Microtubule-associated protein 1B
Ercc6l	DNA excision repair protein ERCC-6-like
Serinc1	Serine incorporator 1
Klf3;LOC100046855	Krueppel-like factor 3
Smarca4	Putative uncharacterized protein
Aak1	Uncharacterized protein FLJ45252 homolog
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2
Ndr1	Protein NDRG1
Melk	Maternal embryonic leucine zipper kinase
Arhgef17	Isoform 1 of Rho guanine nucleotide exchange factor 17
Grit	Isoform 2 of Rho/Cdc42/Rac GTPase-activating protein RICS
Mdc1	mediator of DNA damage checkpoint 1

Gene Symbol	Annotation
Nfkb2	NF-kB2 splice variant 4
Pcm1	Isoform 1 of Pericentriolar material 1 protein
Mybbp1a	Myb-binding protein 1A
Sf3b1	Splicing factor 3B subunit 1
Atrx	Transcriptional regulator ATRX
Ccdc88a	Isoform 2 of Girdin
Baz1b	Isoform 1 of Tyrosine-protein kinase BAZ1B
Nedd4l	Isoform 3 of E3 ubiquitin-protein ligase NEDD4-like
Orc6l	Origin recognition complex subunit 6
Trp53bp1	Transformation related protein 53 binding protein 1
Map3k2	Mitogen-activated protein kinase kinase kinase 2
Hectd2	Hectd2 protein
Usp10	Ubiquitin carboxyl-terminal hydrolase 10
D830031N03Rik	similar to mKIAA0754 protein
Nck1	non-catalytic region of tyrosine kinase adaptor protein 1
Exosc9	Exosome complex exonuclease RRP45
Dap	Death-associated protein 1
Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1
Lmna	Isoform C2 of Lamin-A/C
Sltm	Isoform 1 of SAFB-like transcription modulator
Sh3pxd2a	Isoform 1 of SH3 and PX domain-containing protein 2A
Finc	Isoform 1 of Filamin-C
Oxr1	Isoform 2 of Oxidation resistance protein 1
Rin2	Isoform 1 of Ras and Rab interactor 2
Nek9	Serine/threonine-protein kinase Nek9
Pebp1	Phosphatidylethanolamine-binding protein 1
Pop1	Processing of 1 ribonuclease P/MRP family
Serhl	Serine hydrolase-like protein
Epb4.1l3	Isoform 1 of Band 4.1-like protein 3
Hnrpll	Isoform 1 of Heterogeneous nuclear ribonucleoprotein L-like
Samhd1	SAM domain and HD domain-containing protein 1
Zfp828	Zinc finger protein 828
Larp7	Isoform 1 of La-related protein 7
Myc	myc proto-oncogene protein
Myo9a	Isoform 2 of Myosin-IXa
Gsk3b	Glycogen synthase kinase-3 beta
Zfp395	zinc finger protein 395
Bend3	BEN domain-containing protein 3
Akap12	Isoform 1 of A-kinase anchor protein 12
Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1
Eif4b	Eukaryotic translation initiation factor 4B
Dock7	Isoform 2 of Dedicator of cytokinesis protein 7
Patl1	Protein PAT1 homolog 1

Gene Symbol	Annotation
Slc7a11	Cystine/glutamate transporter
Myo9b	Isoform 1 of Myosin-IXb
Setd2	SET domain containing 2
Gphn	Gephyrin
Erf	ETS domain-containing transcription factor ERF
Spnb2	Isoform 2 of Spectrin beta chain brain 1
Phip	PH-interacting protein
Sdpr	Serum deprivation-response protein
Tcof1	Treacle protein
Pwp1	Periodic tryptophan protein 1 homolog
Rbl1	Isoform Long of Retinoblastoma-like protein 1
Eef1b2	Elongation factor 1-beta
Phactr4	Isoform 1 of Phosphatase and actin regulator 4
C230081A13Rik	Tyrosine-protein kinase-protein kinase SgK269
Ahnak2	Putative uncharacterized protein

Table 2. Names and annotations of proteins identified to harbor phosphopeptides whose intensities decrease after Ku-0063794 treatment (Ku-0063794 screen). Note that the light cells were treated with rapamycin and serve as controls whereas the heavy cells were treated with a combination of rapamycin and Ku-0063794. Protein sequences and phosphorylation sites can be identified from the identifiers provided in the tables and the database provided herein.

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Table 3:

IPI Reference	Peptide	SEQ ID NO	Gene Name	Class
IPI00121418.1	K.DGEGPDNLEPACPLSLPLQGNHTAADMYLS*PLRS*PK.K	30	Rb1	1
IPI00221581.1	R.TGS*ESS*QTGASATSGR.N	31	Eif4b	1
IPI00929786.1	R.TAS*ISSS*PSEGTPAVGSYGCT*PQS*LPK@.F	32	Larp1	1
IPI00929786.1	R.TAS*ISSS*PSEGTPAVGSYGCT*PQS*LPK@.F	33	Larp1	1
IPI00929786.1	R.T*AS*ISSSPSEGTPAVGS*YGCTPQSLPK@.F	34	Larp1	1
IPI00317401.6	R.AES*PETSVESTQST*PQK@.G	35	Pds5b	1
IPI00107958.1	K.TSDIFGS*PVTATAPLAHPNK@PK@.D	36	Hn1l	1
IPI00108454.2	R.R^LS*S^LR^A	37	Rps6	1
IPI00225062.2	R.R^SS*SELS*PEVVEK@.V	38	Srrm2	1
IPI00761759.1	R.S*SSGS*EHST*EGSVSLGDGPLSR^S	39	Larp4	1
IPI00761759.1	R.SSS*GS*EHST*EGSVSLGDGPLSR^S	40	Larp4	1
IPI00225062.2	R.RSS*SELS*PEVVEK.V	41	Srrm2	1
IPI00122594.4	R.TTPLAS*PSLS*PGR^S	42	Ahctf1	1
IPI00136107.1	R.THS*TSS*S^IGSGESPFSR^S	43	Ndr3	1
IPI00136107.1	R.THS*TSSS^IGSGESPFSR^S	44	Ndr3	1
IPI00136107.1	R.THS*TSS*S^IGSGESPFSR^S	45	Ndr3	1
IPI00136107.1	R.THS*TSSS^IGSGESPFSR^S	46	Ndr3	1
IPI00136107.1	R.T^HST*S^SSIGSGESPFSR^S	47	Ndr3	1
IPI00136107.1	R.T^HSTSSS^IGSGESPFSR^S	48	Ndr3	1
IPI00136107.1	R.THS*TSSS^IGSGESPFSR^S	49	Ndr3	1
IPI00136107.1	R.T^HSTSS^SIGSGESPFSR^S	50	Ndr3	1
IPI00136107.1	R.THS*TSSS^IGSGESPFSR^S	51	Ndr3	1
IPI00551454.3	R.ER^QES*ESEQLVVK@.R	52	Pdcd11	1
IPI00117229.3	R.TS*PAGGTWSSVVGVP.R	53	Atxn2	1
IPI00348442.1	R.SK@FDS*DEEDEDENLEAVSSGK@.V	54	Sfrs18	1
IPI00556837.1	K.DTVIIVS*EPS*EDEESHDLPSVTR.R	55	Smarcad1	1
IPI00153986.2	K.GTS*RPQT*PSAEAASTSLR.A	56	Gtf2f1	1
IPI00225062.2	R.GCS*PPKS*PEKPPQSTSSSESCPPS*PQPTK.V	57	Srrm2	1
IPI00128904.1	R.VMTIPYQMPASS*PVICAGQDR.C	58	Pcbp1	1
IPI00121251.7	R.LSTTPS*PT*NSLHEDGVDDFRR.Q	59	Tox4	1
IPI00320594.5	K.SQPHSSTSNQETS*DS*EMEMAEHYPNGVLESVSTR^I	60	Ranbp10	1
IPI00808277.2	R.SAPASPNHAGVLS*AH*SGAQTPESLS^R^E	61	Foxk2	1
IPI00137166.1	R.SR^DAT*PPVS*PINMEDQER^I	62	Junb	1
IPI00454104.1	K.TTEAPCS*PGSQPPS*PDEL PANVK@.Q	63	Scrib	1
IPI00225062.2	R.GCS*PPK@S*PEK@PPQSTSSSESCPPS*PQPTK@.V	64	Srrm2	1
IPI00153986.2	K.GTS*R^PGTPS*AEAASTSLR^A	65	Gtf2f1	1
IPI00753321.2	K.SVS*ETSEDK@K@DEES*DEEEEEEEEEPLGATTR^S	66	Bod1l	1
IPI00153986.2	K.GT*SR^PGT*PSAEAASTSLR^A	67	Gtf2f1	1
IPI00153986.2	K.GTS*R^PGT*PSAEAASTSLR^A	68	Gtf2f1	1
IPI00929786.1	R.TASIS*SSPS*EGTPAVGSYGCT*PQSLPK@.F	69	Larp1	1
IPI00929786.1	R.TASISS*SPSEGTPAVGSYGCT*PQS*LPK@.F	70	Larp1	1

IPI Reference	Peptide	SEQ ID NO	Gene Name	Class
IPI00130920.1	R.RSES*PFEGK.N	71	Mtap1b	1
IPI00336973.2	K.GLNLDGTPALSTLGGFS*PASK@PSS*PR [^] .E	72	Ccn1	1
IPI00336973.2	K.GLNLDGTPALSTLGGFSPAS*KPS*SPR.E	73	Ccn1	1
IPI00336973.2	K.GLNLDGT*PALSTLGGFSPAS*K@PS*SPR [^] .E	74	Ccn1	1
IPI00336973.2	K.GLNLDGTPALSTLGGFSPAS*K@PS*SPR [^] .E	75	Ccn1	1
IPI00379844.4	R.TAS*EGDGAAGGAGTAGGR [^] PMSVAGS*PLS*PGPVR [^] .A	76	Irs2	1
IPI00336973.2	K.GLNLDGTPALSTLGGFSPAS*KPSS*PR.E	77	Ccn1	1
IPI00336973.2	K.GLNLDGT*PALSTLGGFSPAS*KPSS*PR.E	78	Ccn1	1
IPI00656285.2	R.SLVS*PIPSPT*GTISVPNSCPAS*PR [^] .G	79	Foxk1	1
IPI00656285.2	R.SLVS*PIPS*PTGTISVPNSCPAS*PR.G	80	Foxk1	1
IPI00454104.1	K.TTEAPCS*PGSQPPS*PDELPANVK@.Q	81	Scrib	1
IPI00753321.2	K.S*VSETSEDK@K@DEES*DEEEEEEEEEPLGATTR [^] .S	82	Bod1l	1
IPI00753321.2	K.SVS*ETSEDK@K@DEES*DEEEEEEEEEPLGATTR [^] .S	83	Bod1l	1
IPI00313307.3	R.SYQNS*PSS*EDGIR [^] PLPEYSTEK@.H	84	Med1	1
IPI00225062.2	R.GCS*PPK@S*PEK@PPQSTSS*ESCPPSPQPTK@.V	85	Srrm2	1
IPI00318938.6	R.NS*PVAK@TPPK@DLPAIPGVTS*PTSDEPPMQASQSQL PSSPEDK@.R	86	Eif4ebp1	1
IPI00130920.1	R.SLMS*SPEDLTk@DFEELK@AEEIDVAK@.D	87	Mtap1b	1
IPI00553798.2	R.SS*EVVLS*GDDEDYQR [^] .I	88	Ahnak	1
IPI00129264.1	R.ATSR [^] PINLGSS*PNTEIHWTPYR [^] .A	89	Sorbs3	1
IPI00129264.1	R.ATSRPINLGPS*SPNTEIHWTPYR.A	90	Sorbs3	1
IPI00123410.5	R.TIS*AQDTLAYATALLNEK@.E	91	Usp24	1
IPI00226441.2	R.LHYT*PPLQS*PIT*DGDP LLGQS*PWR [^] .S	92	Lin9	1
IPI00309059.7	R.ST*SPIIGS*PPVR [^] .A	93	Pat1	1
IPI00336713.1	R.CS*PVPGLSSS*PSGSPLHGK@.L	94	Bcas3	1
IPI00320905.7	R.LGEQGPEPGPT*PPQTPT*PPS*TPPLAK.Q	95	Arhgap17	1
IPI00309059.7	R.R [^] S*TS*PIIGS*PPVR [^] .A	96	Pat1	1
IPI00309059.7	R.RSTS*PIIGS*PPVR.A	97	Pat1	1
IPI00309059.7	R.ST*S*PIIGS*PPVR [^] .A	98	Pat1	1
IPI00317599.3	K.SQEDEEEISTS*PGVSEFVSADFDTCSLNQEDLRK.E	99	Syap1	1
IPI00317599.3	K.SQEDEEEIST*SPGVSEFVSADFDTCSLNQEDLRK.E	100	Syap1	1
IPI00656285.2	R.S*LVSPISPT*GTISVPNS*CPASPR [^] .G	101	Foxk1	1
IPI00676574.2	R.RVS*TDLPEGQDVYTAACNSVIHR.C	102	Herc1	1
IPI00458958.2	K.DWDK@ES*EGEEPAGGR [^] .A	103	Rrp15	2
IPI00230719.8	R.R [^] DSS*DDWEIPDGGQITVGQR [^] .I	104	Braf	2
IPI00318938.6	R.VALGDGVQLPPGDYSTT*PGGTLFSTTPGGT [^] .R.I	105	Eif4ebp1	2
IPI00874995.2	R.AS*DDLGE PDVFATAPFR.S	106	Aak1	2
IPI00318938.6	R.VALGDGVQLPPGDYSTT*PGGTLFSTTPGGT [^] .R.I	107	Eif4ebp1	2
IPI00318938.6	R.VALGDGVQLPPGDYSTTPGGT*LFSTT*PGGTR.I	108	Eif4ebp1	2
IPI00318938.6	R.VALGDGVQLPPGDYSTTPGGT*LFSTT*PGGTR [^] .I	109	Eif4ebp1	2
IPI00323045.3	R.S*MDVDLNQAHMEDTPK@.K	110	Melk	2

IPI Reference	Peptide	SEQ ID NO	Gene Name	Class
IPI00623284.4	K.IWDTPSHT*PAGAAT*PGRGDT*PGHAT*PGHGGATSSA R.K	111	Sf3b1	2
IPI00125960.1	R.TAS*GSS*VTSLEGTR.S	112	Ndrp1	2
IPI00318938.6	R.R^VALGDGVQLPPGDYSTT*PGGTLFSTT*PGGTR^I	113	Eif4ebp1	2
IPI00229571.1	R.ISS*K@S*PGHMLVILNQTK@.G	114	Sltm	2
IPI00120095.2	R.DFTK@PQDGDIIAPLIT*PLK@.W	115	Samhd1	2
IPI00340860.5	R.T*AS*EGSEAETPEAPK.Q	116	Larp7	2
IPI00664670.4	R.LGS*FGSITR^Q	117	Flnc	2
IPI00654192.2	R.S*LSFSEPQQPPPTVK@.S	118	Zfp395	2
IPI00225062.2	K.IHTTALTGQSPPLAS*GHQGECDAPSVEPGATNIQQPSS* PAPSTK.Q	119	Srrm2	2
IPI00225062.2	K.IHTTALTGQS*PPLASGHQGECDAPSVEPGATNIQQPSS* PAPST*K@.Q	120	Srrm2	2
IPI00225062.2	K.IHTTALTGQS*PPLASGHQGECDAPSVEPGATNIQQPSS* PAPST*K.Q	121	Srrm2	2
IPI00339428.9	R.MSSHTETS*SFLQTLTGR.L	122	Dock7	2
IPI00225062.2	R.DGSGT*PSRHSL*GS*S*PGMKDTPQT*PSR.G	123	Srrm2	2
IPI00668709.2	R.DRS*SSAPNVHINTIEPVNIDDLIR.D	124	Braf	2
IPI00135660.5	R.RGNN*AVGS*NADLT*IEEDEEEEPVALQQAQVR.Y	125	Sdpr	2
IPI00135660.5	R.R^GNN*AVGS*NADLT*IEEDEEEEPVALQQAQVR^Y	126	Sdpr	2
IPI00404545.2	R.SLS*S*PTVTL*SALEGAK@.D	127	Nedd4l	2
IPI00121892.9	R.R^PPS*PDPNTK@.V	128	Spnb2	2
IPI00322707.5	K.AKQPVIGDQNSDS*DEMLAVLK.E	129	Atrx	2
IPI00929786.1	R.S*LPTTV*PES*PNYR^N	130	Larp1	3
IPI00125319.1	R.TTS*FAESCK@PVQQPSAFGSMK@.V	131	Gsk3b	3

Table 3. Categorization of mTOR targets identified in the rapamycin and Ku-0063794

screens. Class 1 includes downstream effectors of rapamycin-sensitive mTORC1. Class 2 includes downstream effectors of rapamycin-insensitive mTORC1 or mTORC2. Class 3 includes the proteins downstream of both mTORC1 and mTORC2. Name of exemplary genes and sequences of respective phosphopeptides are shown. * represents the site of phosphorylation (Ser, Thr and Tyr); ^ and @ represent heavy Arg and Lys, respectively.

Table 4:

Extracted Term	IPI References
Rapamycin screen	
mTOR signaling pathway	IPI00453603,IPI00318938,IPI00399440,IPI00268673,IPI00467843,IPI00221581,IPI00121335
ErbB signaling pathway	IPI00125319,IPI00453603,IPI00318938,IPI00113563,IPI00268673,IPI00121335
Insulin signaling pathway	IPI00125319,IPI00453603,IPI00116923,IPI00318938,IPI00268673,IPI00379844,IPI00121335
Acute myeloid leukemia	IPI00453603,IPI00318938,IPI00268673,IPI00121335
Focal adhesion	IPI00403938,IPI00125319,IPI00131138,IPI00113563,IPI00671847,IPI00121335
Tight junction	IPI00118143,IPI00380354,IPI00323349,IPI00845596,IPI00121335
Pathways in cancer	IPI00125319,IPI00121418,IPI00381495,IPI00113563,IPI00268673,IPI00380817,IPI00121335
Prostate cancer	IPI00125319,IPI00121418,IPI00268673,IPI00121335
RNA degradation	IPI00169888,IPI00309059,IPI00330066
Glioma	IPI00121418,IPI00268673,IPI00121335
Adipocytokine signaling pathway	IPI00268673,IPI00379844,IPI00121335
VEGF signaling pathway	IPI00111169,IPI00113563,IPI00121335
Chronic myeloid leukemia	IPI00121418,IPI00380817,IPI00121335

Ku-0063794 Screen	
ErbB signaling pathway	IPI00453999,IPI00125319,IPI00453603,IPI00230719,IPI00318938,IPI00668709,IPI00131999
mTOR signaling pathway	IPI00453603,IPI00230719,IPI00318938,IPI00668709,IPI00221581
Acute myeloid leukemia	IPI00453603,IPI00230719,IPI00318938,IPI00668709,IPI00131999
Cell cycle	IPI00125319,IPI00124717,IPI00137864,IPI00131999
Insulin signaling pathway	IPI00125319,IPI00453603,IPI00230719,IPI00318938,IPI00668709
Endometrial cancer	IPI00125319,IPI00230719,IPI00668709,IPI00131999
MAPK signaling pathway	IPI00230719,IPI00117088,IPI00123474,IPI00668709,IPI00664670,IPI00131999
RNA degradation	IPI00309059,IPI00119442,IPI00330066
Focal adhesion	IPI00125319,IPI00230719,IPI00405227,IPI00668709,IPI00664670
Colorectal cancer	IPI00125319,IPI00230719,IPI00668709,IPI00131999
TGF-beta signaling pathway	IPI00453603,IPI00137864,IPI00131999

Table 4. Gene ontology analysis of mTOR targets identified in the rapamycin and Ku-0063794 screens. Pathways that were overrepresented among the rapamycin-sensitive and Ku-sensitive mTOR targets are shown. Also shown is the biological process that the rapamycin-sensitive and Ku-sensitive targets overrepresented.

Table 5:

Screen ID	Bio-replicate	# of tech-replicate combined	Cell line	Drug treatment	# of phosphopeptides (FDR%)	# of phosphoproteins (FDR%)	# of unique phosphosites	Total unique sites	Total phosphoproteins (FDR%)
Rapa	#1	2	TSC2-/-	(L) DMSO (H) rapa	14,635 (0.25%)	1,615 (1.0%)	4,484		
	#2	2	TSC2-/-	(L) rapa (H) DMSO	32,500 (0.28%)	1,866 (0.97%)	6,832	11,271	2,778 (1.7%)
Ku	#1	1	wt MEF	(L) rapa (H) rapa+Ku	34,642 (0.28%)	1,867 (0.97%)	6,220		

Table 5. Summary of the data. Two biological replicates were obtained for the rapamycin screen (each contained data from two technical replicates) and one SILAC experiment was performed for the Ku-0063794 screen. (L), light cells. (H), heavy cells.

Table 6:

Gene Name	Description	Modified Sequence	SEQ ID NO	Amino acid position	Median (treated/ctrl)
Rapa Screen (Proteins with downregulated phosphorylation)					
RPS6	Ribosomal protein S6	RLS*S*LRASTSK	132	S235, S236	30.5
RPS6	Ribosomal protein S6	LSSLRAS*TS*KSES*S*QK	133	S240, S242, S246, S247	4.5
Akt1s1	Proline-rich AKT1 substrate 1	S*LPVSVPVWAFK	134	S184	2.2
Gsk3 β	Glycogen synthase kinase-3 beta	TTS*FAESCKPVQQPSAFGSMK	135	S9	3.3
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2	RNS*PMAQT*PPCHLPNIPGVT SPGALIEDSK	136	S65, T70	39.1
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2	TVAISDAAQLPQDYCTT*PGGT LFSTT*PGGTRIIYDRK	137	T37, T46	2.3
Eif4b	Eukaryotic translation initiation factor 4B	SRT*GS*ESSQTGASATSGR	138	T420, S422	4.3
Eif4b	Eukaryotic translation initiation factor 4B	TGS*ESS*QTGASATSGR	139	S422, S425	4.6
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	NS*PVAKT*PPKDLPAIPGVTSP TSDEPPMQASQSQLPSSPEDK	140	S64, T69	2.8
Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	SFS*KEVEER	141	S1189	2.8
Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1	FIGS*PRT*PVS*PVKFSPGDFW GR	142	S441, T444, S447	2.8
mTOR	Isoform 1 of FKBP12-rapamycin complex-associated protein	AGTTVPES*IHS*FIGDGLVKPE ALNKK	143	S2478, S2481	3.6
ULK1	Serine/threonine-protein kinase ULK1	GGGASS*PAPVVFTVGS*PPSG AT*PPQSTR	144	S747, S757, T763	4.1
Grb10	Isoform 3 of Growth factor receptor-bound protein 10	MNILSS*QS*PLHPSTLNAVIHR	145	S421, S423	27.3
Grb10	Isoform 3 of Growth factor receptor-bound protein 10	T*ASLPAIPNPFPELTGAAPGS* PPSVAPSS*LPPPPSQPPAK	146	T76, S96, S104	5.4
Ku Screen (Proteins with downregulated phosphorylation)					
Flnc	Filamin-C	LGS*FGSITR	147	S2234	2.4
Gsk3 β	Glycogen synthase kinase-3 beta	TTS*FAESCKPVQQPSAFGSMK	148	S9	2.2
Ndrp1	Protein NDRG1	TAS*GSS*VTSLEGTR	149	S330, S333	4.1
Braf	B-Raf protein	DRSSS*APNVHINTIEPVNIDDLI R	150	S312	2.1
Akt1s1	Proline-rich AKT1 substrate 1	LNT*SDFQK	151	T247	31.3
Eif4b	Eukaryotic translation initiation factor 4B	TGS*ESSQTGASATSGR	152	S422	2.2
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	VALGDGVQLPPGDYSTT*PGGT LFSTT*PGGTR	153	T36, T45	7.2
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2	NS*PMAQT*PPCHLPNIPGVTSP GALIEDSK	154	S65	6.8

Table 6. Representative hits identified in the rapamycin and Ku-0063794 screens. Only protein targets with downregulated phosphorylation are shown. Median fold-changes of the

identified phosphopeptides are reported. For the rapamycin screen, hits from the second biological replicate are shown. The control group is DMSO vehicle treated sample whereas the experiment group is the one treated with rapamycin . For the Ku-0063794 screen, the control group was treated with rapamycin whereas the experiment group was treated with a combination of rapamycin and Ku-0063794. An asterisk indicates the site of phosphorylation. 5 Phosphorylation of Grb10 in MNILSS*QS*PLHPSTLNAVIHR (SEQ ID NO: 27) corresponds to S421/S423 in isoform 3 and S501/S503 in isoform 1, respectively. The site designation in the text corresponds to the sites in isoform 1 (mouse sequence).

Table 7:

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
Rapa replicate 1 (light cells were control and heavy cells were treated with rapamycin. L, light; H, heavy)					
IPI:IPI00136419.1	LDGNPINLS*R	155	Epyc	Epiphykan	-7.993
IPI:IPI00108454.2	LSS*LRAS*TSKSESSQK	156	rpS6	29 kDa protein	-7.693
IPI:IPI00108454.2	RLS*S*LRASTSK	157	rpS6	29 kDa protein	-6.817
IPI:IPI00225062.2	TPQAPTPANLVVGPR^S*A HGT*APVNIAGS*R^	158	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-6.606
IPI:IPI00111497.1	VTEGSYSCLAHS*PLGVVA SQVAVVK	159	Igdcc4	Isoform 2 of Immunoglobulin superfamily DCC subclass member 4	-6.062
IPI:IPI00874813.1	MPAT*DTANLTAPWHPR	160	Ldhd	22 kDa protein	-5.745
IPI:IPI00126317.1	NAS*TS*FQELEDKK	161	Dnajc2	DnaJ homolog subfamily C member 2	-5.522
IPI:IPI00187443.1	WLKEAEEEE*S*GGEEDE DENIEVVYSK	162	Eif5;LO C10004 7658	Eukaryotic translation initiation factor 5	-5.378
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFS*TTPGGTR	163	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-5.301
IPI:IPI00225062.2	S*AHGT*APVNIAGSRTPAG LAPTNLS*SSR	164	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-5.098
IPI:IPI00467423.3	GYS*YDDSMESR	165	Gm136 97	Novel protein containing MIF4G and MA3 domains	-5.093
IPI:IPI00467423.3	GYS*YDDSMESR	166	Gm136 97	Novel protein containing MIF4G and MA3 domains	-4.733
IPI:IPI00130920.1	SDISPLT*PR	167	Mtap1b	Microtubule-associated protein 1B	-4.668
IPI:IPI00133685.1	AATATRPPGPPAPQPPS* PAPS*PPRPALAR	168	Akt1s1	Proline-rich AKT1 substrate 1	-4.667
IPI:IPI00154084.2	GFGDS*FGR	169	Myef2	Isoform 2 of Myelin expression factor 2	-4.553
IPI:IPI00338745.4	QADVADQQTTELPAENGET ENQSPAS*EEEKEAKS*D	170	Hmgn1; LOC10 004439 1	Non-histone chromosomal protein HMG-14	-4.546
IPI:IPI00109318.1	RNS*PMAQT*PPCHLPNIPG VTSPGALIEDSK	171	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	-4.531
IPI:IPI00154084.2	GFGDS*FGR	172	Myef2	Isoform 2 of Myelin expression factor 2	-4.429
IPI:IPI00121519.1	SYSESGLMGEPQPQGPPS* WTDECLS*S*QDEEHEADK K	173	Neurod 1	Neurogenic differentiation factor 1	-4.393
IPI:IPI00317794.5	KEDS*DEDEDEDEDDSD*DEDEDEDEDEFEPPIVK	174	Ncl	Nucleolin	-4.345
IPI:IPI00399953.1	VFTSDISDPVVASTSQAPG M#NLSHSASSLS*LQQAFLS ELK	175	Wnk1	Serine/threonine-protein kinase WNK1	-4.306
IPI:IPI00263048.1	VS*SETHQGPPTPEK	176	Numa1	Nuclear mitotic apparatus protein 1	-4.079
IPI:IPI00225062.2	TPPSAPS*QSRM#T*SER	177	Srrm2	Isoform 3 of Serine/arginine repetitive	-4.002

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
				matrix protein 2	
IPI:IPI00263048.1	VSS*ETHQGPGTPESK	178	Numa1	Nuclear mitotic apparatus protein 1	-3.674
IPI:IPI00664808.2	SSSPT*NSLTQPIEMPTLSS S*PTEER*PTVGPGQQDNP LLK@	179	Kdm3b	Isoform 2 of Lysine-specific demethylase 3B	-3.64
IPI:IPI00225062.2	RKETPS*PR	180	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-3.569
IPI:IPI00453603.1	TPVS*PVKFS*PGDFWGR	181	Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1	-3.424
IPI:IPI00318938.6	R*VALGDGVQLPPGDY*ST TPGGTLFSTTPGGT*R^	182	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.386
IPI:IPI00330066.5	DSQDTSAEQS*DHDDEVAS LASASGGFGSK	183	Edc4	Isoform 1 of Enhancer of mRNA-decapping protein 4	-3.347
IPI:IPI00399953.1	DAMNLS*GR	184	Wnk1	Serine/threonine-protein kinase WNK1	-3.343
IPI:IPI00127707.1	LHQLAMQQSHFPMTHGNT GFSGIESSS*PEVK	185	Pcbp2	Isoform 1 of Poly(rC)-binding protein 2	-3.277
IPI:IPI00458068.6	SNS*LSEQLTVNSNPDTVK	186	Fkbp15	Isoform B of FK506-binding protein 15	-3.252
IPI:IPI00116442.1	S*EGLSLER	187	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-3.127
IPI:IPI00116442.1	S*EGLSLER^	188	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-3.127
IPI:IPI00112101.1	TTQSLQDFPVADS*EEEEAE EEFQKELSQWR	189	Tfip11	Tuftelin-interacting protein 11	-3.096
IPI:IPI00750472.3	TESASLSQS*QVNGFFASH LGDR	190	Ptpn13	Tyrosine-protein phosphatase non-receptor type 13	-3.058
IPI:IPI00318938.6	VALGDGVQLPPGDYS*TPP GGT*LFST*TPGGTR	191	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.042
IPI:IPI00317599.3	SQEDEEEISTS*PGVSEFVS DAFDTC*LNQEDLRK	192	Syap1	Synapse-associated protein 1	-3.022
IPI:IPI00116442.1	S*EGLSLER	193	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-3.012
IPI:IPI00553798.2	T*PEMIIQPKIS*M#QDVDL S*LGSK	194	Ahnak	AHNAK nucleoprotein isoform 1	-2.987
IPI:IPI00751009.1	TSEFPTPLFSGPLEPVACG SVISEGSPLTEQEESSPSH DR^S*R^	195	Srpk2	serine/arginine-rich protein-specific kinase 2	-2.951
IPI:IPI00127976.1	MNLSQS*PLHPSTLNAVI HR	196	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	-2.946
IPI:IPI00127976.1	M#NILSS*QSPLHPSTLNAVI HR	197	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	-2.944
IPI:IPI00656285.2	SSGLQTPECLS*REGS*PIP HDPDLGSK	198	Foxk1	Forkhead box protein K1	-2.896
IPI:IPI00830829.1	S*GEQITSS*PVS*PK	199	Hisppd1	140 kDa protein	-2.883
IPI:IPI00380722.1	LAWVGDVFTTT*PTDPRPL TS*PLR	200	Bat2	Large proline-rich protein BAT2	-2.824
IPI:IPI00153986.2	GTS*RPGTPSAEAASSTL R	201	Gtf2f1	General transcription factor IIF subunit 1	-2.802

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00129276.2	LES*LNQR ^A	202	Eif3a	Eukaryotic translation initiation factor 3 subunit A	-2.792
IPI:IPI00121277.1	SAS*ESYQSFQSR	203	Pi4k2a	Phosphatidylinositol 4-kinase type 2-alpha	-2.789
IPI:IPI00470003.3	S*PTPKS*PPSR	204	Parva	Alpha-parvin	-2.746
IPI:IPI00308971.1	AEALSSLHGDDQDS*EDEV LTVPEVK	205	Igf2r	Cation-independent mannose-6-phosphate receptor	-2.738
IPI:IPI00121277.1	SASESYT*QSFQSR	206	Pi4k2a	Phosphatidylinositol 4-kinase type 2-alpha	-2.723
IPI:IPI00130920.1	VLS*PLR ^A S*PPLLGSSEPYE DFLSADSK@	207	Mtap1b	Microtubule-associated protein 1B	-2.715
IPI:IPI00129276.2	LES*LNQR	208	Eif3a	Eukaryotic translation initiation factor 3 subunit A	-2.711
IPI:IPI00111169.1	CSV ^S *LSNVEAR	209	Pla2g4a	Cytosolic phospholipase A2	-2.664
IPI:IPI00458068.6	HS ^S *GNSM#LLPSMSVTM ETSM#IM#SNIQR	210	Fkbp15	Isoform B of FK506-binding protein 15	-2.641
IPI:IPI00751009.1	TVSASS ^T *GDLPK@	211	Srp2	serine/arginine-rich protein-specific kinase 2	-2.607
IPI:IPI00222828.2	S*SPNPFVGSPPK@	212	Dab2	Isoform p93 of Disabled homolog 2	-2.599
IPI:IPI00111169.1	CSV ^S *LSNVEAR	213	Pla2g4a	Cytosolic phospholipase A2	-2.579
IPI:IPI00120886.3	SVGDGET*VEFDVVEGEK	214	Ybx1	Nuclease-sensitive element-binding protein 1	-2.553
IPI:IPI00751009.1	TVS ^A SS ^T *TGDLPK@	215	Srp2	serine/arginine-rich protein-specific kinase 2	-2.534
IPI:IPI00133349.1	DR ^A S ^S *PS*PLR ^A GNVVPS*PL PTR ^A	216	Carhsp1	Calcium-regulated heat stable protein 1	-2.512
IPI:IPI00469392.2	GSGSVDET*LFALPAASEPV IPSSAEK	217	Rtn4	Isoform 1 of Reticulon-4	-2.475
IPI:IPI00127976.1	T*ASLPAIPNPFPELTGAAP GS*PPSVAPSS*LPPPPSQP PAK	218	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	-2.437
IPI:IPI00751009.1	TSEFPTPLFSGPLEPVACG SVISEGSPLTEQEESSPSH DRS ^R	219	Srp2	serine/arginine-rich protein-specific kinase 2	-2.408
IPI:IPI00761677.1	S ^R *RSPVDSPVPASMFAPPEP SS*PGAAR	220	Gtpbp1	GTP-binding protein 1	-2.406
IPI:IPI00468516.3	TRT*VLS*LFDEDEDKVEDE SSTCAPQDGR	221	D6Wsu116e	Isoform 1 of Protein FAM21	-2.398
IPI:IPI00396728.3	R ^V VSGS*ATPNSEAPR ^A	222	Ddx51	ATP-dependent RNA helicase DDX51	-2.351
IPI:IPI00660767.2	KRSDS ^S *GGYTLSDVIQS* PPSAGLLK	223	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	-2.347
IPI:IPI00226750.2	TSST ^C S ^S *NES*LNAGGTPV TPR	224	Tbc1d4	140 kDa protein	-2.275
IPI:IPI00113033.1	RSPASSGSAVPQPS*SPPS *PAQAEPEPR	225	Ighmbp2	DNA-binding protein SMUBP-2	-2.241
IPI:IPI00136107.1	THS ^T TSSS*IGSGESPF ^S R	226	Ndr3	Protein NDRG3	-2.202

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00751009.1	TSEFPTPLFSGPLEPVACG SVISEGSPLTEQEESSPSH DRS*R	227	Srpk2	serine/arginine-rich protein-specific kinase 2	-2.187
IPI:IPI00321647.2	QNPEQS*ADED AEKNEEDS *EGS*S*DEDEDEDGVGNTT FLKK	228	Eif3c	Eukaryotic translation initiation factor 3 subunit C	-2.165
IPI:IPI00453800.4	HSSFADTGAAPSALSPEP VLATS*PEPWGPS*LSASPE SR^	229	Zfp828	Zinc finger protein 828	-2.147
IPI:IPI00136107.1	THS*TSSS*IGSGESPFSR^	230	Ndr3	Protein NDRG3	-2.124
IPI:IPI00377615.2	RSS*RS*FSLDEPPLFIPDNI ATVK	231	Phf3	PHD finger protein 3	-2.124
IPI:IPI00377615.2	R^SSR^S*FS*LDEPPLFIPD NIATVK@	232	Phf3	PHD finger protein 3	-2.124
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVKLLGM#S GK	233	Npm1	Nucleophosmin	-2.101
IPI:IPI00331075.4	SLNFQEDDDT*S*RETFASD TNEALASLDEAQEGPGETK	234	Phax	Phosphorylated adapter RNA export protein	-2.101
IPI:IPI00136107.1	THSTSS*S*IGSGESPFSR^	235	Ndr3	Protein NDRG3	-2.098
IPI:IPI00136107.1	THST*SSS*IGSGESPFSR	236	Ndr3	Protein NDRG3	-2.098
IPI:IPI00669522.4	SRS*DIVNAAASAK	237	Clasp1	Isoform 2 of CLIP-associating protein 1	-2.073
IPI:IPI00117953.2	S*TDSPVAGS*EDDLVAAAP LLHSPEWSEER^	238	Bicc1;4 930533 K18Rik	Isoform 1 of Protein bicaudal C homolog 1	-2.07
IPI:IPI00137229.1	GFQFVSSS*LPDICYR	239	Cnbp	Isoform 2 of Cellular nucleic acid-binding protein	-2.061
IPI:IPI00380309.3	AMLDQLMGTS*R	240	Luc7l2	Isoform 1 of Putative RNA-binding protein Luc7-like 2	-2.046
IPI:IPI00153986.2	GTSRPGT*PSAEAASTSTL R	241	Gtf2f1	General transcription factor IIF subunit 1	-2.035
IPI:IPI00330262.5	S*QDDAMVDYFFQR	242	Pum1	Isoform 1 of Pumilio homolog 1	-2.02
IPI:IPI00312128.3	LDLDLTS*DSQPPVFK	243	Trim28	Isoform 1 of Transcription intermediary factor 1-beta	-2.01
IPI:IPI00667973.3	IRQPS*IDLT*DDDQTSSVPH SAISDIMSSDQETYSCK	244	Cep170	Isoform 1 of Centrosomal protein of 170 kDa	-1.979
IPI:IPI00468516.3	TRT*VLS*LFDEDEDKVEDE SSTCAPQDGR	245	D6Wsu 116e	Isoform 1 of Protein FAM21	-1.956
IPI:IPI00136207.6	YTPTSPSY*SPSSPEYTPAS PK@	246	Polr2a	DNA-directed RNA polymerase II subunit RPB1	-1.95
IPI:IPI00225062.2	SLLPNSSQDELM#EVEKSE QPLSQVLPSLS*PEHK	247	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.937
IPI:IPI00222828.2	S*SPNPFVGSPPK@	248	Dab2	Isoform p93 of Disabled homolog 2	-1.915
IPI:IPI00309059.7	RS*TS*PIIGS*PPVR	249	Pat1	Protein PAT1 homolog 1	-1.901
IPI:IPI00309059.7	RST*S*PIIGS*PPVR	250	Pat1	Protein PAT1 homolog 1	-1.896

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00338745.4	QADVADQQTTELPAENGET ENQSPASEEEKEAKS*D	251	Hmgn1; LOC10044391	Non-histone chromosomal protein HMG-14	-1.895
IPI:IPI00417158.1	SQTPQLHFLDT*DDEISPTS WGDSR^	252	Smg6	Telomerase-binding protein EST1A	-1.895
IPI:IPI00761759.1	SSS*GSEHSTEGSVSLGDG PLSR	253	Larp4	Putative uncharacterized protein	-1.89
IPI:IPI00314502.5	VHGLPT*TSPSGVNMAELA QQVVK	254	Tcfef	Transcription factor EB	-1.887
IPI:IPI00117689.1	ATEEPSGTGS*DELIK@SD QVNGVLVLSLLDK@	255	Ptfr	Polymerase I and transcript release factor	-1.875
IPI:IPI00462949.4	AENIMAS*LER	256	Dock11	Dedicator of cytokinesis protein 11	-1.851
IPI:IPI00471475.1	FDQLFDDDES*DPFEVLK@	257	Serbp1	Isoform 1 of Plasminogen activator inhibitor 1 RNA-binding protein	-1.845
IPI:IPI00471475.1	FDQLFDDDES*DPFEVLK	258	Serbp1	Isoform 1 of Plasminogen activator inhibitor 1 RNA-binding protein	-1.845
IPI:IPI00309059.7	RS*TS*PIIGS*PPVR	259	Pat11	Protein PAT1 homolog 1	-1.837
IPI:IPI00331612.3	K@PAQETEETSS*QES*AE ED	260	Hmga2	High mobility group protein HMGI-C	-1.834
IPI:IPI00929786.1	SLPT*TVPES*PNYR^	261	Larp1	Isoform 1 of La-related protein 1	-1.823
IPI:IPI00112101.1	TTQSLQDFPVADS*EEEEAE EEFQKELSQWR	262	Tfip11	Tuftelin-interacting protein 11	-1.813
IPI:IPI00133685.1	SSDEENGPPSS*PDLDR	263	Akt1s1	Proline-rich AKT1 substrate 1	-1.779
IPI:IPI00761443.2	SLS*ESYELSSDLQDK	264	lqsec1	IQ motif and Sec7 domain 1 isoform b	-1.779
IPI:IPI00318938.6	NS*PVAKTTPPKDLPAIPGVT *SPTSDEPPMQASQSQLPS SPEDK	265	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.776
IPI:IPI00318938.6	NSPVAKT*PPKDLPAIPGVT SPT*SDEPPMQASQSQLPS SPEDK	266	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.776
IPI:IPI00421179.1	SFS*KEVEER	267	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	-1.77
IPI:IPI00379844.4	TYS*LTPPAR	268	Irs2	Insulin receptor substrate 2	-1.769
IPI:IPI00379844.4	TYS*LTPPAR	269	Irs2	Insulin receptor substrate 2	-1.769
IPI:IPI00127989.1	FSEM#M#DHMGGDEDVDL PEVDGADDDDS*QDS*DDEK MPDLE	270	Ptges3; Gm9769;LOC100048119	Prostaglandin E synthase 3	-1.762
IPI:IPI00127989.1	FSEM#M#DHMGGDEDVDL PEVDGADDDDS*QDS*DDEK @MPDLE	271	Ptges3; Gm9769;LOC100048119	Prostaglandin E synthase 3	-1.762

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00320208.3	YGPSSVEDTTGSGAADAK @DDDDIDLFGS*DDEESEE EAK@	272	Eef1b2	Elongation factor 1-beta	-1.754
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAI PGVTSPTSDEPPMQASQS QLPSSPEDK@	273	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.752
IPI:IPI00317794.5	KEDS*DEDEDEDEDDSD*D EDEDEDEDEFEPPIVK	274	Ncl	Nucleolin	-1.75
IPI:IPI00116331.1	S*RTPSAS*HEEQQE	275	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.747
IPI:IPI00116331.1	S*R^TPS*ASHEEQQE	276	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.747
IPI:IPI00553798.2	FGT*FGGLGS*K	277	Ahnak	AHNAK nucleoprotein isoform 1	-1.745
IPI:IPI00130510.1	LQDISSELLAT*GVGLS*DSEV EPDGEHNTTELPQAVAGR^	278	Ppan	Suppressor of SWI4 1 homolog	-1.743
IPI:IPI00330262.5	S*QDDAMVDYFFQR	279	Pum1	Isoform 1 of Pumilio homolog 1	-1.734
IPI:IPI00459468.2	LSESSALKQPAT*PTAAES* S*EGEGEEGDDGGETESR	280	Wmip1	Isoform 1 of ATPase WRNIP1	-1.728
IPI:IPI00130573.1	SLLSHEFQDET*DT*EEETL YSSK	281	Cpd	Carboxypeptidase D	-1.723
IPI:IPI00468516.3	TSALLFSS*DEEDQWNIADS HTK	282	D6Wsu 116e	Isoform 1 of Protein FAM21	-1.718
IPI:IPI00468516.3	TSALLFSS*DEEDQWNIADS HTK	283	D6Wsu 116e	Isoform 1 of Protein FAM21	-1.718
IPI:IPI00109676.6	SSGSSSSGLGTVSS*SPAS QR	284	Phf8	Isoform 1 of PHD finger protein 8	-1.715
IPI:IPI00399953.1	VFTSDISDPVFAST*SQAPG MNLSSHASSLSLQQAFSEL K	285	Wnk1	Serine/threonine-protein kinase WNK1	-1.704
IPI:IPI00399953.1	VFTSDISDPVFASTSQAPG MNLSSHASS*LSLQQAFSE LK@	286	Wnk1	Serine/threonine-protein kinase WNK1	-1.704
IPI:IPI00225062.2	RSSS*ELS*PEVVEK	287	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.702
IPI:IPI00116331.1	S*RTPS*ASHEEQQE	288	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.694
IPI:IPI00116331.1	SRT*PS*ASHEEQQE	289	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.69
IPI:IPI00116331.1	S*R^TPS*ASHEEQQE	290	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.69

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00405752.3	VLQESDVS*PSSSTTSLPIS* PLTEELPFKDITR	291	C13009 2011Rik	Isoform 1 of Uncharacterized protein KIAA1680	-1.689
IPI:IPI00380415.2	ALS*LS*SADS*TDAKR	292	Bat2l	Isoform 1 of Protein BAT2-like	-1.687
IPI:IPI00130510.1	LQDISELLATGVGLS*DS*EV EPDGEHNTTELPQAVAGR	293	Ppan	Suppressor of SWI4 1 homolog	-1.68
IPI:IPI00229859.1	AKPAAQS*EEETATS*PAAS *PTPQSAERS*PSQEPSAP GK	294	Eif3b	Eif3b protein	-1.677
IPI:IPI00224200.1	RLS*S*TGGQTPR	295	Iws1	Isoform 1 of Protein IWS1 homolog	-1.663
IPI:IPI00225062.2	R^SSS*ELS*PEVVEK@	296	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.663
IPI:IPI00331612.3	K@PAQETEETS*SQES*AE ED	297	Hmga2	High mobility group protein HMGI-C	-1.658
IPI:IPI00229645.2	K@GSS*GNAS*EVSVAULT ER^	298	Cytsa	Cytospin-A	-1.657
IPI:IPI00317794.5	KEDS*DEDEDEDEDDSD* EDEDEDEDEFEPPIVK	299	Ncl	Nucleolin	-1.637
IPI:IPI00663627.1	GFLDGVYSFEYYPST*TPGK	300	Flnb	Filamin-B	-1.621
IPI:IPI00312128.3	LDLDTSDS*QPPVFK	301	Trim28	Isoform 1 of Transcription intermediary factor 1-beta	-1.616
IPI:IPI00225062.2	HSGS*TSFY*PK@	302	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.603
IPI:IPI00312414.4	TSTFCGT*PEFLAPEVLTET SYTR^	303	Pkn2	Isoform 1 of Serine/threonine-protein kinase N2	-1.603
IPI:IPI00553798.2	S*NS*FSDER^EFSAPST*PT GT*LEFAGGDAK@	304	Ahnak	AHNAK nucleoprotein isoform 1	-1.602
IPI:IPI00126176.3	VSLGVPVT*T*PEFQLVKTP LSSLSQR	305	Racgap 1	Rac GTPase-activating protein 1	-1.597
IPI:IPI00225062.2	GSLSRSS*S*PVTELTAR	306	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.593
IPI:IPI00399953.1	VFTSDISDPVVASTSQAPG MNLSSH*ASSLSLQAFSE LK	307	Wnk1	Serine/threonine-protein kinase WNK1	-1.588
IPI:IPI00226155.3	VSALEEDMDDVES*S*EEEE EEDEKLER	308	Prpf38a	Isoform 1 of Pre-mRNA-splicing factor 38A	-1.585
IPI:IPI00226155.3	VSALEEDMDDVES*S*EEEE EEDEK@LER^	309	Prpf38a	Isoform 1 of Pre-mRNA-splicing factor 38A	-1.585
IPI:IPI00116331.1	S*RTPS*ASHEEQQE	310	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.58
IPI:IPI00116331.1	S*R^TPS*ASHEEQQE	311	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.58
IPI:IPI00135660.5	SLEETLHNVDLS*S*DDELP R^DEEALEDSAEK@	312	Sdpr	Serum deprivation-response protein	-1.577

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00323349.2	HSSHDMLSHS*WEGNR	313	Tjp2	Tight junction protein ZO-2	-1.566
IPI:IPI00169500.3	TESILDKEDKVPMAVG EGPEQLPAPCPSQTGS*PP VGLIK	314	Atxn2l	Isoform 1 of Ataxin-2-like protein	-1.564
IPI:IPI00118143.1	K@QTPPASPS*QPIEDR^ PPS*SPIYEDAAPFK@	315	Cttn	Src substrate cortactin	-1.556
IPI:IPI00127415.1	TVSLGAGAK@DELHIVEAE AM#NYEGS*PIK@VTLATLK @	316	Npm1	Nucleophosmin	-1.555
IPI:IPI00225062.2	SLLPNSSQDELMEVEK@S EQPLSQVLP SLS*PEHK@	317	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.55
IPI:IPI00225062.2	SLLPNSSQDELMEVEKSEQ PLSQVLP SLS*PEHK	318	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.55
IPI:IPI00320267.1	GDQVLNFS*DAEDLIDDSK @LK@	319	Mcrs1	Microspherule protein 1	-1.55
IPI:IPI00320267.1	GDQVLNFS*DAEDLIDDSKL K	320	Mcrs1	Microspherule protein 1	-1.55
IPI:IPI00553798.2	SNS*FSDER^EFS*APS*TPT *GTLEFAGGDAK@	321	Ahnak	AHNAK nucleoprotein isoform 1	-1.548
IPI:IPI00116331.1	S*RTPS*ASHEEQQE	322	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.543
IPI:IPI00222828.2	SSPNPFVGS*PPK	323	Dab2	Isoform p93 of Disabled homolog 2	-1.531
IPI:IPI00317794.5	KEDS*DEDEDEEDEDSD EDEDDEEDEFEPPIVK	324	Ncl	Nucleolin	-1.531
IPI:IPI00225062.2	RSS*SELS*PEVVEK	325	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.524
IPI:IPI00225062.2	R^SS*S*ELSPEVVEK@	326	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.524
IPI:IPI00116331.1	S*RTPS*ASHEEQQE	327	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.52
IPI:IPI00380415.2	ALS*LS*S*ADSTDAKR	328	Bat2l	Isoform 1 of Protein BAT2-like	-1.519
IPI:IPI00225062.2	RSSS*ELS*PEVVEK	329	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.518
IPI:IPI00225062.2	R^SSS*ELS*PEVVEK@	330	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.518
IPI:IPI00399469.2	VS*PPAS*PTLDVELGAGEA PLQGAVGPELPLGGSHGR	331	Sh3rf1	Isoform 2 of Putative E3 ubiquitin-protein ligase SH3RF1	-1.504
IPI:IPI00225062.2	R^SS*SELS*PEVVEK@	332	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.501
IPI:IPI00137501.1	TEMDS*PFNS*PSPQDS*P R	333	Nfic	Isoform 1 of Nuclear factor 1 C-type	-1.498
IPI:IPI00309059.7	RSTS*PIIGS*PPVR	334	Pat1l	Protein PAT1 homolog 1	-1.498
IPI:IPI00225062.2	RSS*SELS*PEVVEK	335	Srm2	Isoform 3 of Serine/arginine repetitive	-1.497

Reference	Ascore Seq	SEQ ID NO.	Gene Name	Annotation	Log2 Area (H/L) Ratio
				matrix protein 2	
IPI:IPI00116331.1	S*R^TPS*ASHEEQQE	336	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha	-1.493
IPI:IPI00470095.1	HGS*GADS*DYENTQSGDP LLGLEK@	337	Git1	ARF GTPase-activating protein GIT1	-1.488
IPI:IPI00470095.1	HGS*GADS*DYENTQSGDP LLGLEK	338	Git1	ARF GTPase-activating protein GIT1	-1.488
IPI:IPI00225062.2	IHTTALTGQS*PPLASGHQG EGDAPSVPGATNIQQPSS *PAPS*TK	339	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.479
IPI:IPI00116442.1	TRLAS*ESANDDNEDS	340	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-1.456
IPI:IPI00225062.2	GSLSRSS*S*PVTELTAR	341	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.454
IPI:IPI00320267.1	GDQVLNFS*DAEDLIDDSK	342	Mcrs1	Microspherule protein 1	-1.454
IPI:IPI00225062.2	RSSS*ELS*PEVVEK	343	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.445
IPI:IPI00661508.3	S*IDPDSIQSALLASGLGSK @	344	Sbno1	Isoform 2 of Protein strawberry notch homolog 1	-1.442
IPI:IPI00661508.3	S*IDPDSIQSALLASGLGSK	345	Sbno1	Isoform 2 of Protein strawberry notch homolog 1	-1.442
IPI:IPI00317794.5	K@EDS*DEDEDEEDEDSDS* DEDEDEEDEFEPPIVK@	346	Ncl	Nucleolin	-1.441
IPI:IPI00225267.6	ATPTESPEKPPPPAVQRDE DDDALFS*EPALAQISSNV LLK	347	231002 2B05Ri k	Uncharacterized protein C1orf198 homolog	-1.438
IPI:IPI00122594.4	EVS*VSS*VTEEPKLDSSQL PLQTGLDVPATPR	348	Ahctf1	AT-hook-containing transcription factor 1	-1.437
IPI:IPI00129356.1	SAFTPATATGS*S*PSPVLG QGEK@VEGLQAQALYPWR ^	349	Itsn1	Isoform 1 of Intersectin-1	-1.43
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGV TSPTSDEPPMQASQSQLPS S*PEDK	350	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.412
IPI:IPI00224200.1	VVCDADDS*DSDVSDK@	351	Iws1	Isoform 1 of Protein IWS1 homolog	-1.403
IPI:IPI00321647.2	QNPEQSADEDAEK@NEED S*EGS*S*DEDEDEDGVGN TTFLK@	352	Eif3c	Eukaryotic translation initiation factor 3 subunit C	-1.399
IPI:IPI00664808.2	VSESVADDS*SS*RDSFTQS LESLSGLCK	353	Kdm3b	Isoform 2 of Lysine-specific demethylase 3B	-1.393
IPI:IPI00122863.2	RGQS*PQPDQGP	354	Rarg	Isoform 2 of Retinoic acid receptor gamma	-1.387
IPI:IPI00453853.2	TPVASECTQTDGAEVAGS CPQTTTHS*PPSK@	355	Bap1	Ubiquitin carboxyl-terminal hydrolase BAP1	-1.38
IPI:IPI00132028.1	K@GS*DDGGDS*PVQDID TPEVDLYQLQVNTLR^	356	Sap30	Histone deacetylase complex subunit SAP30	-1.376

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00132028.1	KGS*DDGGDS*PVQDIDT PEVDLYQLQVNTLR	357	Sap30	Histone deacetylase complex subunit SAP30	-1.376
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGV TSPTSDEPPMQASQSQLPS S*PEDK	358	Elf4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.374
IPI:IPI00116442.1	TRLAS*ESANDDNEDS	359	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-1.358
IPI:IPI00153986.2	GTS*RPGT*PSAEAASTSS LR	360	Gtf2f1	General transcription factor IIF subunit 1	-1.348
IPI:IPI00226149.6	GSASES*PSASVAEATTTD VQVTP TALLQLDR^	361	Rsl1d1	Putative uncharacterized protein	-1.342
IPI:IPI00226149.6	GS*ASESPSASVAEATTTD VQVTP TALLQLDR^	362	Rsl1d1	Putative uncharacterized protein	-1.342
IPI:IPI00313307.3	SYQNSPS*S*EDGIRPLPEY STEK	363	Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1	-1.337
IPI:IPI00656285.2	S*LVS*PIPSPTGTISVPNSC PAS*PR	364	Foxk1	Forkhead box protein K1	-1.327
IPI:IPI00320208.3	YGPSSVEDTTGSGAADAK @DDDDIDLFGSDDEEES*E EAK@	365	Eef1b2	Elongation factor 1-beta	-1.324
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGV TSPTSDEPPMQASQSQLPS S*PEDK	366	Elf4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.322
IPI:IPI00136572.4	SSTHASVS*PASEPSR	367	Zc3hav 1	Isoform 1 of Zinc finger CCCH-type antiviral protein 1	-1.318
IPI:IPI00116442.1	TRLAS*ES*ANDDNEDS	368	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-1.315
IPI:IPI00116442.1	TR^LAS*ES*ANDDNEDS	369	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-1.315
IPI:IPI00226149.6	GS*ASESPSASVAEATTTD VQVTP TALLQLDR^	370	Rsl1d1	Putative uncharacterized protein	-1.314
IPI:IPI00169500.3	R^SPGGT*SPPNGGLPGPL TAT^AAPPGPAAVSPCLG PAAAAGSGLR^	371	Atxn2l	Isoform 1 of Ataxin-2-like protein	-1.308
IPI:IPI00467362.6	S*ESLIDASEDS*QLEAAIR	372	Ubxn7	UBX domain-containing protein 7	-1.307
IPI:IPI00124753.3	RNTFIGTPY*WMAPEVIACD ENPDATYDYR	373	Mink1	misshapen-like kinase 1 isoform 2	-1.302
IPI:IPI00110247.7	SLSQS*FENLLDEPAYGLIQ K@	374	Tbc1d1 5	TBC1 domain family member 15	-1.301
IPI:IPI00276222.1	KLDDQS*EDEALELEGPLIM PGSGSIYSS*PGLYSK	375	Fermt2	Fermitin family homolog 2	-1.293
IPI:IPI00460668.2	EVDYSDS*LTEK@	376	Smarca 4	Putative uncharacterized protein	-1.293
IPI:IPI00380736.1	STTPT*PSVITR	377	Zfp516	Zinc finger protein 516	-1.259
IPI:IPI00153986.2	GTS*R^PGT*PSAEAASTSS TLR^	378	Gtf2f1	General transcription factor IIF subunit 1	-1.251
IPI:IPI00230486.3	LSSKLS*AVS*LR	379	Snx17	Sorting nexin-17	-1.24
IPI:IPI00116331.1	SR^T*PSAS*HEEQQE	380	Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing	-1.239

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
				protein alpha	
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGV TSPTSDEPPMQASQSQLPS SPEDK	381	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.238
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGV TSPTSDEPPMQASQSQLPS SPEDK	382	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.238
IPI:IPI00749954.8	LR^TDNAS*DAS*ESS*DAE SSSK@	383	Jmjd1c	jumonji domain containing 1C	-1.235
IPI:IPI00225062.2	SVSSPR^T*K@	384	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.234
IPI:IPI00136107.1	THS*TSSSIGSGESPF ^{SR}	385	Ndr3	Protein NDRG3	-1.23
IPI:IPI00136107.1	THST*SSSIGSGESPF ^{SR}	386	Ndr3	Protein NDRG3	-1.23
IPI:IPI00113377.1	K@EESEES*EDDMGFLF D	387	Rplp1	60S acidic ribosomal protein P1	-1.229
IPI:IPI00553798.2	GGVT*GSPEAS*IS*GSK@G DLK@	388	Ahnak	AHNAK nucleoprotein isoform 1	-1.228
IPI:IPI00330240.7	S*QDAESYQNVVELK@	389	Peg3	Isoform 1 of Paternally-expressed gene 3 protein	-1.221
IPI:IPI00122845.1	LGS*QEPER^	390			-1.219
IPI:IPI00224200.1	VVCDADDS*DSDVSDK@	391	Iws1	Isoform 1 of Protein IWS1 homolog	-1.219
IPI:IPI00465879.2	LCS*SSSDTSPR^	392	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.207
IPI:IPI00116442.1	TR^LAS*ES*ANDDNEDS	393	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-1.206
IPI:IPI00116442.1	TRLAS*ES*ANDDNEDS	394	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	-1.206
IPI:IPI00322095.4	IDEPNT*PYHNMIGDDEDAY S*DSEGNEVMTPDILAK	395	Ppp1r2	Putative uncharacterized protein	-1.204
IPI:IPI00322095.4	IDEPNTPY*HNMIGDDEDAY S*DSEGNEVMTPDILAK	396	Ppp1r2	Putative uncharacterized protein	-1.204
IPI:IPI00387384.3	LLCQEETPEAT*EDERDEE R	397	Mett10d	Isoform 1 of Putative methyltransferase METT10D	-1.202
IPI:IPI00330246.2	WAAHGTS*PEDFSLTLGAR ^	398	Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1	-1.202
IPI:IPI00330246.2	WAAHGTS*PEDFSLTLGAR	399	Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1	-1.202
IPI:IPI00678133.3	SSHQDATDPEALWGVHQT EADS*T*S*EGPEDEAQR^	400	Inf2	Isoform 1 of Inverted formin-2	-1.199
IPI:IPI00465879.2	LCS*SSSDTSPR^	401	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.189
IPI:IPI00313513.6	S*VDIFGSTPFQPFVSASK	402	Bmp2k	Isoform 1 of BMP-2-inducible protein kinase	-1.18
IPI:IPI00465879.2	LCS*SSSDTSPR	403	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.172
IPI:IPI00465879.2	LCS*SSSDTSPR	404	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.171

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00553798.2	EFSAPST*PT*GTLEFAGGD AK@	405	Ahnak	AHNAK nucleoprotein isoform 1	-1.169
IPI:IPI00317794.5	K@EDS*DEDEDEDEDDSD* DEDEDEDEDEFEPPIVK@	406	Ncl	Nucleolin	-1.167
IPI:IPI00465879.2	LCS*SSSDTSPR^	407	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.163
IPI:IPI00465879.2	LCS*SSSDTSPR	408	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.163
IPI:IPI00229739.4	LVVSS*PT*SPKGK	409	Plekhm 1	Pleckstrin homology domain-containing family M member 1	-1.159
IPI:IPI00465879.2	LCS*SSSDTSPR	410	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.156
IPI:IPI00465879.2	LCS*SSSDTSPR^	411	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.155
IPI:IPI00225616.3	DGAGS*PLR^T*SPPSTPSS PDDTFFNLGDLQNGR^	412	Dennd2 a	DENN domain-containing protein 2A	-1.15
IPI:IPI00720110.2	VLANSNPSS*PSAAK	413	160002 7N09Rik	RIKEN cDNA 1600027N09 gene	-1.148
IPI:IPI00465879.2	LCS*SSSDTSPR	414	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	-1.143
IPI:IPI00461396.6	STRHS*PSALQDVFVELLS* PHSK	415	Baz1a	bromodomain adjacent to zinc finger domain 1A	-1.134
IPI:IPI00222828.2	SSPNPFVGS*PPK@	416	Dab2	Isoform p93 of Disabled homolog 2	-1.134
IPI:IPI00222828.2	SSPNPFVGS*PPK	417	Dab2	Isoform p93 of Disabled homolog 2	-1.134
IPI:IPI00222828.2	SSPNPFVGS*PPK	418	Dab2	Isoform p93 of Disabled homolog 2	-1.134
IPI:IPI00225062.2	GCS*PPKS*PEKPPQSTSS* ESCPPSPQPTK	419	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.133
IPI:IPI00553798.2	GGVTGS*PEAS*IS*GSK@G DLK@	420	Ahnak	AHNAK nucleoprotein isoform 1	-1.132
IPI:IPI00318671.2	DK@PVYDELFTLS*PINGK @	421	Ehd4	EH-domain containing 4-KJR (Fragment)	-1.131
IPI:IPI00129388.1	HDHAVSLTAAST*ISLLLE R	422	Scrib	Isoform 3 of Protein LAP4	-1.13
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA SKPSS*PR	423	Ccnl1	Isoform 1 of Cyclin-L1	-1.124
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA SK@PSS*PR^	424	Ccnl1	Isoform 1 of Cyclin-L1	-1.124
IPI:IPI00317401.6	METVSNASSSSNPSS*PGR ^	425	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	-1.12
IPI:IPI00317401.6	METVSNASSSSNPSS*PGR	426	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	-1.12
IPI:IPI00471475.1	HSGSDR^S*SFSHYGLK@	427	Serbp1	Isoform 1 of Plasminogen activator inhibitor 1 RNA-binding protein	-1.119
IPI:IPI00330240.7	S*QDAESYQNVVELK@	428	Peg3	Isoform 1 of Paternally-expressed gene 3 protein	-1.108
IPI:IPI00153986.2	GTS*RPGTSAEAASTSSL R	429	Gtf2f1	General transcription factor IIF subunit 1	-1.102

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00453656.2	KVAPLS*SSLDTSLDFSK	430	Uvrug	UV radiation resistance associated	-1.098
IPI:IPI00127976.1	SVS*ENS*LVAMDFSGQIGR	431	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	-1.097
IPI:IPI00135443.2	KTS*FDQDS*DVDIFPSDFT SEPPALPR	432	Top2b	DNA topoisomerase 2-beta	-1.092
IPI:IPI00331612.3	KPAQETEETSS*QES*AEED	433	Hmga2	High mobility group protein HMGI-C	-1.078
IPI:IPI00331612.3	K@PAQETEETSS*QES*AE ED	434	Hmga2	High mobility group protein HMGI-C	-1.078
IPI:IPI00320208.3	YGPSSVEDTTGSGAADAK @DDDDIDLFGS*DDEESEE EAK@	435	Eef1b2	Elongation factor 1-beta	-1.075
IPI:IPI00321884.1	ESLPLDLS*DDQNSNK	436	Nvl	Nuclear valosin-containing protein-like	-1.071
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK@LLGMS GK@	437	Npm1	Nucleophosmin	-1.071
IPI:IPI00553798.2	GGVTGS*PEAS*ISGS*K@G DLK@	438	Ahnak	AHNAK nucleoprotein isoform 1	-1.067
IPI:IPI00136107.1	THST*SS*SIGSGESPF SR	439	Ndr3	Protein NDRG3	-1.054
IPI:IPI00130920.1	VLS*PLR*SPPLLGSES*PYE DFLSADSK@	440	Mtap1b	Microtubule-associated protein 1B	-1.054
IPI:IPI00349069.4	GPQQDS*DS*DDGEALGGN PMVAGFQDDVDIEDQTHG K	441	B23020 8H17Rik	Putative GTP-binding protein Parf	-1.048
IPI:IPI00349069.4	GPQQDS*DS*DDGEALGGN PMVAGFQDDVDIEDQTHG K@	442	B23020 8H17Rik	Putative GTP-binding protein Parf	-1.048
IPI:IPI00408803.6	GR^ES*DEDT*EDAS*ETDL AK@	443	Suds3	Sin3 histone deacetylase corepressor complex component SDS3	-1.047
IPI:IPI00109311.3	SASS*DTS^EELNS*QDSPK @R^	444	Slc9a3r1	Isoform 1 of Na(+)/H(+) exchange regulatory cofactor NHE-RF1	-1.047
IPI:IPI00136107.1	THSTSS*SIGSGESPF SR^	445	Ndr3	Protein NDRG3	-1.042
IPI:IPI00114560.5	FRT*ITSSYYR	446	Rab1	Ras-related protein Rab-1A	-1.042
IPI:IPI00123410.5	TIS*AQDTLAYATALLNEK	447	Usp24	Isoform 1 of Ubiquitin carboxyl-terminal hydrolase 24	-1.04
IPI:IPI00169477.1	NT*PSQHSQHS*PER^	448	Bclaf1	Isoform 2 of Bcl-2-associated transcription factor 1	-1.036
IPI:IPI00317401.6	AES*PESAVESTQST*PQK	449	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	-1.036
IPI:IPI00317401.6	METVSNASSSSNPSS*PGR ^	450	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	-1.035
IPI:IPI00317401.6	METVSNASSSSNPSS*PGR	451	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	-1.035
IPI:IPI00229702.1	KDS*PPLVT*PPQS*PPSSQ PPAMTQAPR	452	Smtnl2	Smoothelin-like protein 2	-1.03
IPI:IPI00107999.1	SSPS*ILAVQR	453	Chd1	Chromodomain-helicase-DNA-binding protein 1	-1.019

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00107999.1	SS*PSILAVQR^	454	Chd1	Chromodomain-helicase-DNA-binding protein 1	-1.019
IPI:IPI00118120.1	TSS*IADEGTYTLDSILR	455	Myo5a	Myosin-Va	-1.018
IPI:IPI00453848.5	SAFK@LDS*DS*DEEDAQF FSMASGVPTPAPEPSR^R ^	456	Atg2a	Protein	-1.014
IPI:IPI00330773.3	AS*YSGTSPSHSFISGEPDR ^	457	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	-1.013
IPI:IPI00225062.2	GCS*PPKS*PEKPPQSTSS* ESCPPSPQPTK	458	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.003
IPI:IPI00229613.3	SSS*SASQSNHSCSTMPSS PATPASGTK	459	Macf1	Isoform 3 of Microtubule-actin cross-linking factor 1	-1.003
IPI:IPI00136107.1	THS*TSSS*IGSGESPFSR^	460	Ndr3	Protein NDRG3	-1.002
IPI:IPI00121135.5	R.S*Ks*PPKS*PEEEGAVS* S.	461	Sfrs2	Splicing factor	-1
IPI:IPI00126338.5	R.SST*PLPTVS*SS*AENTR ^Q	462	Tmpo	Isoform Alpha of Lamina-associated polypeptide 2	-1
IPI:IPI00623249.4	R.T*DSVIIADQT*PT*PTR^F	463	Atf7	Activating transcription factor 7	-1
Rapa replicate 2 (Note: heavy cells were control and light cells were treated with rapamycin. L, light; H, heavy.)					
IPI:IPI00330112.1	VAPAGSAIS*NASGER^	464	Mib1	E3 ubiquitin-protein ligase MIB1	9.6909
IPI:IPI00108454.2	R^LS*S*LR^AS*TSK@	465	rpS6	29 kDa protein	9.6182
IPI:IPI00108454.2	R^LS*S*LR^AS*TSK@	466	rpS6	29 kDa protein	9.6182
IPI:IPI00225062.2	ELS*HSPPRENSFESSLEFK	467	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	9.4619
IPI:IPI00108454.2	R^LS*S*LR^AS*TSK@	468	rpS6	29 kDa protein	9.4253
IPI:IPI00346155.4	NFLS*MDS*LK@	469	Gm130 99	Novel protein similar to preferentially expressed antigen in melanoma-like family	9.2638
IPI:IPI00649156.4	NLAITGGVTLs*VIASPVIAAV SVGIGVPIMLAY*VY*GVVPI SLCR^	470	Rnf19b	IBR domain containing 3	9.1171
IPI:IPI00108454.2	R^LS*S*LR^AS*TSK@	471	rpS6	29 kDa protein	9.0561
IPI:IPI00133349.1	TR^TFS*ATVR^	472	Carhsp 1	Calcium-regulated heat stable protein 1	8.7001
IPI:IPI00133349.1	TR^TFS*ATVR^	473	Carhsp 1	Calcium-regulated heat stable protein 1	8.6779
IPI:IPI00133349.1	TR^TFS*ATVR^	474	Carhsp 1	Calcium-regulated heat stable protein 1	8.6519
IPI:IPI00108454.2	R^LS*S*LR^AS*TSK@	475	rpS6	29 kDa protein	8.6271
IPI:IPI00351206.5	GLCSGPGAGEESPAAT*LP R^M#K@	476	Pgrmc2	Membrane-associated progesterone receptor component 2	8.5943
IPI:IPI00108454.2	LS*SLR^AS*TSK@	477	rpS6	29 kDa protein	7.5465
IPI:IPI00108454.2	LSS*LR^AS*TSK@	478	rpS6	29 kDa protein	7.5465

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00131138.1	AHVAPCFDAS*K@	479			7.3937
IPI:IPI00125530.1	WTNDYSMVLTGAAIY*HK@	480	Ext1	Exostosin-1	7.3545
IPI:IPI00108454.2	LSS*LR^AS*TSK@	481	rpS6	29 kDa protein	7.1711
IPI:IPI00108454.2	LSS*LR^AS*TSK@	482	rpS6	29 kDa protein	7.1711
IPI:IPI00108454.2	R^LSS*LR^AS*TSK@	483	rpS6	29 kDa protein	7.0714
IPI:IPI00131138.1	AHVAPCFDAS*K@	484			7.0413
IPI:IPI00378564.4	LVY*PEVK@ES*K@FK@	485	Gm14085	Novel protein similar to solute carrier family 28 (Sodium-coupled nucleoside transporter) member 2	6.9768
IPI:IPI00108454.2	R^LSS*LR^AS*TSK@	486	rpS6	29 kDa protein	6.9459
IPI:IPI00133685.1	AATATRPPGPPAPQPPS*PAPS*PPRPALAR	487	Akt1s1	Proline-rich AKT1 substrate 1	6.9065
IPI:IPI00316922.1	R^LGAAM#T^FPR^PPSR^	488	Gm9757	Putative uncharacterized protein	6.6604
IPI:IPI00118875.4	ATAPQTQHVS*PMR^	489	Eef1d	eukaryotic translation elongation factor 1 delta isoform a	6.5442
IPI:IPI00109318.1	R^NS*PMAQT*PPCHLPNIPGVTSPGALIEDSK@	490	Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2	6.5094
IPI:IPI00109318.1	R^NS*PMAQT*PPCHLPNIPGVTSPGALIEDSK@	491	Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2	6.4811
IPI:IPI00131138.1	AHVAPCFDAS*K@	492			6.4769
IPI:IPI00757687.1	LK@PDS*K@PFSR^	493	Gon4l	RIKEN cDNA 5830417110 gene	6.4593
IPI:IPI00121027.4	ES^LS*HVLSK@	494	Mogat1	2-acylglycerol O-acyltransferase 1	6.0819
IPI:IPI00115681.1	TECGS*TGS*PASSFHFK@	495	Eef2k	Elongation factor 2 kinase	5.912
IPI:IPI00115681.1	TECGS*T^GSPASSFHFK@	496	Eef2k	Elongation factor 2 kinase	5.912
IPI:IPI00128818.2	LYTEK@AY*K@	497	Dhx15	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	5.9047
IPI:IPI00118438.4	SR^VS*VS*PGR^	498	Srrm1	Isoform 2 of Serine/arginine repetitive matrix protein 1	5.834
IPI:IPI00323238.5	R^K@T^VSFS^AAEEAPVPEPSTAAPLQAK@	499	Setd1a	SET domain containing 1A	5.7891
IPI:IPI00323238.5	R^K@T^VSFS^AAEEAPVPEPSTAAPLQAK@	500	Setd1a	SET domain containing 1A	5.6797
IPI:IPI00323238.5	R^K@T^VSFS^AAEEAPVPEPSTAAPLQAK@	501	Setd1a	SET domain containing 1A	5.6797
IPI:IPI00405470.1	SGHSLT*WDSAMSALSSAS*SSSCCTLR^	502	D830015G02Rik	Putative uncharacterized protein	5.6705
IPI:IPI00137148.2	R^K@Y^GMLHTQESSSVFYPSQDEGLSPGSGNCAK@	503	Vwa5b1	von Willebrand factor A domain-containing protein 5B1	5.6371
IPI:IPI00660767.2	SDSS*GGYTLSDVIQS*PPSAGLLK@	504	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	5.5816
IPI:IPI00660767.2	SDSS*GGYTLSDVIQS*PPSAGLLK@	505	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	5.4166
IPI:IPI00351206.5	GLCSGPGAGEESPAAT*LP	506	Pgrmc2	Membrane-associated progesterone	5.4066

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
	R^M#K@			receptor component 2	
IPI:IPI00117731.1	TFWS*PELK@K@	507	Erc1;LOC100048600	Isoform 1 of ELKS/RAB6-interacting/CAST family member 1	5.3901
IPI:IPI00115681.1	TECGS*TGSPAS*SFHFK@	508	Eef2k	Elongation factor 2 kinase	5.3519
IPI:IPI00351206.5	GLCSGPGAGEES*PAATLP R^M#K@	509	Pgrmc2	Membrane-associated progesterone receptor component 2	5.2793
IPI:IPI00108454.2	LSS*LR^AS*TSK@SESSQK@	510	rpS6	29 kDa protein	5.274
IPI:IPI00108454.2	LSS*LR^ASTS*K@SESSQK@	511	rpS6	29 kDa protein	5.274
IPI:IPI00108454.2	R^LS*S*LR^	512	rpS6	29 kDa protein	5.2699
IPI:IPI00108454.2	RLS*S*LR	513	rpS6	29 kDa protein	5.2699
IPI:IPI00108454.2	LS*SLR^ASTS*K@SESSQK@	514	rpS6	29 kDa protein	5.257
IPI:IPI00331280.1	AALDQT*SGLPGGAAQDPG GR^	515	Adamts 2	A disintegrin and metalloproteinase with thrombospondin motifs 2	5.2222
IPI:IPI00108454.2	RLS*S*LR	516	rpS6	29 kDa protein	5.1769
IPI:IPI00108454.2	R^LS*S*LR^	517	rpS6	29 kDa protein	5.1745
IPI:IPI00127976.1	MNLS*SQS*PLHPSTLNAVI HR^	518	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	5.0363
IPI:IPI00127976.1	MNLS*SQS*PLHPSTLNAVI HR^	519	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	5.0363
IPI:IPI00656285.2	SLVSPIS*PTGTISVPNSCP AS*PR^	520	Foxk1	Forkhead box protein K1	5.0164
IPI:IPI00461419.2	IR^S*S*LAR^	521	Gm6988	similar to hCG1640785	4.998
IPI:IPI00108454.2	R^LS*S*LR^ASTSK@	522	rpS6	29 kDa protein	4.9653
IPI:IPI00127976.1	MNLS*SQS*PLHPSTLNAVI HR^	523	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.9297
IPI:IPI00403938.2	LLDPQEFT*LS*GT*QR^	524	Tnc	Isoform 1 of Tenascin	4.9074
IPI:IPI00108454.2	R^LS*S*LR^ASTSK@	525	rpS6	29 kDa protein	4.8929
IPI:IPI00929786.1	TASISSSPS*EGTPAVGS*Y GCT*PQSLPK@	526	Larp1	Isoform 1 of La-related protein 1	4.8902
IPI:IPI00169986.4	SLLVLR^GT*AYT*R^	527	Alkbh6	24 kDa protein	4.8761
IPI:IPI00127976.1	MNLS*SQS*PLHPSTLNAVI HR^	528	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.774
IPI:IPI00929786.1	T*ASISSP*PSEGTPAVGSY GCT*PQS*LPK@	529	Larp1	Isoform 1 of La-related protein 1	4.758
IPI:IPI00929786.1	T*ASISSP*PSEGTPAVGSY* GCT*PQSLPK@	530	Larp1	Isoform 1 of La-related protein 1	4.758
IPI:IPI00115681.1	TECGS*TGS*PASSFHK@	531	Eef2k	Elongation factor 2 kinase	4.7395
IPI:IPI00929786.1	TAS*ISSP*PSEGTPAVGSY GCT*PQS*LPK@	532	Larp1	Isoform 1 of La-related protein 1	4.7282

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00127976.1	M#NILSS*QS*PLHPSTLNAV IHR ^A	533	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.7179
IPI:IPI00340860.5	TAS*EGS*EAETPEAPK@Q PAK@K@	534	Larp7	Isoform 1 of La-related protein 7	4.7122
IPI:IPI00340860.5	TAS*EGS*EAETPEAPK@Q PAK@K@	535	Larp7	Isoform 1 of La-related protein 7	4.7105
IPI:IPI00127976.1	MNILSSQS*PLHPSTLNAVH R ^A	536	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.6623
IPI:IPI00127976.1	MNILSSQS*PLHPSTLNAVH R ^A	537	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.6623
IPI:IPI00929786.1	TASIS*SSPSEGT*PAVGSY GCTPQS*LPK@	538	Larp1	Isoform 1 of La-related protein 1	4.5768
IPI:IPI00115681.1	TECGS*TGSPAS*SFHFK@	539	Eef2k	Elongation factor 2 kinase	4.562
IPI:IPI00553798.2	VK@T*PEMIQK@PK@	540	Ahnak	AHNAK nucleoprotein isoform 1	4.557
IPI:IPI00929786.1	T*ASISSS*PSEGTPAVGSY* GCT*PQSLPK@	541	Larp1	Isoform 1 of La-related protein 1	4.4981
IPI:IPI00929786.1	TAS*ISSS*PSEGTPAVGSY GCT*PQS*LPK@	542	Larp1	Isoform 1 of La-related protein 1	4.4981
IPI:IPI00320208.3	YGPSSVEDTTGSGAADAK @DDDDIDLFGS*DDEESEE EAK@K@	543	Eef1b2	Elongation factor 1-beta	4.4765
IPI:IPI00320208.3	YGPSSVEDTTGSGAADAKD DDDIDLFGS*DDEESEEAK K	544	Eef1b2	Elongation factor 1-beta	4.4765
IPI:IPI00474916.3	AVVPFLGVGFSSLDMS*LCV VLY*VASS*LFLM#IMYFFFR ^VR ^A	545	Qsox2	Isoform 3 of Sulfhydryl oxidase 2	4.4747
IPI:IPI00399953.1	K@FS*APGQLCVPMTSNLG GSTPISAASATSLGHFTK@	546	Wnk1	Serine/threonine-protein kinase WNK1	4.3426
IPI:IPI00654415.2	MT*S*T*DYS*LSGTCGM#D R ^A	547	Megf11	Isoform 4 of Multiple epidermal growth factor-like domains 11	4.325
IPI:IPI00660767.2	SDS*SGGYTLSDVIQS*PPS AGLLK@	548	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	4.2681
IPI:IPI00660767.2	K@R*SDSSGGYT*LSDVIQS *PPSAGLLK@	549	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	4.2613
IPI:IPI00127976.1	MNILSSQS*PLHPSTLNAVH R ^A	550	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.2564
IPI:IPI00127976.1	MNILSSQSPLHPS*TLNAVH R ^A	551	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.2564
IPI:IPI00127976.1	M#NILSSQS*PLHPSTLNAV IHR ^A	552	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.2332
IPI:IPI00313653.2	QFCQEGQPHVLEALS*PPQ TSGLS*PSR ^A	553	Maf1	Repressor of RNA polymerase III transcription MAF1 homolog	4.2077
IPI:IPI00929786.1	TAS*ISSS*PSEGTPAVGSY GCT*PQS*LPK@	554	Larp1	Isoform 1 of La-related protein 1	4.18
IPI:IPI00127976.1	M#NILSSQS*PLHPSTLNAV IHR ^A	555	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.1504
IPI:IPI00127976.1	M#NILSSQS*PLHPSTLNAV IHR ^A	556	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.1504

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00122594.4	EVS*VSS*VTEEPK@LDSSQ LPLQTGLDVPAT*PR^	557	Ahctf1	AT-hook-containing transcription factor 1	4.144
IPI:IPI00127976.1	MNIISSQS*PLHPSTLNAVIH R^	558	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.133
IPI:IPI00127976.1	MNIISSQS*PLHPSTLNAVIH R^	559	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.133
IPI:IPI00109318.1	R^NS*PMAQT*PPCHLPNIP GVTSPGALIEDSK@	560	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	4.0914
IPI:IPI00109318.1	R^NS*PMAQT*PPCHLPNIP GVTSPGALIEDSK@	561	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	4.0914
IPI:IPI00122521.1	K@DELSDDS*LAGEDDR^E TR^	562	Fxr1	Isoform E of Fragile X mental retardation syndrome-related protein 1	4.0773
IPI:IPI00127976.1	MNIISS*QSPLHPSTLNAVIH R	563	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.0585
IPI:IPI00127976.1	MNIISS*QS*PLHPSTLNAVI HR^	564	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	4.0417
IPI:IPI00313653.2	QFCQEGQPHVLEALS*PPQ TSGLS*PSR^	565	Maf1	Repressor of RNA polymerase III transcription MAF1 homolog	4.0213
IPI:IPI00127976.1	MNIISS*QSPLHPSTLNAVIH R	566	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	3.9734
IPI:IPI00127976.1	MNIISSQS*PLHPSTLNAVIH R^	567	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	3.9734
IPI:IPI00127976.1	MNIISSQS*PLHPSTLNAVIH R^	568	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	3.9734
IPI:IPI00127976.1	MNIISS*QSPLHPSTLNAVIH R	569	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	3.9734
IPI:IPI00120691.3	QADSET*K@EITEEPS*EEE ADMPK@PK@	570	Ddx21	Nucleolar RNA helicase 2	3.9589
IPI:IPI00226441.2	LHYT*PPLQS*PIT*DGDPLL GQS*PWR^	571	Lin9	Isoform 2 of Lin-9 homolog	3.8536
IPI:IPI00127976.1	MNIISSQS*PLHPSTLNAVIH R^	572	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	3.8383
IPI:IPI00127976.1	MNIISSQS*PLHPSTLNAVIH R^	573	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	3.8383
IPI:IPI00656285.2	SSGLQTPECLS*REGS*PIP HDPDLGSK	574	Foxk1	Forkhead box protein K1	3.7948
IPI:IPI00656285.2	SSGLQTPECLS*R^EGS*PIP HDPDLGSK@	575	Foxk1	Forkhead box protein K1	3.7948
IPI:IPI00468516.3	SHILESVP TLPGS*VEAGVS FDLPAQADTLHSANK@	576	D6Wsu 116e	Isoform 1 of Protein FAM21	3.7932
IPI:IPI00751009.1	TSEFPTPLFSGPLEPVACGS VISEGSPLEQEESPSHDR ^S*R^	577	SrpK2	serine/arginine-rich protein-specific kinase 2	3.7653
IPI:IPI00929786.1	TASISSPS*EGTPAVGSYG CT*PQS*LPK@	578	Larp1	Isoform 1 of La-related protein 1	3.756
IPI:IPI00929786.1	TASISSPS*EGTPAVGSY* GCT*PQSLPK@	579	Larp1	Isoform 1 of La-related protein 1	3.756
IPI:IPI00656285.2	SSGLQTPECLS*R^EGS*PIP HDPDLGSK@	580	Foxk1	Forkhead box protein K1	3.7214

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00400017.2	TQS*GNFNTDAPGMAEFR [^]	581	Ppfbp2	Isoform 4 of Liprin-beta-2	3.6603
IPI:IPI00660767.2	SDSS*GGYTLSDVIQS*PPS AGLLK@	582	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	3.6519
IPI:IPI00116442.1	S*EGLSLER [^]	583	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	3.6501
IPI:IPI00379844.4	TAS*EGDGAAGGAGTAG GR [^] PMSVAGS*PLS*PGPVR [^]	584	Irs2	Insulin receptor substrate 2	3.6492
IPI:IPI00929786.1	T*ASISSS*PSEGTPAVGS*Y GCTPQSLPK@	585	Larp1	Isoform 1 of La-related protein 1	3.6217
IPI:IPI00929786.1	T*ASISSS*PSEGTPAVGS*Y GCTPQSLPK@	586	Larp1	Isoform 1 of La-related protein 1	3.6217
IPI:IPI00116442.1	R [^] S*EGLSLER [^]	587	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	3.6142
IPI:IPI00656285.2	SLVS*PIPSPTGT*ISVPNSC PAS*PR [^]	588	Foxk1	Forkhead box protein K1	3.6065
IPI:IPI00656285.2	SLVS*PIPS*PTGTISVPNSC PAS*PR [^]	589	Foxk1	Forkhead box protein K1	3.6065
IPI:IPI00656285.2	SLVSPISPT*GTISVPNSCP AS*PR [^]	590	Foxk1	Forkhead box protein K1	3.605
IPI:IPI00654417.1	HSS*PPLTVK	591	Tinf2	Putative uncharacterized protein	3.5562
IPI:IPI00830829.1	R [^] R [^] S*GEQIT*SS*PVS*PK@	592	Hisppd1	140 kDa protein	3.5492
IPI:IPI00118875.4	GATPAEDDEDKDIDLFGS*D EEEEEDKEAAR	593	Eef1d	eukaryotic translation elongation factor 1 delta isoform a	3.5469
IPI:IPI00118875.4	GATPAEDDEDKDIDLFGS*D EEEEEDKEAAR	594	Eef1d	eukaryotic translation elongation factor 1 delta isoform a	3.5469
IPI:IPI00169888.3	SQDVAIS*PQQQQCSK@S* YVDR [^]	595	Edc3	Enhancer of mRNA-decapping protein 3	3.5277
IPI:IPI00134029.8	VS*SS*VS*VGPSM#SGET*L PR [^]	596	Aim1l	Absent in melanoma 1-like	3.5092
IPI:IPI00654417.1	HSS*PPLTVK	597	Tinf2	Putative uncharacterized protein	3.4997
IPI:IPI00676574.2	RVS*TDLPEGQDVYTAACN SVIHR	598	Herc1	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1	3.4866
IPI:IPI00762234.2	SGDPR [^] S*CEEES*DPEPDP DPDTQAEAYVAR [^]	599	Fbxw9	F-box and WD-40 domain protein 9	3.4479
IPI:IPI00660767.2	VDTAASSSWLAGS*CS*PVS PPVVDLR [^]	600	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	3.398
IPI:IPI00169888.3	SQDVAIS*PQQQQCS*K@S YVDR [^]	601	Edc3	Enhancer of mRNA-decapping protein 3	3.3665
IPI:IPI00169888.3	SQDVAISPQQQQCS*K@SY *VDR [^]	602	Edc3	Enhancer of mRNA-decapping protein 3	3.3665
IPI:IPI00122521.1	K@DELSDW*LAGEDDR [^] E TR [^]	603	Fxr1	Isoform E of Fragile X mental retardation syndrome-related protein 1	3.3379
IPI:IPI00761443.2	RSS*AGS*LESNVEGSISS* PHMR	604	Iqsec1	IQ motif and Sec7 domain 1 isoform b	3.3179
IPI:IPI00761443.2	R [^] S*SAGS*LESNVEGSISS* PHMR [^]	605	Iqsec1	IQ motif and Sec7 domain 1 isoform b	3.3179

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00828461.1	GPPDFS*S*DEER^EPTVL GSGASVGR^	606	Tmpo	thymopoietin isoform delta	3.3038
IPI:IPI00828461.1	GPPDFS*S*DEER^EPTVL GSGASVGR^	607	Tmpo	thymopoietin isoform delta	3.3038
IPI:IPI00126317.1	NAS*TS*FQELEDK@K@EL SEESEDEELQLEEFMLK@	608	Dnajc2	DnaJ homolog subfamily C member 2	3.2768
IPI:IPI00227934.3	TSASCS*PAPES*PMSSSES VK@	609	Cux1	cut-like homeobox 1 isoform a	3.1887
IPI:IPI00116442.1	S*EGLSLER^	610	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	3.1751
IPI:IPI00468516.3	SHILESVPTLPGS*VEAGVS FDLPAQADTLHSANK@	611	D6Wsu 116e	Isoform 1 of Protein FAM21	3.1635
IPI:IPI00468516.3	SHILESVPTLPGS*VEAGVS FDLPAQADTLHSANK@	612	D6Wsu 116e	Isoform 1 of Protein FAM21	3.1635
IPI:IPI00762234.2	SGDPR^S*CEES*DPEPDP DPDTQAEAYVAR^	613	Fbxw9	F-box and WD-40 domain protein 9	3.1508
IPI:IPI00320208.3	YGPSSVEDTTGSGAADA K DDDIDLFGS*DDEESEEEK	614	Eef1b2	Elongation factor 1-beta	3.1436
IPI:IPI00320594.5	SQPHSSTSNQETS*DS*EM EMEAHPNGVLESVSTR^	615	Ranbp1 0	Ran-binding protein 10	3.1377
IPI:IPI00808277.2	S*APASPNHAGVLSAHSSG AQTPE*LSR^EGS*PAPLE PEPGASQPK@	616	Foxk2	Isoform 1 of Forkhead box protein K2	3.1204
IPI:IPI00808277.2	SAPAS*PNHAGVLSAHSSG AQTPE*LSR^EGS*PAPLE PEPGASQPK@	617	Foxk2	Isoform 1 of Forkhead box protein K2	3.1105
IPI:IPI00753321.2	S*VSETSEDK@K@DEES*D EEEEEEEEEPLGATTR^	618	Bod1l	biorientation of chromosomes in cell division 1-like	3.106
IPI:IPI00420464.3	SNT*PS*PLNLSSTSSK@	619	Zeb2	Zinc finger E-box-binding homeobox 2	3.0996
IPI:IPI00116442.1	S*EGLSLER^	620	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	3.0974
IPI:IPI00808277.2	SAPAS*PNHAGVLSAHSSG AQT*PES*LSR^	621	Foxk2	Isoform 1 of Forkhead box protein K2	3.0877
IPI:IPI00830829.1	R^R^S*GEQITSS*PVS*PK@	622	Hisppd1	140 kDa protein	3.0712
IPI:IPI00117932.2	S*PPVQPHTPVTISLGTAPS LQNNQPVEFNHAINYVNK@	623	Sin3a	Isoform 1 of Paired amphipathic helix protein Sin3a	3.0565
IPI:IPI00117932.2	S*PPVQPHTPVTISLGTAPS LQNNQPVEFNHAINYVNK@	624	Sin3a	Isoform 1 of Paired amphipathic helix protein Sin3a	3.0565
IPI:IPI00320594.5	SQPHSSTSNQETS*DS*EM EMEAHPNGVLESVSTR^	625	Ranbp1 0	Ran-binding protein 10	3.0328
IPI:IPI00227934.3	TS*ASCSPAPES*PMSSSES VK@	626	Cux1	cut-like homeobox 1 isoform a	3.0118
IPI:IPI00380817.6	GR^SS*ESSCGLDGDYEDA ELNPR^	627	Bcr	Breakpoint cluster region protein	3.0087
IPI:IPI00656285.2	SLVSPIPS*PTGTISVPNSCP AS*PR^	628	Foxk1	Forkhead box protein K1	2.9994
IPI:IPI00656285.2	SLVS*PIPS*PTGTISVPNSC	629	Foxk1	Forkhead box protein K1	2.9989

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
	PAS*PR^				
IPI:IPI00127976.1	MNILS*SQS*PLHPSTLNAVIHR^	630	Grb10	Isoform 3 of Growth factor receptor-bound protein 10	2.9784
IPI:IPI00551454.3	ER^QES*ESEQELVNK@	631	Pdcd11	Protein RRP5 homolog	2.9603
IPI:IPI00226155.3	VSALEEDMDDVES*S*EEEEEEDEKLER	632	Prpf38a	Isoform 1 of Pre-mRNA-splicing factor 38A	2.9547
IPI:IPI00753321.2	SVSETS*EDK@K@DEES*D EEEEEEEEEPLGATTR^	633	Bod1l	biorientation of chromosomes in cell division 1-like	2.9525
IPI:IPI00753321.2	SVSET*SEDK@K@DEES*D EEEEEEEEEPLGATTR^	634	Bod1l	biorientation of chromosomes in cell division 1-like	2.9525
IPI:IPI00108454.2	LSS*LR^ASTS*K@S*ESSQK@	635	-	29 kDa protein	2.9394
IPI:IPI00553798.2	HR^SNS*FS*DER^EFSAPS* TPTGTLEFAGGDAK@	636	Ahnak	AHNAK nucleoprotein isoform 1	2.9368
IPI:IPI00551454.3	ER^QES*ESEQELVNK@	637	Pdcd11	Protein RRP5 homolog	2.9308
IPI:IPI00468516.3	SHILESVPTLPGS*VEAGVS FDLPAQADTLHSANK@	638	D6Wsu 116e	Isoform 1 of Protein FAM21	2.9286
IPI:IPI00420464.3	SNT*PS*PLNLSSTSSK@	639	Zeb2	Zinc finger E-box-binding homeobox 2	2.9204
IPI:IPI00656285.2	SLVS*PIPS*PTGTISVPNSC PAS*PR^	640	Foxk1	Forkhead box protein K1	2.8837
IPI:IPI00330773.3	K@MLLASTSSDDFDR^AS* Y*SGTSPSHSFISGEPDR^	641	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	2.8699
IPI:IPI00551454.3	ER^QES*ESEQELVNK@	642	Pdcd11	Protein RRP5 homolog	2.8488
IPI:IPI00656285.2	SLVS*PIPSPT*GTISVPNS*C PASPR^	643	Foxk1	Forkhead box protein K1	2.818
IPI:IPI00660767.2	VDTAASSSWLAGS*CS*PVS PPVVDLR^	644	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	2.8109
IPI:IPI00656285.2	SLVS*PIPS*PTGTISVPNSC PAS*PR^	645	Foxk1	Forkhead box protein K1	2.8019
IPI:IPI00656285.2	SLVS*PIPS*PTGTISVPNSC PAS*PR^	646	Foxk1	Forkhead box protein K1	2.8019
IPI:IPI00656285.2	SLVSPISPT*GT*ISVPNSC PAS*PR	647	Foxk1	Forkhead box protein K1	2.8019
IPI:IPI00107958.1	TSDIFGS*PVTATAPLAHPN K@PK@	648	Hn1l	Hematological and neurological expressed 1-like protein	2.7751
IPI:IPI00129298.1	EIDVLEFGESAPAASKENSA APS*PGRPQSASPAKEEQK	649	Palm	Isoform 1 of Paralemmmin	2.7684
IPI:IPI00320208.3	YGPSSVEDTTGSGAADAK @DDDDIDLFGS*DDEESEE EAK@K@	650	Eef1b2	Elongation factor 1-beta	2.7577
IPI:IPI00929786.1	TASISSS*PSEGT*PAVGSY GCT*PQS*LPK@	651	Larp1	Isoform 1 of La-related protein 1	2.7577
IPI:IPI00377615.2	R^SS*R^S*FSLDEPPLFIPD NIATVK@	652	Phf3	PHD finger protein 3	2.7452
IPI:IPI00113563.3	YMEDST*YY*K@ASK@	653	Ptk2	Isoform 1 of Focal adhesion kinase 1	2.7394
IPI:IPI00553283.1	MMPS*PSDSSR^	654	111001	Putative uncharacterized protein	2.7037

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
			3L07Rik		
IPI:IPI00314502.5	VHGLPTTSPS*GVNMAELAQQVVK@	655	Tcfef	Transcription factor EB	2.6958
IPI:IPI00314502.5	VHGLPTTSPS*GVNMAELAQQVVK@	656	Tcfef	Transcription factor EB	2.6958
IPI:IPI00122594.4	EVS*VSS*VTEEPK@LDSSQLPLQTGLDVPAT*PR^	657	Ahctf1	AT-hook-containing transcription factor 1	2.6674
IPI:IPI00377615.2	S*S*R^SFSLEPPLFIPDNIA TVK@K@	658	Phf3	PHD finger protein 3	2.6537
IPI:IPI00468516.3	SHILESVPTLPGS*VEAGVS FDLPAQADTLHSANK@	659	D6Wsu116e	Isoform 1 of Protein FAM21	2.6436
IPI:IPI00122521.1	SSISSVLK@DPDSNPYSLLDNTES*DQTADT*DAS*ESHHSTNR^	660	Fxr1	Isoform E of Fragile X mental retardation syndrome-related protein 1	2.618
IPI:IPI00625723.2	TGTGSPFAGNS*PAR^EGEQDAGSLK@DVFK@	661	Zc3h4	Isoform 2 of Zinc finger CCCH domain-containing protein 4	2.5583
IPI:IPI00625723.2	TGTGSPFAGNS*PAR^EGEQDAGSLK@DVFK@	662	Zc3h4	Isoform 2 of Zinc finger CCCH domain-containing protein 4	2.5583
IPI:IPI00122559.3	EIQNGTLR^ES*DSEHVPR^	663	Ktn1	Isoform 1 of Kinectin	2.5547
IPI:IPI00136379.1	GGGSAAAAAASGGGV S*PDNSIEHSDYR^	664	Pbx2	Pre-B-cell leukemia transcription factor 2	2.554
IPI:IPI00330246.2	SGPLPSSSGSSSSSSQLSVAT*LGR^SPS*PK@	665	Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1	2.5309
IPI:IPI00330246.2	SGPLPSSSGSSSSSSQLSVAT*LGR^SPS*PK@	666	Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1	2.5309
IPI:IPI00377615.2	S*S*R^SFSLEPPLFIPDNIA TVK@K@	667	Phf3	PHD finger protein 3	2.5121
IPI:IPI00125505.2	TTGNSHWTLEAPFSSS*CANLETER^	668	Cdgap	Cdc42 GTPase-activating protein	2.4733
IPI:IPI00551454.3	ER^QES*ESEQELVNK@	669	Pdcd11	Protein RRP5 homolog	2.4392
IPI:IPI00320594.5	SQPHSSTSNQETS*DS*EM EMEAHPNGVLESVSTR^	670	Ranbp10	Ran-binding protein 10	2.4384
IPI:IPI00126317.1	NAS*TS*FQELEDK@K@ELSEESEDEELQLEEFMLK@	671	Dnajc2	DnaJ homolog subfamily C member 2	2.438
IPI:IPI00129276.2	LES*LNIQR^	672	Eif3a	Eukaryotic translation initiation factor 3 subunit A	2.429
IPI:IPI00553798.2	SS*EVVLS*GDDEDYQR^	673	Ahnak	AHNAK nucleoprotein isoform 1	2.4187
IPI:IPI00226750.2	T*S*S*TCSNESLNAGGTPVTPR^	674	Tbc1d4	140 kDa protein	2.4185
IPI:IPI00377615.2	R^SSR^S*FS*LDEPPLFIPDNIATVK@	675	Phf3	PHD finger protein 3	2.409
IPI:IPI00377615.2	R^SSR^S*FS*LDEPPLFIPDNIATVK@	676	Phf3	PHD finger protein 3	2.409
IPI:IPI00114227.7	SIST*CGPLDK@DDPGGQK@	677	Dennd4a	hypothetical protein LOC102442	2.3733
IPI:IPI00339693.1	LGDSELALVCSQR^PAS*LSQSPR^	678	Wdr91	WD repeat-containing protein 91	2.3532

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00137166.1	SR ^Δ DAT*PPVS*PINMEDQE R ^Δ	679	Junb	Transcription factor jun-B	2.3444
IPI:IPI00751009.1	TVS*ASS*TGDLPK@	680	SrpK2	serine/arginine-rich protein-specific kinase 2	2.3444
IPI:IPI00751009.1	TVS*ASS*TGDLPK@	681	SrpK2	serine/arginine-rich protein-specific kinase 2	2.3444
IPI:IPI00751009.1	TVS*ASS*TGDLPK	682	SrpK2	serine/arginine-rich protein-specific kinase 2	2.3444
IPI:IPI00226750.2	TSST*CS*NESLNAGGTPVT PR ^Δ	683	Tbc1d4	140 kDa protein	2.3429
IPI:IPI00221581.1	SR ^Δ T*GS*ESSQTGASATSG R ^Δ	684	Eif4b	Eukaryotic translation initiation factor 4B	2.3268
IPI:IPI00122521.1	SSISSVLK@DPDSNPYSLLD NTES*DQT*ADT*DASESHH STNR ^Δ	685	Fxr1	Isoform E of Fragile X mental retardation syndrome-related protein 1	2.3266
IPI:IPI00116442.1	K@R ^Δ S*EGLS*LER ^Δ	686	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	2.3042
IPI:IPI00828461.1	GPPDFS*S*DEER ^Δ EPT*PVL GS*GASVGR ^Δ	687	Tmpo	thymopoietin isoform delta	2.3011
IPI:IPI00463493.1	S*ATDADMVNSGWLVGK	688	Gbf1	Golgi-specific brefeldin A-resistance factor 1	2.294
IPI:IPI00129276.2	LES*LNQR ^Δ	689	Eif3a	Eukaryotic translation initiation factor 3 subunit A	2.2772
IPI:IPI00751009.1	TVS*ASS*TGDLPK@	690	SrpK2	serine/arginine-rich protein-specific kinase 2	2.2686
IPI:IPI00137166.1	SR ^Δ DAT*PPVS*PINMEDQE R ^Δ	691	Junb	Transcription factor jun-B	2.2666
IPI:IPI00221581.1	SR ^Δ TGS*ESS*QTGASATSG R ^Δ	692	Eif4b	Eukaryotic translation initiation factor 4B	2.2646
IPI:IPI00221581.1	SR ^Δ TGS*ESS*QTGASATSG R ^Δ	693	Eif4b	Eukaryotic translation initiation factor 4B	2.2646
IPI:IPI00221581.1	SRT*GS*ESSQTGASATSGR	694	Eif4b	Eukaryotic translation initiation factor 4B	2.2646
IPI:IPI00268688.3	TSS*S*ETEEK@K@TEK@P LILQLGSR ^Δ	695	Cd2ap	CD2-associated protein	2.2567
IPI:IPI00268688.3	TSS*S*ETEEKKTEKPLILQP LGSR	696	Cd2ap	CD2-associated protein	2.2567
IPI:IPI00226750.2	TSST*CS*NES*LNAGGTPV TPR ^Δ	697	Tbc1d4	140 kDa protein	2.2548
IPI:IPI00221581.1	SRT*GS*ESSQTGASATSGR	698	Eif4b	Eukaryotic translation initiation factor 4B	2.2395
IPI:IPI00221581.1	SR ^Δ TGS*ESS*QTGASATSG R ^Δ	699	Eif4b	Eukaryotic translation initiation factor 4B	2.2395
IPI:IPI00122594.4	EVS*VSS*VTEEPK@LDSSQ LPLQTGLDVPATPR ^Δ	700	Ahctf1	AT-hook-containing transcription factor 1	2.2291
IPI:IPI00122594.4	EVSVS*S*VTEEPKLDSSQL PLQTGLDVPATPR	701	Ahctf1	AT-hook-containing transcription factor 1	2.2291
IPI:IPI00676574.2	RVST*DLPEGQDVYTAACN SVIHR	702	Herc1	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1	2.2125

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00268688.3	TSS*S*ETEEK@K@TEK@P LILQLGSR^	703	Cd2ap	CD2-associated protein	2.1992
IPI:IPI00320905.7	LGEQGPEPGPT*PPQTPT*P PS*TPPLAK	704	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	2.1798
IPI:IPI00108454.2	LSSLRAS*TS*KSES*S*QK	705	-	29 kDa protein	2.1655
IPI:IPI00929786.1	TASIS*S*SPSEGTPAVGSY GCT*PQSLPK@	706	Larp1	Isoform 1 of La-related protein 1	2.1557
IPI:IPI00381495.5	TVSSPIPYTPSPSSSR^PIS* PGLSY*ASHTVGFTPPTS LT R^	707	Ccdc6	coiled-coil domain containing 6	2.1555
IPI:IPI00221581.1	TGS*ESS*QTGASATSGR^	708	Eif4b	Eukaryotic translation initiation factor 4B	2.1437
IPI:IPI00221581.1	TGS*ESS*QTGASATSGR^	709	Eif4b	Eukaryotic translation initiation factor 4B	2.1437
IPI:IPI00137166.1	SR^DAT*PPVS*PINMEDQE R^	710	Junb	Transcription factor jun-B	2.1419
IPI:IPI00929786.1	S*LPTTVPES*PNYR^	711	Larp1	Isoform 1 of La-related protein 1	2.1397
IPI:IPI00929786.1	S*LPTTVPESPNY*R	712	Larp1	Isoform 1 of La-related protein 1	2.1397
IPI:IPI00406045.3	SESSAGICVPLSTS*PQVSE AAHIPSK@K@PVIPVVSST VLPSTYQIR^	713	Pik3r4	Phosphoinositide 3-kinase regulatory subunit 4	2.1394
IPI:IPI00122594.4	ER^EVS*VS*SVTEEPK@LD SSQLPLQTGLDVPATPR^	714	Ahctf1	AT-hook-containing transcription factor 1	2.1312
IPI:IPI00929786.1	S*LPTTVPES*PNYR^	715	Larp1	Isoform 1 of La-related protein 1	2.1207
IPI:IPI00929786.1	S*LPTTVPES*PNYR	716	Larp1	Isoform 1 of La-related protein 1	2.1207
IPI:IPI00929786.1	SLPT*TVPES*PNYR^	717	Larp1	Isoform 1 of La-related protein 1	2.1207
IPI:IPI00929786.1	S*LPTTVPES*PNYR	718	Larp1	Isoform 1 of La-related protein 1	2.1207
IPI:IPI00625723.2	TGTGSPFAGNS*PAR^EGE QDAGSLK@DVFK@	719	Zc3h4	Isoform 2 of Zinc finger CCCH domain-containing protein 4	2.1078
IPI:IPI00221581.1	T*GSESS*QTGASATSGR^	720	Eif4b	Eukaryotic translation initiation factor 4B	2.103
IPI:IPI00221581.1	T*GSESS*QTGASATSGR^	721	Eif4b	Eukaryotic translation initiation factor 4B	2.103
IPI:IPI00221581.1	TGS*ESS*QTGASATSGR	722	Eif4b	Eukaryotic translation initiation factor 4B	2.103
IPI:IPI00625723.2	TGTGSPFAGNS*PAR^EGE QDAGSLK@DVFK@	723	Zc3h4	Isoform 2 of Zinc finger CCCH domain-containing protein 4	2.0988
IPI:IPI00379844.4	GEQGSLAQSQPQPGDK@N S*WSR^	724	Irs2	Insulin receptor substrate 2	2.0959
IPI:IPI00136107.1	T*HST*SSS*IGSGESPFGR^	725	Ndr3	Protein NDRG3	2.0759
IPI:IPI00467843.2	GGGAS*SPAPVFTVGS*PP S*GATPPQSTR^	726	Ulk1	Putative uncharacterized protein	2.0752
IPI:IPI00127415.1	LK@CGSGPVHISGQHLVAV EEDAES*EDEDEEDVK@LL GM#SGK@	727	Npm1	Nucleophosmin	2.0591

Reference	Ascore Seq	SEQ ID NO.	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00320905.7	LGEQGPEPGPT*PPQTPT*P PS*TPPLAK	728	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	2.0572
IPI:IPI00622946.2	QFIAAQNLGPASGLPTPTSS *PSSSSLPSPLSPT*PR^PFG R^	729	Palld	Isoform 4 of Palladin	2.0517
IPI:IPI00467843.2	GGGASS*PAPVVFTVGS*PP S*GATPPQSTR^	730	Ulk1	Putative uncharacterized protein	2.0359
IPI:IPI00929786.1	TASISSSPS*EGTPAVGSYG CT*PQSLPK@	731	Larp1	Isoform 1 of La-related protein 1	2.0315
IPI:IPI00309059.7	ST*S*PIIGS*PPVR^	732	Pat1	Protein PAT1 homolog 1	2.0311
IPI:IPI00929786.1	TASIS*SSPS*EGTPAVGSY GCT*PQS*LPK@	733	Larp1	Isoform 1 of La-related protein 1	2.0277
IPI:IPI00107958.1	TSDIFGS*PVTATAPLAHPN KPK	734	Hn1l	Hematological and neurological expressed 1-like protein	2.0059
IPI:IPI00336713.1	CS*PVPGLSSS*PSGSPHKG K@	735	Bcas3	Isoform 1 of Breast carcinoma- amplified sequence 3 homolog	1.9848
IPI:IPI00136107.1	THST*SSS*IGSGESPFSR^	736	Ndr3	Protein NDRG3	1.9707
IPI:IPI00136107.1	THSTSS*S*IGSGESPFSR^	737	Ndr3	Protein NDRG3	1.9707
IPI:IPI00830210.1	LSESPAS*LPSCLPVETALIN QR^	738	Atg2a	Autophagy-related protein 2 homolog A	1.9651
IPI:IPI00225062.2	GCSPPK@S*PEK@PPQST SS*ESCPPS*PQPTK@	739	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.9354
IPI:IPI00122594.4	ER^EVS*VSS*VTEEPK@LD SSQLPLQTGLDVPATPR^	740	Ahctf1	AT-hook-containing transcription factor 1	1.9159
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA SKPSS*PR	741	Ccn1	Isoform 1 of Cyclin-L1	1.8986
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA SKPSS*PR	742	Ccn1	Isoform 1 of Cyclin-L1	1.896
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA SK@PS*SPR^	743	Ccn1	Isoform 1 of Cyclin-L1	1.896
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA S*KPSSPR	744	Ccn1	Isoform 1 of Cyclin-L1	1.896
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA S*K@PS*SPR^	745	Ccn1	Isoform 1 of Cyclin-L1	1.896
IPI:IPI00137166.1	SR^DAT*PPVS*PINMEDQE R^	746	Junb	Transcription factor jun-B	1.8916
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA S*KPSSPR	747	Ccn1	Isoform 1 of Cyclin-L1	1.8893
IPI:IPI00467930.2	LVIGS*LPAHLSPHLFGGFK @	748	Znrf2	E3 ubiquitin-protein ligase ZNRF2	1.8798
IPI:IPI00225062.2	R^SSS*ELS*PEVVEK@	749	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.8718
IPI:IPI00309059.7	ST*S*PIIGS*PPVR^	750	Pat1	Protein PAT1 homolog 1	1.8673
IPI:IPI00751009.1	TSEFPTPLFSGPLEPVACGS VISEGSPLT*EQEESSPSHD R^SR^	751	Srp2	serine/arginine-rich protein-specific kinase 2	1.859

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00808277.2	SAPASPNHAGVLSAHSSGA QT*PES*LSR*EGS*PAPLEP EPGASQPK@	752	Foxk2	Isoform 1 of Forkhead box protein K2	1.8546
IPI:IPI00136107.1	THS*TSSS*IGSGESPFSSR^	753	Ndr3	Protein NDRG3	1.8482
IPI:IPI00761759.1	SSSGSEHST*EGSVSLGDG PLSR^	754	Larp4	Putative uncharacterized protein	1.8482
IPI:IPI00122594.4	EVS*VSS*VTEEPK@LDSSQ LPLQTGLDVPATPR^	755	Ahctf1	AT-hook-containing transcription factor 1	1.8472
IPI:IPI00122594.4	EVS*VSS*VTEEPK@LDSSQ LPLQTGLDVPATPR^	756	Ahctf1	AT-hook-containing transcription factor 1	1.8472
IPI:IPI00268673.5	AGTTVPES*IHS*FIGDGLVK @PEALNK@K@	757	Mtor	Isoform 1 of FKBP12-rapamycin complex-associated protein	1.8442
IPI:IPI00314502.5	VHGLPTTS*PSGVNMAELA QQVVK@	758	Tcf3	Transcription factor EB	1.8426
IPI:IPI00125319.1	TTS*FAESCK@PVQQPSAF GSMK@	759	Gsk3b	Glycogen synthase kinase-3 beta	1.8417
IPI:IPI00125319.1	TTS*FAESCK@PVQQPSAF GSMK@	760	Gsk3b	Glycogen synthase kinase-3 beta	1.8417
IPI:IPI00116285.2	SQDSYPVS*PR*PFSSPSMS *PSHGMSIHLAPGK@	761	Ranbp9	RAN binding protein 9	1.8399
IPI:IPI00323510.5	TDNSVAS*SPSSAISTATPS* PK@	762	Kdm6a	Isoform 1 of Lysine-specific demethylase 6A	1.8307
IPI:IPI00229859.1	GHPSAGAEIEEGGS*DGS*A AEAEP	763	Eif3b	Eif3b protein	1.826
IPI:IPI00136107.1	THS*TSS*SIGSGESPFSSR^	764	Ndr3	Protein NDRG3	1.8106
IPI:IPI00136107.1	T*HSTSSSIGS*GESPFSSR^	765	Ndr3	Protein NDRG3	1.8106
IPI:IPI00225062.2	GCS*PPK@S*PEK@PPQST SSESCPPS*PQPTK@	766	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.8106
IPI:IPI00405752.3	VCLASS*LS*PYR*EGR^	767	C13009 2011Rik	Isoform 1 of Uncharacterized protein KIAA1680	1.8087
IPI:IPI00136107.1	THSTSS*S*IGSGESPFSSR^	768	Ndr3	Protein NDRG3	1.8041
IPI:IPI00130920.1	RSES*PFEGK	769	Mtap1b	Microtubule-associated protein 1B	1.7981
IPI:IPI00136107.1	THS*TSS*S*IGSGESPFSSR^	770	Ndr3	Protein NDRG3	1.7967
IPI:IPI00336713.1	CS*PVPGLSSS*PSGSPLHG K@	771	Bcas3	Isoform 1 of Breast carcinoma-amplified sequence 3 homolog	1.7932
IPI:IPI00323349.2	GYPPPIAAK@PAFGR*PILK @PST*PVPMPPESEEVGES* TEEQEDAPR^	772	Tjp2	Tight junction protein ZO-2	1.7869
IPI:IPI00225062.2	GCS*PPK@S*PEK@PPQST SSESCPPS*PQPTK@	773	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7868
IPI:IPI00225062.2	GCS*PPKS*PEKPPQSTSSE SCPPS*PQPTK	774	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7868
IPI:IPI00808277.2	SAPASPNHAGVLSAHSSGA QT*PES*LSR*EGS*PAPLEP EPGASQPK@	775	Foxk2	Isoform 1 of Forkhead box protein K2	1.7848

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00136107.1	THS*TSS*S*IGSGESPFSR^	776	Ndrp3	Protein NDRG3	1.7706
IPI:IPI00107958.1	TSDIFGS*PVTATAPLAHPN K@PK@	777	Hn1l	Hematological and neurological expressed 1-like protein	1.7561
IPI:IPI00136107.1	THS*TSSS*IGSGESPFSR^	778	Ndrp3	Protein NDRG3	1.7555
IPI:IPI00136107.1	THS*TSSS*IGSGESPFSR^	779	Ndrp3	Protein NDRG3	1.7525
IPI:IPI00130920.1	RSES*PFEGK	780	Mtap1b	Microtubule-associated protein 1B	1.7508
IPI:IPI00130920.1	RSES*PFEGK	781	Mtap1b	Microtubule-associated protein 1B	1.7508
IPI:IPI00136107.1	THS*TSS*SIGSGESPFSR^	782	Ndrp3	Protein NDRG3	1.7499
IPI:IPI00136107.1	THS*TSS*SIGSGESPFSR	783	Ndrp3	Protein NDRG3	1.7499
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFS*TTGGTRIYYDR	784	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.7456
IPI:IPI00468516.3	R^LAAQES*SEAEDVTVDRA GPVAQLSSS*PVLPNHGQP LLQPR^	785	D6Wsu 116e	Isoform 1 of Protein FAM21	1.7446
IPI:IPI00137501.1	TEMDKS*PFNSPS*PQDS*P R	786	Nfic	Isoform 1 of Nuclear factor 1 C-type	1.7419
IPI:IPI00225062.2	GCS*PPK@S*PEK@PPQS* TSSESCPPSPQPTK@	787	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7403
IPI:IPI00225062.2	GCS*PPK@S*PEK@PPQST SSESCPPS*PQPTK@	788	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7403
IPI:IPI00225062.2	GCS*PPKS*PEKPPQSTSS* ESCPPSPQPTK	789	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7403
IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA SK@PS*SPR^	790	Ccn1	Isoform 1 of Cyclin-L1	1.7368
IPI:IPI00107958.1	TSDIFGS*PVTATAPLAHPN K@PK@	791	Hn1l	Hematological and neurological expressed 1-like protein	1.7353
IPI:IPI00227209.3	R^LSS*T*SLASGHSVR^	792	Prkd2	Serine/threonine-protein kinase D2	1.7328
IPI:IPI00225062.2	RSS*SELS*PEVVEK	793	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7324
IPI:IPI00225062.2	R^SS*SELS*PEVVEK@	794	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7324
IPI:IPI00225062.2	RSS*SELS*PEVVEK	795	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7324
IPI:IPI00225062.2	R^SSS*ELS*PEVVEK@	796	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.7324
IPI:IPI00929779.1	S*EGLSQEATPSQDLIQHSC SPVDHSEPEAR^	797	Usp36	Ubiquitin specific peptidase 36	1.7192
IPI:IPI00467930.2	LVIGS*LPAHLS*PHLFGGFK	798	Znrf2	E3 ubiquitin-protein ligase ZNRF2	1.7137
IPI:IPI00467930.2	LVIGS*LPAHLS*PHLFGGFK @	799	Znrf2	E3 ubiquitin-protein ligase ZNRF2	1.7137
IPI:IPI00459443.5	DLQSEFGVATDSHHSSFGS SSWSQDTSQNYSLGGR^S* PVGDTGLGK@	800	Tnks1b p1	182 kDa tankyrase-1-binding protein	1.7011
IPI:IPI00785400.1	LTSHTPGLDDEKEAS*ENET *DIEDPREIQADSWR	801	Syne2	Syne2 protein	1.7003

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00136107.1	THST*SSSIGSGESPF ^{SR}	802	Ndr3	Protein NDRG3	1.6838
IPI:IPI00136107.1	THST*SSSIGSGESPF ^{SR}	803	Ndr3	Protein NDRG3	1.6838
IPI:IPI00336713.1	QGGRCS*PVPGLSSS*PSG SPLHGK	804	Bcas3	Isoform 1 of Breast carcinoma-amplified sequence 3 homolog	1.6818
IPI:IPI00336713.1	QGGR ^{CS} *PVPGLSS*SPSG SPLHGK@	805	Bcas3	Isoform 1 of Breast carcinoma-amplified sequence 3 homolog	1.6818
IPI:IPI00380354.1	LQES*PKLSQANGTR	806	Lig1	lethal giant larvae homolog 1 isoform 1	1.6806
IPI:IPI00128904.1	VMTIPYQPM ^{PASS} *PVICAG GQDR	807	Pcbp1	Poly(rC)-binding protein 1	1.6782
IPI:IPI00380107.4	LVIPS*ATTKSPPEITVT*PPT*PTLLSPK	808	Cabin1	calcineurin binding protein 1	1.6782
IPI:IPI00153375.1	SACFS*PVSL ^S *PR ^A *PCS*PF STPPPTSPVALSK@	809	Pdlim2	PDZ and LIM domain protein 2	1.6659
IPI:IPI00467930.2	LVIGS*LPAHLSPHLFGGFK@	810	Znf2	E3 ubiquitin-protein ligase ZNRF2	1.6655
IPI:IPI00467930.2	LVIGS*LPAHLSPHLFGGFK@	811	Znf2	E3 ubiquitin-protein ligase ZNRF2	1.6655
IPI:IPI00221581.1	S ^R *TGS*ESS*QTGASATS GR ^A	812	Eif4b	Eukaryotic translation initiation factor 4B	1.6642
IPI:IPI00318938.6	NS*PVA ^K @T*PPK@DLPAIP GVTSP ^T SDEPPMQASQSQL PSSPEDK@	813	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.6633
IPI:IPI00120529.2	NK@PLS*PIK@LTPTS ^V LDY FGTESVQR ^A	814	Rfc1	Rfc1 protein	1.6568
IPI:IPI00225062.2	RSS*SELS*PEVVEK	815	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.6324
IPI:IPI00225062.2	R ^{AS} *SELS*PEVVEK@	816	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.6324
IPI:IPI00225062.2	R ^{AS} *SELS*PEVVEK@	817	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.6324
IPI:IPI00225062.2	RSS*SELS*PEVVEK	818	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.6324
IPI:IPI00225062.2	R ^{AS} *SELS*PEVVEK@	819	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.6324
IPI:IPI00225062.2	R ^{AS} *SELS*PEVVEK@	820	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.6324
IPI:IPI00761759.1	SSSGSEHSTEGS*VSLGDG PLSR ^A	821	Larp4	Putative uncharacterized protein	1.6294
IPI:IPI00309059.7	R ^{AS} *TS*PIGS*PPVR ^A	822	Pat1	Protein PAT1 homolog 1	1.6275
IPI:IPI00309059.7	R ^{AS} *TS*PIGS*PPVR ^A	823	Pat1	Protein PAT1 homolog 1	1.6245
IPI:IPI00317401.6	AES*PETS ^A VESTQS*TPQK@GR ^A	824	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.623
IPI:IPI00317401.6	AES*PETS ^A VESTQST*PQK@GR ^A	825	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.623
IPI:IPI00115620.1	AS*LYNAVTTEDVEK	826	Psat1	Phosphoserine aminotransferase	1.6216
IPI:IPI00126124.2	T ^F SECS*YPETEEEEALP GR ^A	827	St5	Isoform 1 of Suppression of tumorigenicity 5	1.6159

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00421179.1	SFS*K@EVEER^	828	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.6081
IPI:IPI00225062.2	GCSPPK@S*PEK@PPQST* SSESCPPS*PQPTK@	829	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.608
IPI:IPI00227934.3	AAPSS*EGDS*CDGVEATDA EPPGGNIVATK@	830	Cux1	cut-like homeobox 1 isoform a	1.6068
IPI:IPI00314240.5	K@LEK@EEEEEGIS*QES*S* EEEQ	831	Hmga1	Isoform HMG-I of High mobility group protein HMG-I/HMG-Y	1.6058
IPI:IPI00111754.6	LDT*FCGSPPYAAPELFQGK	832	Mark2	Isoform 2 of Serine/threonine-protein kinase MARK2	1.5994
IPI:IPI00125319.1	TTS*FAESCK@PVQQPSAF GSMK@	833	Gsk3b	Glycogen synthase kinase-3 beta	1.5966
IPI:IPI00320905.7	LGEQGPEPGPT*PPQT*PTP PS*TPPLAK	834	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	1.5946
IPI:IPI00380737.1	TSSVS*S*LASACTGGIPSSS R^	835	Pom12 1	Nuclear envelope pore membrane protein POM 121	1.5883
IPI:IPI00122594.4	TTPLAS*PSLS*PGR^	836	Ahctf1	AT-hook-containing transcription factor 1	1.5845
IPI:IPI00125319.1	TTS*FAESCK@PVQQPSAF GSMK@	837	Gsk3b	Glycogen synthase kinase-3 beta	1.5821
IPI:IPI00381019.1	KRS*PS*PSPTPEAK	838	Smarcc 2	Isoform 2 of SWI/SNF complex subunit SMARCC2	1.5795
IPI:IPI00111754.6	LDT*FCGSPPYAAPELFQGK @	839	Mark2	Isoform 2 of Serine/threonine-protein kinase MARK2	1.578
IPI:IPI00111754.6	LDT*FCGSPPYAAPELFQGK @	840	Mark2	Isoform 2 of Serine/threonine-protein kinase MARK2	1.578
IPI:IPI00136107.1	THS*TSSSIGSGESPF SR^	841	Ndr3	Protein NDRG3	1.576
IPI:IPI00136107.1	THS*TSSSIGSGESPF SR^	842	Ndr3	Protein NDRG3	1.576
IPI:IPI00128904.1	VMTIPYQMPASS*PVICAG GQDR	843	Pcbp1	Poly(rC)-binding protein 1	1.5752
IPI:IPI00225062.2	S*SS*PVTELTAR^	844	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.5701
IPI:IPI00421179.1	SFS*KEVEER	845	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.5642
IPI:IPI00421179.1	SFS*K@EVEER^	846	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.5642
IPI:IPI00421179.1	SFS*KEVEER	847	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.5642
IPI:IPI00421179.1	SFS*K@EVEER^	848	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.5642
IPI:IPI00115492.1	HSLSSSQAPEDIAPPGS*S PHANR^	849	Eps8l2	Isoform 1 of Epidermal growth factor receptor kinase substrate 8-like protein 2	1.564
IPI:IPI00761759.1	S*SS*GS*EHSTEGSVSLGD GPLSR^	850	Larp4	Putative uncharacterized protein	1.5621
IPI:IPI00136107.1	THSTS*SSIGSGESPF SR^	851	Ndr3	Protein NDRG3	1.5584
IPI:IPI00111754.6	LDT*FCGSPPYAAPELFQGK	852	Mark2	Isoform 2 of Serine/threonine-protein kinase MARK2	1.5403

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00336973.2	GLNLDGT*PALSTLGGFS*PASK@PS*SPR^	853	Ccn1l	Isoform 1 of Cyclin-L1	1.5363
IPI:IPI00229739.4	LVVSS*PTS*PK@GK@	854	Plekhn1	Pleckstrin homology domain-containing family M member 1	1.5286
IPI:IPI00126124.2	TFSECS*Y*PETEEEEALPGR^	855	St5	Isoform 1 of Suppression of tumorigenicity 5	1.526
IPI:IPI00122594.4	TTPLAS*PSLS*PGR^	856	Ahctf1	AT-hook-containing transcription factor 1	1.5177
IPI:IPI00229739.4	LVVSS*PTS*PKGK	857	Plekhn1	Pleckstrin homology domain-containing family M member 1	1.515
IPI:IPI00421179.1	SFS*K@EVEER^	858	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.5113
IPI:IPI00421179.1	SFS*KEVEER	859	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.5113
IPI:IPI00349069.4	LFGT*SPAAEVTPSPPEPAPALEAPAR^	860	B230208H17Rik	Putative GTP-binding protein Parf	1.5073
IPI:IPI00605037.1	KET*ES*EAEDDNLDDLER	861	Srrm1	Isoform 1 of Serine/arginine repetitive matrix protein 1	1.5038
IPI:IPI00381244.8	KEELGASS*PGYGPPNLGCVDS*PSAGPHLGGLELK	862	Mll2	similar to myeloid/lymphoid or mixed-lineage leukemia 2	1.4993
IPI:IPI00421179.1	SFS*K@EVEER^	863	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.4913
IPI:IPI00421179.1	SFS*KEVEER	864	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.4913
IPI:IPI00421179.1	SFS*KEVEER	865	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.4913
IPI:IPI00421179.1	SFS*K@EVEER^	866	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	1.4913
IPI:IPI00136572.4	YEENPAWPGTSTHNGPNGFSQIMDET*PNVSK@SSPTGFGIK@	867	Zc3hav1	Isoform 1 of Zinc finger CCCH-type antiviral protein 1	1.4864
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAIPGVTSPTSDEPPMQASQSQLPSSPEDK@	868	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.4819
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAIPGVTSPTSDEPPMQASQSQLPSSPEDK@	869	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.4819
IPI:IPI00318938.6	NSPVAKT*PPKDLPAIPGVT*SPTSDEPPMQASQSQLPSSPEDK	870	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.4819
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAIPGVTSPTSDEPPMQASQSQLPSSPEDK@	871	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.4819
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT*SPTSDEPPMQASQSQLPSSPEDK	872	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.4819
IPI:IPI00228948.3	S*FGDK@DLILPNGGTPAGTASPASSSSLLNR^	873	Snx30	Sorting nexin-30	1.4774

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00330246.2	WAAHGTS*PEDFSLTLGAR [^]	874	Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1	1.474
IPI:IPI00229739.4	LVVSS*PTS*PK@GK@	875	Plekhn1	Pleckstrin homology domain-containing family M member 1	1.4728
IPI:IPI00229739.4	LVVSS*PT*SPKGK	876	Plekhn1	Pleckstrin homology domain-containing family M member 1	1.4728
IPI:IPI00453603.1	FIGS*PR [^] T*PVS*PVK@FSP GDFWGR [^]	877	Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1	1.4727
IPI:IPI00136107.1	THS*TSSSIGSGESPF [^] SR [^]	878	Ndr3	Protein NDRG3	1.4724
IPI:IPI00136107.1	THS*TSSSIGSGESPF [^] SR [^]	879	Ndr3	Protein NDRG3	1.4724
IPI:IPI00317401.6	AES*PETS [^] AVESTQST*PQK@GR [^]	880	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.4711
IPI:IPI00317401.6	AES*PETS [^] AVESTQST*PQK@GR [^]	881	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.4711
IPI:IPI00453603.1	FIGS*PRT*PVS*PVKFSPGD FWGR	882	Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1	1.4689
IPI:IPI00453603.1	FIGS*PR [^] T*PVS*PVK@FSP GDFWGR [^]	883	Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1	1.4689
IPI:IPI00453603.1	FIGS*PR [^] T*PVS*PVK@FSP GDFWGR [^]	884	Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1	1.4689
IPI:IPI00380737.1	TS*SVSS*LASACTGGIPSS [^] SR [^]	885	Pom121	Nuclear envelope pore membrane protein POM 121	1.4684
IPI:IPI00380737.1	TS*SVSS*LASACTGGIPSS [^] SR [^]	886	Pom121	Nuclear envelope pore membrane protein POM 121	1.4684
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPMQASQSQLPSS PEDK	887	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.4676
IPI:IPI00317401.6	AES*PETS [^] AVESTQST*PQK@GR [^]	888	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.4613
IPI:IPI00317401.6	AES*PETS [^] AVESTQST*PQK@GR [^]	889	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.4526
IPI:IPI00317401.6	AES*PETS [^] AVESTQST*PQK@GR [^]	890	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.4526
IPI:IPI00136107.1	S*RT*HSTSSSIGSGESPF [^] SR	891	Ndr3	Protein NDRG3	1.451
IPI:IPI00118438.4	KPPAPPSPVQS*QSPS*T*N WS*PAVPAKK	892	Srm1	Isoform 2 of Serine/arginine repetitive matrix protein 1	1.45
IPI:IPI00123410.5	TIS*AQDTLAYATALLNEK@	893	Usp24	Isoform 1 of Ubiquitin carboxyl-terminal hydrolase 24	1.4486
IPI:IPI00411026.1	SLHPWYGITPTSS*PK@	894	Micall1	Isoform 1 of MICAL-like protein 1	1.4479
IPI:IPI00761759.1	SSS*GSEHS*T*EGSVSLGD GPLSR [^]	895	Larp4	Putative uncharacterized protein	1.4347
IPI:IPI00313307.3	SYQNSPS*S*EDGIR*PLPEY STEK@	896	Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1	1.4214
IPI:IPI00313307.3	SYQNS*PSS*EDGIR*PLPEY STEK@	897	Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1	1.4158
IPI:IPI00129264.1	ATSR*PINLGPSS*PNTEIHW TPYR [^]	898	Sorbs3	Vinexin	1.4122

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00330773.3	ASYSGTS*PSHS*FISGEPDR [^]	899	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.403
IPI:IPI00116442.1	TR [^] LAS*ES*ANDDNEDS	900	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	1.3985
IPI:IPI00309059.7	STS*PIIGS*PPVR [^]	901	Pat11	Protein PAT1 homolog 1	1.3955
IPI:IPI00309059.7	STS*PIIGS*PPVR [^]	902	Pat11	Protein PAT1 homolog 1	1.3937
IPI:IPI00309059.7	STS*PIIGS*PPVR [^]	903	Pat11	Protein PAT1 homolog 1	1.3937
IPI:IPI00309059.7	STS*PIIGS*PPVR	904	Pat11	Protein PAT1 homolog 1	1.3937
IPI:IPI00318938.6	NS*PVAK@TPPK@DLPAIPGVT SPTSPTS*DEPPMQASQSQ LPSSPEDK@	905	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.3906
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPMQASQSQ LPSSPEDK	906	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.3906
IPI:IPI00108388.1	R [^] PYTGPNQYTYNNWS*PP VQSNETSNGYFLER [^]	907	Usp9x	Probable ubiquitin carboxyl-terminal hydrolase FAF-X	1.3905
IPI:IPI00108388.1	RPYTGPNQYTYNNWS*PPV QSNETSNGYFLER	908	Usp9x	Probable ubiquitin carboxyl-terminal hydrolase FAF-X	1.3905
IPI:IPI00309059.7	STS*PIIGS*PPVR [^]	909	Pat11	Protein PAT1 homolog 1	1.3897
IPI:IPI00309059.7	STS*PIIGS*PPVR [^]	910	Pat11	Protein PAT1 homolog 1	1.3897
IPI:IPI00556837.1	DTVIVS*EPS*EDEESHDLPSVTR	911	Smardc1	Isoform 1 of SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A containing DEAD/H box 1	1.3868
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPMQASQSQ LPSSPEDK	912	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	1.3764
IPI:IPI00467843.2	GGGASSPAPVVFTVGS*PP SGAT*PPQSTR [^]	913	Ulk1	Putative uncharacterized protein	1.3745
IPI:IPI00467843.2	GGGASSPAPVVFTVGS*PP SGATPPQST* [^] R [^]	914	Ulk1	Putative uncharacterized protein	1.3745
IPI:IPI00467843.2	GGGASSPAPVVFTVGS*PP SGAT*PPQSTR [^]	915	Ulk1	Putative uncharacterized protein	1.3702
IPI:IPI00330773.3	ASYSGTS*PSHSFISGEPDR [^]	916	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.3697
IPI:IPI00330773.3	AS*YSGTSPSHSFISGEPDR	917	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.3697
IPI:IPI00330773.3	ASYSGTS*PSHSFISGEPDR [^]	918	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.3697
IPI:IPI00117932.2	SPPVQPHTPVTIS*LG TAPS LQNNQPVFHNAINVYVVK@	919	Sin3a	Isoform 1 of Paired amphipathic helix protein Sin3a	1.3566
IPI:IPI00309059.7	STS*PIIGS*PPVR [^]	920	Pat11	Protein PAT1 homolog 1	1.3334
IPI:IPI00309059.7	STS*PIIGS*PPVR [^]	921	Pat11	Protein PAT1 homolog 1	1.3334
IPI:IPI00224153.6	VHHS*VQTFQEDSLPVAHS* LQEVSEPLTAAR [^]	922	Ptpn21	Tyrosine-protein phosphatase non-receptor type 21	1.3332

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00224153.6	VHHSVQT*FQEDSLPVAHS* LQEVSEPLTAAR	923	Ptpn21	Tyrosine-protein phosphatase non-receptor type 21	1.3332
IPI:IPI00136572.4	FHHNS*LEVLSTVS*PLGSG PPS*PDVTGCK@DPLEDVS ADVTKQK@	924	Zc3hav 1	Isoform 1 of Zinc finger CCCH-type antiviral protein 1	1.3312
IPI:IPI00309059.7	STS*PIIGS*PPVR	925	Pat11	Protein PAT1 homolog 1	1.3311
IPI:IPI00309059.7	STS*PIIGS*PPVR^	926	Pat11	Protein PAT1 homolog 1	1.3311
IPI:IPI00309059.7	STS*PIIGS*PPVR^	927	Pat11	Protein PAT1 homolog 1	1.3311
IPI:IPI00309059.7	STS*PIIGS*PPVR	928	Pat11	Protein PAT1 homolog 1	1.3311
IPI:IPI00309059.7	R^STS*PIIGS*PPVR^	929	Pat11	Protein PAT1 homolog 1	1.3267
IPI:IPI00229739.4	LVVSSPT*S*PK@	930	Plekhn 1	Pleckstrin homology domain-containing family M member 1	1.3252
IPI:IPI00321774.2	HSSIS*PVR^LPLNSSLGAEL SR^	931	Crkrs	Isoform 2 of Cell division cycle 2-related protein kinase 7	1.3231
IPI:IPI00129264.1	ATSR^PINLGPS*SPNTEIHW TPYR^	932	Sorbs3	Vinexin	1.3226
IPI:IPI00380354.1	LQES*PKLSQANGTR	933	Lgl1	lethal giant larvae homolog 1 isoform 1	1.3225
IPI:IPI00320905.7	LGEQGPEPGPT*PPQT*PT* PPST*PPLAK	934	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	1.3166
IPI:IPI00381495.5	TVSS*PIPYTPSPS*SSR^PIS *PGLSYASHTVGFT*PPTSL TR^	935	Ccdc6	coiled-coil domain containing 6	1.3165
IPI:IPI00330773.3	ASYSGTS*PSHS*FISGEPD R^	936	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.3149
IPI:IPI00660767.2	VDTAASSSWLAGS*CS*PVS PPVVDLR^	937	Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase	1.3143
IPI:IPI00309059.7	RSTS*PIIGS*PPVR	938	Pat11	Protein PAT1 homolog 1	1.3126
IPI:IPI00309059.7	R^STS*PIIGS*PPVR^	939	Pat11	Protein PAT1 homolog 1	1.3126
IPI:IPI00309059.7	R^STS*PIIGS*PPVR^	940	Pat11	Protein PAT1 homolog 1	1.3126
IPI:IPI00309059.7	RSTS*PIIGS*PPVR	941	Pat11	Protein PAT1 homolog 1	1.3123
IPI:IPI00309059.7	RSTS*PIIGS*PPVR	942	Pat11	Protein PAT1 homolog 1	1.3122
IPI:IPI00309059.7	R^STS*PIIGS*PPVR^	943	Pat11	Protein PAT1 homolog 1	1.3122
IPI:IPI00309059.7	R^STS*PIIGS*PPVR^	944	Pat11	Protein PAT1 homolog 1	1.3122
IPI:IPI00112593.2	S*T*S*S*PK@	945	Spert	Isoform 2 of Spermatid-associated protein	1.3085
IPI:IPI00129264.1	ATSR^PINLGPSS*PNTEIHW TPYR^	946	Sorbs3	Vinexin	1.3056
IPI:IPI00129264.1	ATSRPINLGPSS*PNTEIHW TPYR	947	Sorbs3	Vinexin	1.3056
IPI:IPI00116442.1	TR^LAS*ES*ANDDNEDS	948	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	1.3036
IPI:IPI00313307.3	SYQNS*PSS*EDGIRPLPEY STEK	949	Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1	1.298
IPI:IPI00313307.3	SYQNS*PSS*EDGIR^PLPEY STEK@	950	Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1	1.298

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00313307.3	SYQNS*PSS*EDGIR*PLPEY STEK@	951	Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1	1.298
IPI:IPI00330773.3	ASYSGTS*PSHSFISGEPDR [^]	952	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.2944
IPI:IPI00330773.3	ASYSGTS*PSHSFISGEPDR	953	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.2944
IPI:IPI00330773.3	ASYSGTS*PSHSFISGEPDR [^]	954	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.2944
IPI:IPI00153986.2	GTS*R*PGTPS*AEAASTSS TLR [^]	955	Gtf2f1	General transcription factor IIF subunit 1	1.2876
IPI:IPI00153986.2	GTSRPGT*PS*AEAASTSS TLR	956	Gtf2f1	General transcription factor IIF subunit 1	1.2876
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTIFS*TPGGTR*IIYDR [^] K@	957	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.2862
IPI:IPI00221581.1	SR*TGS*ESSQTGASATSG R [^]	958	Eif4b	Eukaryotic translation initiation factor 4B	1.2845
IPI:IPI00454104.1	TTEAPCSPGS*QQPPS*PDE LPANVK@	959	Scrib	Isoform 1 of Protein LAP4	1.2842
IPI:IPI00454104.1	TTEAPCS*PGSQPPS*PDE LPANVK	960	Scrib	Isoform 1 of Protein LAP4	1.2842
IPI:IPI00454104.1	TTEAPCS*PGSQPPS*PDE LPANVK	961	Scrib	Isoform 1 of Protein LAP4	1.2842
IPI:IPI00320905.7	LGEQGPEPGTPPQT*PT*P PST*PPLAK@	962	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	1.2828
IPI:IPI00381495.5	TVSS*PIPYTPS*PSSSR*PIS *PGLSYASHTVGFT*PPTS*L TR [^]	963	Ccdc6	coiled-coil domain containing 6	1.2808
IPI:IPI00381495.5	TVSS*PIPYTPS*PSS*SRPIS PGLSYASHTVGFT*PPTSLT R	964	Ccdc6	coiled-coil domain containing 6	1.2808
IPI:IPI00381495.5	TVSS*PIPYTPS*PSSSRPIS PGLS*YASHTVGFT*PPTSL TR	965	Ccdc6	coiled-coil domain containing 6	1.2808
IPI:IPI00309059.7	RSTS*PIIGS*PPVR	966	Pat1	Protein PAT1 homolog 1	1.2745
IPI:IPI00336973.2	GLNLDGT*PALSTLGGFS*P ASK@PS*SPR [^]	967	Ccn1	Isoform 1 of Cyclin-L1	1.273
IPI:IPI00336973.2	GLNLDGT*PALSTLGGFS*P ASKPSS*PR	968	Ccn1	Isoform 1 of Cyclin-L1	1.273
IPI:IPI00309059.7	R*STS*PIIGS*PPVR [^]	969	Pat1	Protein PAT1 homolog 1	1.2725
IPI:IPI00309059.7	R*STS*PIIGS*PPVR [^]	970	Pat1	Protein PAT1 homolog 1	1.2725
IPI:IPI00309059.7	RSTS*PIIGS*PPVR	971	Pat1	Protein PAT1 homolog 1	1.2725
IPI:IPI00309059.7	R*STS*PIIGS*PPVR [^]	972	Pat1	Protein PAT1 homolog 1	1.2723
IPI:IPI00309059.7	RSTS*PIIGS*PPVR	973	Pat1	Protein PAT1 homolog 1	1.2723
IPI:IPI00309059.7	R*STS*PIIGS*PPVR [^]	974	Pat1	Protein PAT1 homolog 1	1.2723
IPI:IPI00309059.7	RSTS*PIIGS*PPVR	975	Pat1	Protein PAT1 homolog 1	1.2723
IPI:IPI00129264.1	ATSR*PINLGPS*SPNTEIHW TPYR [^]	976	Sorbs3	Vinexin	1.2719

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAIP GVTSPSTDEPPM#QASQSQ LPSSPEDK@	977	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.2719
IPI:IPI00115492.1	HSLSSESQAPEDIAPPGS*S PHANR^	978	Eps8l2	Isoform 1 of Epidermal growth factor receptor kinase substrate 8-like protein 2	1.2678
IPI:IPI00381495.5	TVSS*PIPYTPS*PSSSR^PIS *PGLSYASHTVGFT*PPTSL TR^	979	Ccdc6	coiled-coil domain containing 6	1.2638
IPI:IPI00381495.5	TVSS*PIPYTPS*PSSSRPIS* PGLSYASHTVGFT*PPTSLT R	980	Ccdc6	coiled-coil domain containing 6	1.2638
IPI:IPI00381495.5	TVSS*PIPYTPS*PSSSRPIS* PGLSYASHTVGFT*PPTSLT R	981	Ccdc6	coiled-coil domain containing 6	1.2638
IPI:IPI00381495.5	TVSS*PIPYTPSPSS*SR^PIS PGLSYAS*HTVGFTPPTS*L TR^	982	Ccdc6	coiled-coil domain containing 6	1.2638
IPI:IPI00133917.1	YAQGFLPEK@PPQQDHTT* TTDSEMEEPYLQESK@EE GTPK@	983	Phc2	Isoform 1 of Polyhomeotic-like protein 2	1.2624
IPI:IPI00227209.3	R^LS*S*TSASGHSVR^	984	Prkd2	Serine/threonine-protein kinase D2	1.2605
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFST*TPGGTR^	985	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.2599
IPI:IPI00230368.1	SSS*LGNS*PDR^GPLR^PF VPEQELLR^	986	261011 OG12Ri k	Isoform 1 of UPF0635 protein C6orf134 homolog	1.2571
IPI:IPI00845596.1	LFS*QGQDVSDK@VK@	987	Mlt4	Isoform 3 of Afadin	1.2551
IPI:IPI00378026.4	VSSPSCDS*QGLHPEEAPS* SEPQSPVAQTLGWACSTP LPLVSR^	988	Nacc1	Nucleus accumbens-associated protein 1	1.253
IPI:IPI00458460.1	SLS*ESS*VMDR^	989	Zfp106	Isoform 1 of Zinc finger protein 106	1.2522
IPI:IPI00399440.2	HLEDAGST*PS*IGENDLK@ FPK@	990	Rictor	Isoform 1 of Rapamycin-insensitive companion of mTOR	1.2463
IPI:IPI00109318.1	TVAISDAAQLPQDYCTT*PG GTLFST*TPGGTR^IYDR^K @	991	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	1.2423
IPI:IPI00109318.1	TVAISDAAQLPQDYCTT*PG GTLFST*TPGGTRIYDRK	992	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	1.2423
IPI:IPI00379682.1	R^ANTLS*HFPVECPAPPEP AQ*SPGVSQR^	993	Tbc1d1	Isoform 1 of TBC1 domain family member 1	1.2355
IPI:IPI00454104.1	TTEAPCS*PGSQPPS*PDE LPANVK	994	Scrib	Isoform 1 of Protein LAP4	1.2352
IPI:IPI00454104.1	TTEAPCS*PGSQPPS*PDE LPANVK@	995	Scrib	Isoform 1 of Protein LAP4	1.2352
IPI:IPI00454104.1	TTEAPCS*PGSQPPS*PDE LPANVK@	996	Scrib	Isoform 1 of Protein LAP4	1.2352

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00109318.1	TVAISDAAQLPQDYCT*TPG GTLFSTT*PGGTR^IYDR^K @	997	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	1.2336
IPI:IPI00378438.6	S*QSVPGAWPGASPLSSQP LLGSS*R^QSHPLTQSR^	998	Tns1	tensin 1	1.2303
IPI:IPI00118143.1	KQT*PPAS*PS*PQIEDRPP SS*PIYEDAAPFKAEPSYR	999	Ctnn	Src substrate cortactin	1.2254
IPI:IPI00330773.3	ASYSGTSPS*HSFISGEPDR ^	1000	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.2251
IPI:IPI00330773.3	ASYSGTS*PSHSFISGEPDR ^	1001	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.2251
IPI:IPI00127071.3	GATEEEQQDS*GS*EPR^G DEDDIPLGPQSNVSLLDQH QHLLK@	1002	Ddx41	Probable ATP-dependent RNA helicase DDX41	1.223
IPI:IPI00153986.2	GTSR^PGT*PS^AEAASTSS TLR^	1003	Gtf2f1	General transcription factor IIF subunit 1	1.2226
IPI:IPI00153986.2	GTS*R^PGT*PSAEAASTSS TLR^	1004	Gtf2f1	General transcription factor IIF subunit 1	1.2226
IPI:IPI00153986.2	GTS*RPGT*PSAEAASTSS LR	1005	Gtf2f1	General transcription factor IIF subunit 1	1.2226
IPI:IPI00117277.2	R^GS*GDTISMDTEASIR^	1006	Lrrfp1	Isoform 2 of Leucine-rich repeat flightless-interacting protein 1	1.2213
IPI:IPI00661508.3	LYSLLGIDLTAPSNNS*SPR^ DS*PCK@ENK@	1007	Sbno1	Isoform 2 of Protein strawberry notch homolog 1	1.2147
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT *SPTSDEPPMQASQSQLPS S*PEDK	1008	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.2095
IPI:IPI00116442.1	TRLAS*ES*ANDDNEDS	1009	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	1.1963
IPI:IPI00116442.1	TRLAS*ES*ANDDNEDS	1010	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	1.1963
IPI:IPI00929761.1	R^CPS*QSSSR^PATGISQP PTTPTGQATR^	1011	Larp1	Isoform 2 of La-related protein 1	1.1959
IPI:IPI00320905.7	LGEQGPEPGPT*PPQT*PT* PPS*TPPLAK@	1012	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	1.1918
IPI:IPI00420509.2	S*IEDLQPPNALSAPFTNSLA R	1013	Fmn13	Isoform 1 of Fomin-like protein 3	1.1892
IPI:IPI00153986.2	GTS*RPGT*PSAEAASTSS LR	1014	Gtf2f1	General transcription factor IIF subunit 1	1.1888
IPI:IPI00153986.2	GT*SR^PGT*PSAEAASTSS TLR^	1015	Gtf2f1	General transcription factor IIF subunit 1	1.1888
IPI:IPI00153986.2	GTS*RPGT*PSAEAASTSS LR	1016	Gtf2f1	General transcription factor IIF subunit 1	1.1888
IPI:IPI00153986.2	GTS*R^PGTPS^AEAASTSS TLR^	1017	Gtf2f1	General transcription factor IIF subunit 1	1.1888
IPI:IPI00320905.7	LGEQGPEPGPT*PPQT*PT* PPST*PPLAK	1018	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	1.1882
IPI:IPI00330773.3	ASYSGTS*PSHSFISGEPDR	1019	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.1879

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00330773.3	ASYSGTSPS*HSFISGEPDR ^Λ	1020	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.1879
IPI:IPI00330773.3	ASYSGTS*PSHSFISGEPDR ^Λ	1021	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.1879
IPI:IPI00330773.3	SDELLGDLTRT*PPSSSAFLK	1022	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.185
IPI:IPI00330773.3	SDELLGDLTR ^Λ T*PPSSSAFLK@	1023	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.185
IPI:IPI00340860.5	TAS*EGS*EAETPEAPK@QPAK@K@	1024	Larp7	Isoform 1 of La-related protein 7	1.1845
IPI:IPI00340860.5	TAS*EGS*EAETPEAPK@QPAK@K@	1025	Larp7	Isoform 1 of La-related protein 7	1.1845
IPI:IPI00129264.1	ATSRPINLGPSS*PNTEIHWTPYR	1026	Sorbs3	Vinexin	1.175
IPI:IPI00129264.1	ATSR ^Λ PINLGPSS*PNTEIHWTPYR ^Λ	1027	Sorbs3	Vinexin	1.175
IPI:IPI00129264.1	ATSRPINLGPS*SPNTEIHWTPYR	1028	Sorbs3	Vinexin	1.175
IPI:IPI00381495.5	T*VSSPIPYTPS*PSSS* ^Λ PI SPGLSYASHTVGFT*PPTSLTR ^Λ	1029	Ccdc6	coiled-coil domain containing 6	1.1749
IPI:IPI00153986.2	GTS* ^Λ R ^Λ PGT*PSAEAASTSSLR ^Λ	1030	Gtf2f1	General transcription factor IIF subunit 1	1.1748
IPI:IPI00153986.2	GTS*RPGT*PSAEAASTSSLR	1031	Gtf2f1	General transcription factor IIF subunit 1	1.1748
IPI:IPI00153986.2	GTS* ^Λ R ^Λ PGT*PSAEAASTSSLR ^Λ	1032	Gtf2f1	General transcription factor IIF subunit 1	1.1748
IPI:IPI00153986.2	GTS*RPGT*PSAEAASTSSLR	1033	Gtf2f1	General transcription factor IIF subunit 1	1.1748
IPI:IPI00136572.4	YEENPAWPGTSTHNGPNGFSQIMDETPNVSK@SS*PTGFGIK@	1034	Zc3hav1	Isoform 1 of Zinc finger CCCH-type antiviral protein 1	1.1738
IPI:IPI00225062.2	GSLS* ^Λ R ^Λ SS* ^Λ S*PVTELTAR ^Λ	1035	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.1701
IPI:IPI00133685.1	S*LPVSVPVWAFK@	1036	Akt1s1	Proline-rich AKT1 substrate 1	1.1669
IPI:IPI00133685.1	S*LPVSVPVWAFK@	1037	Akt1s1	Proline-rich AKT1 substrate 1	1.1669
IPI:IPI00133685.1	S*LPVSVPVWAFK@	1038	Akt1s1	Proline-rich AKT1 substrate 1	1.1669
IPI:IPI00225062.2	GSLS*RSS* ^Λ S*PVTELTAR	1039	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.1669
IPI:IPI00225062.2	GSLS* ^Λ R ^Λ SS* ^Λ S*PVTELTAR ^Λ	1040	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.1669
IPI:IPI00929786.1	S*LPTTVPESPNYR ^Λ	1041	Larp1	Isoform 1 of La-related protein 1	1.1655
IPI:IPI00929786.1	S*LPTTVPESPNYR	1042	Larp1	Isoform 1 of La-related protein 1	1.1655
IPI:IPI00116442.1	TRLAS*ES*ANDDNEDS	1043	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	1.1626
IPI:IPI00116442.1	TR ^Λ LAS*ES*ANDDNEDS	1044	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	1.1626

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00116442.1	TR ¹ LAS*ES*ANDDNEDS	1045	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	1.1626
IPI:IPI00116442.1	TRLAS*ES*ANDDNEDS	1046	Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2	1.1626
IPI:IPI00317599.3	SQEDEEEIST*SPGVSEFVS DAFDTCSLNQEDLRK	1047	Syap1	Synapse-associated protein 1	1.1567
IPI:IPI00317599.3	SQEDEEEIST*PGVSEFVS DAFDTCSLNQEDLR ¹ K@	1048	Syap1	Synapse-associated protein 1	1.1567
IPI:IPI00317599.3	SQEDEEEIST*PGVSEFVS DAFDTCSLNQEDLR ¹ K@	1049	Syap1	Synapse-associated protein 1	1.1567
IPI:IPI00317599.3	SQEDEEEIST*PGVSEFVS DAFDTCSLNQEDLRK	1050	Syap1	Synapse-associated protein 1	1.1567
IPI:IPI00126124.2	T ¹ FSECS*YPETEEAEALP GR ¹	1051	St5	Isoform 1 of Suppression of tumorigenicity 5	1.1565
IPI:IPI00312600.2	LSSDENSNPDLS*GDENDD AVSIESGTNTER ¹ PDTPTNT PNAPGR ¹ K@	1052	Eed	Isoform 1 of Polycomb protein EED	1.1553
IPI:IPI00312600.2	LSSDENSNPDLS*GDENDD AVSIESGTNTERPDTPTNTP NAPGRK	1053	Eed	Isoform 1 of Polycomb protein EED	1.1553
IPI:IPI00229990.7	RPPGDVLETFNFLENADDS* DEEENDMIEGIPEGKDK	1054	Strm3	Striatin-3	1.1544
IPI:IPI00229990.7	R ¹ PPGDVLETFNFLENADDS *DEEENDMIEGIPEGK@DK @	1055	Strm3	Striatin-3	1.1544
IPI:IPI00121418.1	DGEGPDNLEPACPLSLPLQ GNHTAADMYLS*PLRS*PK	1056	Rb1	Retinoblastoma-associated protein	1.152
IPI:IPI00121418.1	DGEGPDNLEPACPLSLPLQ GNHTAADMYLS*PLR ¹ S*PK @	1057	Rb1	Retinoblastoma-associated protein	1.152
IPI:IPI00121418.1	DGEGPDNLEPACPLSLPLQ GNHTAADMYLS*PLR ¹ S*PK @	1058	Rb1	Retinoblastoma-associated protein	1.152
IPI:IPI00136386.2	GDT ¹ S*ET*ASAT*PAY ¹ R ¹	1059	Tssk4	Isoform 2 of Testis-specific serine/threonine-protein kinase 4	1.15
IPI:IPI00515576.5	TGVNENTVVSAGKDLSTS*P KPS*PIPS*PVLGQKPNASQ SLLAWCR	1060	Ehbp1	Isoform 2 of EH domain-binding protein 1	1.1492
IPI:IPI00420143.1	STSSVDSILSSSHS*S*DTL CNADSAQIPLANGLDHSIT SSR ¹	1061	Usp47	Isoform 2 of Ubiquitin carboxyl-terminal hydrolase 47	1.1474
IPI:IPI00109318.1	TVAISDAAQLPQDYCTT*PG GTLFSTT*PGGTRIYDRK	1062	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	1.147
IPI:IPI00109318.1	TVAISDAAQLPQDYCT*TPG GTLFSTT*PGGTR ¹ IYDR ¹ K @	1063	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	1.147
IPI:IPI00330773.3	SDELLGDLTR ¹ T*PPSSSAA FLK@	1064	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.1466
IPI:IPI00330773.3	SDELLGDLTRT*PPSSSAAF LK	1065	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.1466

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00229697.3	GT*FSDQELDAQS*LDEDD SLQHAVHPALNRFS*PS*PR	1066	-	68 kDa protein	1.1465
IPI:IPI00133685.1	S*LPVSVPVWAFK@	1067	Akt1s1	Proline-rich AKT1 substrate 1	1.1417
IPI:IPI00133685.1	S*LPVSVPVWAFK	1068	Akt1s1	Proline-rich AKT1 substrate 1	1.1417
IPI:IPI00133685.1	S*LPVSVPVWAFK@	1069	Akt1s1	Proline-rich AKT1 substrate 1	1.1417
IPI:IPI00133685.1	S*LPVSVPVWAFK	1070	Akt1s1	Proline-rich AKT1 substrate 1	1.1417
IPI:IPI00130920.1	SLMSS*PEDLTk@DFEELK @AEEIDVAK@	1071	Mtap1b	Microtubule-associated protein 1B	1.1401
IPI:IPI00130920.1	SLMSSPEDLT*KDFEELKAE EIDVAK	1072	Mtap1b	Microtubule-associated protein 1B	1.1401
IPI:IPI00828355.1	GTLVHTT*SDSDS*EDGDQE AEESSSLDTQK@PTTVVLC EPSQEPK@	1073	Fmn1	Isoform 5 of Formin-1	1.1401
IPI:IPI00381495.5	T*VSSPIPYTPSPS*SSR^PIS PGLSYASHT*VGFT*PPTSL TR^	1074	Ccdc6	coiled-coil domain containing 6	1.1376
IPI:IPI00929761.1	CPS*QSSSRPATGISQPPTT PTGQATR	1075	Larp1	Isoform 2 of La-related protein 1	1.1372
IPI:IPI00379682.1	R^ANTLS*HFPVECPAPPEP AQSS*PGVSQR^	1076	Tbc1d1	Isoform 1 of TBC1 domain family member 1	1.1351
IPI:IPI00379682.1	RANT*LSHFPVECPAPPEPA QSS*PGVSQR	1077	Tbc1d1	Isoform 1 of TBC1 domain family member 1	1.1351
IPI:IPI00381495.5	T*VSSPIPYTPSPSS*SR^PIS PGLS*YASHTVGFT*PPTSL TR^	1078	Ccdc6	coiled-coil domain containing 6	1.1342
IPI:IPI00381495.5	T*VSSPIPYTPS*PSSSRPIS PGLSYASHT*VGFT*PPTSL TR	1079	Ccdc6	coiled-coil domain containing 6	1.1342
IPI:IPI00225062.2	M#SCFS*R^PSMS*PTPLDR ^	1080	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.1322
IPI:IPI00133374.5	EVDPTGELQS*LQMPES*E GPS*SLDPSQEGPTGLK@	1081	Sqstm1	Isoform 1 of Sequestosome-1	1.1315
IPI:IPI00133374.5	EVDPTGELQS*LQMPES*E GPS*SLDPSQEGPTGLK@	1082	Sqstm1	Isoform 1 of Sequestosome-1	1.1315
IPI:IPI00133374.5	EVDPTGELQS*LQMPES*E GPS*SLDPSQEGPTGLK@	1083	Sqstm1	Isoform 1 of Sequestosome-1	1.1315
IPI:IPI00133374.5	EVDPTGELQS*LQMPES*E GPS*SLDPSQEGPTGLK	1084	Sqstm1	Isoform 1 of Sequestosome-1	1.1315
IPI:IPI00465879.2	LCS*SSS*SDTSPR^	1085	Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK	1.1277
IPI:IPI00468802.5	YEMACIAIDAFNLPSSHLR^ PITDS*PVIGAQR^PK@	1086	Mat2b	Isoform 1 of Methionine adenosyltransferase 2 subunit beta	1.1262
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDD FR^R^	1087	Tox4	TOX high mobility group box family member 4	1.1209
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDD FR^R^	1088	Tox4	TOX high mobility group box family member 4	1.1209
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDD FRR	1089	Tox4	TOX high mobility group box family member 4	1.1209

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00127554.1	R^FS*VQEQDWETT*PPK@K@	1090	Emg1	Probable ribosome biogenesis protein NEP1	1.1179
IPI:IPI00127554.1	RFS*VQEQDWET*TPPKK	1091	Emg1	Probable ribosome biogenesis protein NEP1	1.1179
IPI:IPI00459443.5	GEGVSQVGPGTTPAPES*P RKPISGVQGNDPGISLPQR	1092	Tnks1b p1	182 kDa tankyrase-1-binding protein	1.1175
IPI:IPI00225062.2	MELGT*PLR^HSGSTS*PYP K@	1093	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.1138
IPI:IPI00225062.2	MELGT*PLRHSGST*SPYPK	1094	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.1138
IPI:IPI00225062.2	MELGT*PLR^HSGSTS*PYP K@	1095	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.1138
IPI:IPI00127764.2	EIS*QSR^NPS*VSEHLPDEK @	1096	Pcm1	Isoform 1 of Pericentriolar material 1 protein	1.1126
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAIP GVTSPTSDEPPMQASQSQL PSS*PEDK@	1097	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.1074
IPI:IPI00116923.2	SGFAR^PGDLEFEDFS*QVI NR^VPSDSSLGT*PDGR^PE LR^	1098	Trip10	Isoform 3 of Cdc42-interacting protein 4	1.1069
IPI:IPI00121335.1	CGS*PSDSSTSEMMEVAVN K@	1099	LOC10048123;Akt2	RAC-beta serine/threonine-protein kinase	1.1028
IPI:IPI00356608.4	VGS*LT*PPS*SPK@	1100	Aak1	Isoform 2 of AP2-associated protein kinase 1	1.1012
IPI:IPI00828461.1	GPPDFS*SDEER^EPT*PVL GSGASVGR^	1101	Tmpo	thymopoietin isoform delta	1.1001
IPI:IPI00381495.5	TVSSPIPYTPS*PS*SSR^PIS PGLSYASHTVGFTPTSLTR ^	1102	Ccdc6	coiled-coil domain containing 6	1.0993
IPI:IPI00381495.5	TVSSPIPYTPS*PSSSRPISP GLSY*ASHTVGFTPTSLTR	1103	Ccdc6	coiled-coil domain containing 6	1.0993
IPI:IPI00127554.1	R^FS*VQEQDWETT*PPK@K @	1104	Emg1	Probable ribosome biogenesis protein NEP1	1.0981
IPI:IPI00127554.1	R^FS*VQEQDWETT*PPK@K @	1105	Emg1	Probable ribosome biogenesis protein NEP1	1.0981
IPI:IPI00121251.7	LSTT*PSPTNS*LHEDGVDD FRR	1106	Tox4	TOX high mobility group box family member 4	1.0844
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDD FR^R^	1107	Tox4	TOX high mobility group box family member 4	1.0844
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDD FR^R^	1108	Tox4	TOX high mobility group box family member 4	1.0844
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAIP GVTSPTSDEPPMQASQSQL PSS*PEDK@	1109	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.0842
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT S*PTSDEPPMQASQSQLPS SPEDK	1110	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.0842
IPI:IPI00169771.1	S^SASGTHSES*PEK@LQC PVTEPGQGILENTGTEPGE	1111	BC031781	UPF0667 protein C1orf55 homolog	1.0823

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
	TSDK@ECNER^				
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAIP GVTSPTSDEPPMQASQSQL PSS*PEDK@	1112	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.0778
IPI:IPI00127764.2	EISQS*RNPS*VSEHLPDEK	1113	Pcm1	Isoform 1 of Pericentriolar material 1 protein	1.074
IPI:IPI00112597.1	SQSS*EGVSSLSSS*PSNSL ETQSQSLSR^	1114			1.0712
IPI:IPI00112597.1	SQS*SEGVSSLSSS*PSNSL ETQSQSLSR^	1115			1.0712
IPI:IPI00225062.2	S*RSSSPDS*KMELGTPLR	1116	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1.0696
IPI:IPI00330773.3	ASYSGTS*PSHS*FISGEPD R^	1117	Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2	1.0688
IPI:IPI00330246.2	WAAHGTS*PEDFSLTLGAR^	1118	Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1	1.068
IPI:IPI00122594.4	NGVSLFNSPK@T*EQPSPV VHSFPHPELPEAFVGTPI SN TSQR^	1119	Ahctf1	AT-hook-containing transcription factor 1	1.0661
IPI:IPI00122594.4	NGVSLFNS*PKTEQPSPVV HSFPHPELPEAFVGTPI SN TSQR	1120	Ahctf1	AT-hook-containing transcription factor 1	1.0661
IPI:IPI00122594.4	NGVSLFNSPK@TEQPSPVV HS*FPHPELPEAFVGTPI SN TSQR^	1121	Ahctf1	AT-hook-containing transcription factor 1	1.0661
IPI:IPI00121418.1	DGEGPDNLEPACPLSLPLQ GNHTAADMYLS*PLR^S*PK @	1122	Rb1	Retinoblastoma-associated protein	1.0618
IPI:IPI00121418.1	DGEGPDNLEPACPLSLPLQ GNHTAADMYLS*PLRS*PK	1123	Rb1	Retinoblastoma-associated protein	1.0618
IPI:IPI00320905.7	LGEQGPEPGPT*PPQT*PT* PPST*PPLAK	1124	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	1.0618
IPI:IPI00403116.9	NGS*PVPVDPDISQEPDGPAL S*GGEEDAEDGAEPLEVAL EPAEPR^	1125	Ncaph2	Isoform 3 of Condensin-2 complex subunit H2	1.0598
IPI:IPI00403116.9	NGS*PVPVDPDISQEPDGPAL S*GGEEDAEDGAEPLEVAL EPAEPR	1126	Ncaph2	Isoform 3 of Condensin-2 complex subunit H2	1.0598
IPI:IPI00403116.9	NGS*PVPVDPDIS*QEPDGPAL LSGGEEDAEDGAEPLEVAL EPAEPR^	1127	Ncaph2	Isoform 3 of Condensin-2 complex subunit H2	1.0598
IPI:IPI00230237.1	TAVTATNVSAHGSQANS*P STPNSAGGY*PSPCYQPDR ^R^	1128	Pbx1	Isoform PBX1b of Pre-B-cell leukemia transcription factor 1	1.054
IPI:IPI00421139.8	SS*SHLDPAATPHSTLQGSS AGTPEHPSVIDPLMEQDEG PGTPPAK@	1129	Dlg5	Putative uncharacterized protein	1.0498
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDD FRR	1130	Tox4	TOX high mobility group box family member 4	1.0342

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDD FR ^A	1131	Tox4	TOX high mobility group box family member 4	1.0342
IPI:IPI00121431.4	S*INSELDQFPSELEK	1132	Hells	Isoform 1 of Lymphocyte-specific helicase	1.0332
IPI:IPI00121431.4	S*INSELDQFPSELEK@	1133	Hells	Isoform 1 of Lymphocyte-specific helicase	1.0332
IPI:IPI00121431.4	S*INSELDQFPSELEK@	1134	Hells	Isoform 1 of Lymphocyte-specific helicase	1.0332
IPI:IPI00454039.3	VGS*EHSLDPPGK	1135	ErbB2ip	Isoform 1 of Protein LAP2	1.0307
IPI:IPI00109318.1	TVAISDAAQLPQDYCTT*PG GTLFSTT*PGGTR ^A IIYDR ^A	1136	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	1.0271
IPI:IPI00109318.1	TVAISDAAQLPQDYCTT*PG GTLFSTT*PGGTRIIYDR	1137	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	1.0271
IPI:IPI00226228.5	ANNAGASIYPTGPADPCPP ASES*S*PEQWQSPEDKPQ DIHSQGEAR	1138	Azi1	5-azacytidine-induced protein 1	1.0268
IPI:IPI00317401.6	AES*PETSVESTQST*PQK @	1139	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.0246
IPI:IPI00317401.6	AES*PETSVESTQST*PQK @	1140	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.0246
IPI:IPI00317401.6	AES*PETSVESTQST*PQK	1141	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1.0246
IPI:IPI00113389.5	HNLFEDNM#ALPSES ^V SS ^L TDLK	1142	Fam129 a	Protein Niban	1.0232
IPI:IPI00318938.6	NS*PVAK@T*PPK@DLPAIP GVTSP ^T SDEPPM#QASQSQ LPSSPEDK@	1143	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.0227
IPI:IPI00463074.6	SRS*S*PSTDHYSQEV ^P VE ^P NR	1144	Shroom 2	shroom family member 2	1.0176
IPI:IPI00463074.6	SRS*S*PSTDHYSQEV ^P VE ^P NR	1145	Shroom 2	shroom family member 2	1.0176
IPI:IPI00463074.6	SR ^A S*S*PSTDHYSQEV ^P VE ^P PNR ^A	1146	Shroom 2	shroom family member 2	1.0176
IPI:IPI00553798.2	S*NS*FSDER ^A EFSAPSTPT GTLEFAGGDAK@	1147	Ahnak	AHNAK nucleoprotein isoform 1	1.0143
IPI:IPI00553798.2	S*NS*FSDER ^A EFSAPSTPTG TLEFAGGDAK	1148	Ahnak	AHNAK nucleoprotein isoform 1	1.0143
IPI:IPI00553798.2	S*NS*FSDER ^A EFSAPSTPTG TLEFAGGDAK	1149	Ahnak	AHNAK nucleoprotein isoform 1	1.0143
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPT*SDEPPMQASQSQLPS S*PEDK	1150	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1.0129
IPI:IPI00127131.6	GPS*PSPVGS*PASVAQSR ^A	1151	Arid1a	AT rich interactive domain 1A	1.0107
IPI:IPI00113389.5	HNLFEDNMALPSES ^V SSLT DLK@TAMGS*NQAS*PAR ^A R ^A	1152	Fam129 a	Protein Niban	1.0048
IPI:IPI00113389.5	HNLFEDNMALPSES ^V SSLT* DLK@TAMGS*NQAS*PAR ^A R ^A	1153	Fam129 a	Protein Niban	1.0048

Reference	Ascore Seq	SEQ ID NO:	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00454109.2	FPPST*PSEVLS*PTEDPRS*PPACSSSSSSSLFSAVVAR	1154	Erf	ETS domain-containing transcription factor ERF	1.0039
IPI:IPI00120095.2	CDGS*PR^T*PPS*TPPATANLSADDDFQNTDLR^	1155	Samhd1	SAM domain and HD domain-containing protein 1	1.0027
IPI:IPI00117229.3	TS*PAGGTWSSVVGVPRA	1156	Atxn2	ataxin 2	1.0015
IPI:IPI00117229.3	TS*PAGGTWSSVVGVPRA	1157	Atxn2	ataxin 2	1.0015
IPI:IPI00320594.5	SQDSYPGS*PSLS*PR	1158	Ranbp10	Ran-binding protein 10	1.0009
IPI:IPI00320594.5	SQDSYPGS*PSLS*PR^	1159	Ranbp10	Ran-binding protein 10	1.0009
IPI:IPI00320594.5	SQDSYPGS*PSLS*PR^	1160	Ranbp10	Ran-binding protein 10	1.0009
IPI:IPI00320594.5	SQDS*YPGS*PSLSPR	1161	Ranbp10	Ran-binding protein 10	1.0009
IPI:IPI00320594.5	SQDSYPGS*PSLS*PR^	1162	Ranbp10	Ran-binding protein 10	1.0009
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDDFR^R^	1163	Tox4	TOX high mobility group box family member 4	1.0005
IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDDFRR	1164	Tox4	TOX high mobility group box family member 4	1.0005

Table 7. Phosphopeptides whose intensities decrease after rapamycin treatment (Rapamycin screen).

Table 8:

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
Ku (light cells: control (rapamycin treated); heavy cells: treated with rapamycin+Ku-0063794. L, light; H, heavy)					
IPI:IPI00648918.3	DQEEELDEQAGS*IQM#LEQLK	1165	Myo18a	Isoform 4 of Myosin-XVIIIa	-7.171
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1166	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-7.159
IPI:IPI00318938.6	VALGDGVQLPPGDYS*TT*P GGTLFSTT*PGGTR	1167	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-7.127
IPI:IPI00622700.2	TAPPVLPTGYDS*EEEEESR ^PMSYDEK@	1168	Brd2	Isoform 2 of Bromodomain-containing protein 2	-6.823
IPI:IPI00458153.2	ENPPSPPT*SPAAPQPR^	1169	633057 7E15Ri k	Uncharacterized protein C10orf78 homolog	-6.819
IPI:IPI00454090.1	DSVDLQS*LM#TEM#NR	1170	Best3	Bestrophin-3	-6.498
IPI:IPI00274140.4	LSPFFTLDL*PTDDKSSKP SSFTEK	1171	Grit	Isoform 2 of Rho/Cdc42/Rac GTPase- activating protein RICS	-6.465
IPI:IPI00929786.1	SLPT*TVPES*PNYR	1172	Larp1	Isoform 1 of La-related protein 1	-6.159
IPI:IPI00224969.2	VAPS*MSSLNS*LAS*S*CFD LTDVSLNTEAGDSR	1173	Fam62c	Isoform 1 of Extended synaptotagmin-3	-6.023
IPI:IPI00929786.1	S*LPTTVPES*PNYR	1174	Larp1	Isoform 1 of La-related protein 1	-5.98
IPI:IPI00458039.3	IFTEANLVS*VGS*KK	1175	Mdn1	Midasin homolog	-5.907
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPMQASQSQLPS* SPEDK	1176	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-5.874
IPI:IPI00130920.1	TLEVVSQS SVTGS*AGHTP YYQS*PTDEK	1177	Mtap1b	Microtubule-associated protein 1B	-5.86
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1178	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-5.685
IPI:IPI00270767.3	VVK@EDGVMS*PEK@	1179	Rtn4	Isoform 2 of Reticulon-4	-5.681
IPI:IPI00121430.2	DLKPETDYVVNVY*S*VVED EYSEPLKGT*EK	1180	Col12a 1	Isoform 1 of Collagen alpha-1(XII) chain	-5.655
IPI:IPI00169506.7	QAVY*Y*LTQAT*DGGNQS TT*TALEITLLDINDNPPVVR	1181	Pcdh24	Pcdh24 protein	-5.499
IPI:IPI00133685.1	LNT*SDFQK	1182	Akt1s1	Proline-rich AKT1 substrate 1	-5.419
IPI:IPI00876080.1	LPDLRS*R	1183	Gpr157	Putative uncharacterized protein (Fragment)	-5.334
IPI:IPI00850983.1	TPGPPS*SQGSPVDTQPAA QK	1184	Synj1	similar to mKIAA0910 protein	-5.321
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPMQASQSQLPSS *PEDK	1185	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-4.991
IPI:IPI00282808.7	T*PGVPKQKPCSPLS*EPDA FLK	1186	Zfp318	zinc finger protein 318 isoform 1	-4.923
IPI:IPI00133374.5	EVDPTGELQSLQMPESSEG PS*SLDPSQEGPTGLK@	1187	Sqstm1	Isoform 1 of Sequestosome-1	-4.888
IPI:IPI00133374.5	EVDPTGELQSLQMPESSEG PS*SLDPSQEGPTGLK@	1188	Sqstm1	Isoform 1 of Sequestosome-1	-4.882

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00133685.1	LNT*SDFQK	1189	Akt1s1	Proline-rich AKT1 substrate 1	-4.871
IPI:IPI00623114.5	DMPAAGS*LGSSS*R	1190	Fat1	FAT tumor suppressor homolog 1	-4.85
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGT*LFSTTPGGTR	1191	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-4.78
IPI:IPI00125442.4	VPMVSS*QPTS*SM#VPPPI KPLNR	1192	Alpk3	myocyte induction differentiation originator	-4.621
IPI:IPI00380641.3	KLPVVSS*VVK	1193	Zc3h14	Isoform 2 of Zinc finger CCCH domain-containing protein 14	-4.368
IPI:IPI00338745.4	QADVADQQTELPAENGET ENQSPAS*EEEKEAK	1194	Hmgn1; LOC10 004439 1	Non-histone chromosomal protein HMG-14	-4.324
IPI:IPI00338745.4	QADVADQQTELPAENGET ENQS*PASEEEKEAK	1195	Hmgn1; LOC10 004439 1	Non-histone chromosomal protein HMG-14	-4.324
IPI:IPI00271998.4	GPNS*PPPGMPLR	1196	231005 7M21Ri k	Uncharacterized protein C10orf88 homolog	-4.316
IPI:IPI00338976.3	FTISAIS*K	1197	Fcrls	Fc receptor-like protein 2 scavenger isoform	-4.254
IPI:IPI00352984.4	IVHFS*VNACLT*PICSLHHV AVTT*VEGIGNTKK	1198	Xdh	Xanthine dehydrogenase/oxidase	-4.21
IPI:IPI00318938.6	VALGDGVQLPPGDYS*TTP GGTLFSTT*PGGTR	1199	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-4.196
IPI:IPI00330246.2	K@GSFS*GR*LS*PAYSLGS LTGASPR^	1200	Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1	-4.16
IPI:IPI00330066.5	T*RSPDVISSASTALSQDIPE IASEALSR	1201	Edc4	Isoform 1 of Enhancer of mRNA-decapping protein 4	-4.045
IPI:IPI00225062.2	RKETPS*PR	1202	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-4.005
IPI:IPI00405665.6	K@IETM#SS*PK@	1203	Kif20b	Isoform 1 of M-phase phosphoprotein 1	-3.928
IPI:IPI00311187.4	S*AASGS*SGES*MDSVSVS *S*CESNHS*EAEEGPVTPM DTPDEPQKK	1204	Rgl1	Ral guanine nucleotide dissociation stimulator-like 1	-3.911
IPI:IPI00153724.1	VHS*PPASLVPR^	1205	111000 7A13Ri k	UPF0557 protein C10orf119 homolog	-3.905
IPI:IPI00121277.1	VAAAAGSGPS*PPCS*PGH DR	1206	Pi4k2a	Phosphatidylinositol 4-kinase type 2-alpha	-3.904
IPI:IPI00331556.5	MQVDQEEPHTEEQQQQPQ TPAENKAEESEEM#ET*SQA GSK	1207	Hspa4	Heat shock 70 kDa protein 4	-3.897
IPI:IPI00135443.2	KTSFDQDS*DVDIFPSDFTS EPPALPR	1208	Top2b	DNA topoisomerase 2-beta	-3.873
IPI:IPI00469938.3	VGSGAEPGEGS*PGSR*PG PIQADS*PK@	1209	BC0213 81	Isoform 2 of Uncharacterized protein KIAA1931	-3.843
IPI:IPI00331361.2	SPT*KAEPATPAEAAQSDR	1210	Mybbp1 a	Myb-binding protein 1A	-3.83

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00625898.3	RQS*S*ESDIESVMYTIEAVAK	1211	Bbx	Isoform 1 of HMG box transcription factor BBX	-3.809
IPI:IPI00405227.3	S*LGEIAALTSK	1212	Vcl	Vinculin	-3.804
IPI:IPI00109318.1	RNS*PMAQTTPCHLPNIPGV TSPGALIEDSK	1213	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	-3.791
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1214	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.751
IPI:IPI00318938.6	RVALGDGVQLPPGDY*STT PGGTLFSTT*PGGTR	1215	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.726
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1216	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.726
IPI:IPI00318938.6	VALGDGVQLPPGDYSTTPG GTLFS*TT*PGGTR	1217	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.705
IPI:IPI00929814.1	KEANEVLS*DS*AGEDHPAE LR	1218	Morc2a	microrchidia 2A isoform 2	-3.673
IPI:IPI00229645.2	S*NDDLLAGMAGGVNVTNG IK	1219	Cytsa	Cytospin-A	-3.632
IPI:IPI00553798.2	AGAIS*ASGPELEGAGHSK	1220	Ahnak	AHNAK nucleoprotein isoform 1	-3.608
IPI:IPI00756424.3	TAR*PNSEAPLS*GS*EDAD DSNK@	1221	Eif5b	Isoform 1 of Eukaryotic translation initiation factor 5B	-3.543
IPI:IPI00121760.5	LKTEEGEIVY*SAEESNR	1222	Hnrpl	Isoform 1 of Heterogeneous nuclear ribonucleoprotein L-like	-3.51
IPI:IPI00458958.2	DWDKES*EGEEPAGGR	1223	Rrp15	RRP15-like protein	-3.46
IPI:IPI00458958.2	DWDK@ES*EGEEPAGGR^	1224	Rrp15	RRP15-like protein	-3.46
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1225	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.429
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTTP GGT*LFSTT*PGGTR	1226	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.429
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1227	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.429
IPI:IPI00109695.3	IEILDS*PASK	1228	D10Ws u102e	Uncharacterized protein C12orf45 homolog	-3.403
IPI:IPI00230719.8	RDS*SDDWEIPDGQITVGQ R	1229	Braf	Isoform 1 of B-Raf proto-oncogene serine/threonine-protein kinase	-3.372
IPI:IPI00377925.2	SS*PVCSTAPVETEPK	1230	Atg2b	Isoform 1 of Autophagy-related protein 2 homolog B	-3.353
IPI:IPI00221723.1	MGQEFVES*K	1231	Wasf2	Wiskott-Aldrich syndrome protein family member 2	-3.314
IPI:IPI00165794.1	LWHTSDQQVSAISNPSPC AS*VTAEGK	1232	Tmem4 8	Nucleoporin NDC1	-3.255
IPI:IPI00848747.1	DDS*TCLGGILPAGLEPGS* S*T*R	1233	493056 8B11Rik	hypothetical protein LOC75873	-3.253
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1234	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.239
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK@	1235	Npm1	Nucleophosmin	-3.232
IPI:IPI00318938.6	VALGDGVQLPPGDYST*TP GGTLFST*TPGGTR	1236	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.209

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00318938.6	VALGDGVQLPPGDYS*TTP GGTLFSTT*PGGTR	1237	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.209
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1238	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.175
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFS*TTPGGTR	1239	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.175
IPI:IPI00120133.1	EDGDILAS*S*FSVDTQVAYI LSLGVVK	1240	Nat15	N-acetyltransferase 15	-3.163
IPI:IPI00154109.2	SNS*APLIHGLSDSS*PVFQA EAPSAR	1241	Fam122 a	Protein FAM122A	-3.124
IPI:IPI00138199.5	DGY*Y*GES*T*S*GR^	1242	Pcsk5	proprotein convertase subtilisin/kexin type 5	-3.103
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1243	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.092
IPI:IPI00130920.1	TELS*PSFINPNLEWFAGE EPTEESEKPLTQSGGAPPP SGGK	1244	Mtap1b	Microtubule-associated protein 1B	-3.089
IPI:IPI00131725.3	HQIVCINNDLS*EEES*DDES *EEDEIK@LCGILPAK@	1245	Npm3	Nucleoplasmin-3	-3.087
IPI:IPI00330066.5	T*RSPDVISSASTALSQDIPE IASEALSR	1246	Edc4	Isoform 1 of Enhancer of mRNA- decapping protein 4	-3.084
IPI:IPI00756765.3	ALVIQESPPPS*PPPS*PDR ^R^	1247	Ehmt2	Euchromatic histone lysine N- methyltransferase 2	-3.071
IPI:IPI00221889.2	ILS*DDEDEDEEDAFK	1248	Ercc6l	DNA excision repair protein ERCC-6- like	-3.063
IPI:IPI00130920.1	TELS*PSFINPNLEWFAGE EPTEESEKPLTQSGGAPPP SGGK	1249	Mtap1b	Microtubule-associated protein 1B	-3.052
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTTPGGT*R	1250	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.033
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1251	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.031
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1252	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.031
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1253	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-3.031
IPI:IPI00137465.1	S*DGSLDDGDGIHR	1254	Serinc1	Serine incorporator 1	-3.027
IPI:IPI00130920.1	QGFPDRES*PVSDLTSTGLY QDK	1255	Mtap1b	Microtubule-associated protein 1B	-3
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTTPGGT*R	1256	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.995
IPI:IPI00109318.1	RNSPMAQT*PPCHLPNIPGV TSPGALIEDSK	1257	Eif4ebp 2	Eukaryotic translation initiation factor 4E-binding protein 2	-2.988
IPI:IPI00122757.1	TDYYPEEMS*PPLMNPVSP PQALLQENHPS*VIVQPGK @	1258	Klf3;LO C10004 6855	Krueppel-like factor 3	-2.986
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1259	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.972
IPI:IPI00126006.6	TQT*PPLGQTPQLGLK	1260	Eif4g2	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 2	-2.956

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00460668.2	KAENAEQTPAIGPDGEPL DETSQM#S*DLPVK	1261	Smarca4	Putative uncharacterized protein	-2.915
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPMQASQSQLPS* SPEDK	1262	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.908
IPI:IPI00127764.2	EGENVKPVNSGTWVAS*NS *ELTPSESLVTT*DDETFEK	1263	Pcm1	Isoform 1 of Pericentriolar material 1 protein	-2.9
IPI:IPI00874995.2	AS*DDLGE PDVFATAPFR	1264	Aak1	Uncharacterized protein FLJ45252 homolog	-2.899
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPMQASQSQLPSS PEDK	1265	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.888
IPI:IPI00318938.6	VALGDGVQLPPGDYSTTPG GT*LFSTT*PGGTR	1266	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.884
IPI:IPI00128564.1	R*AAAAASAAEAGIAT*PGTE DSDDALLK@	1267	Psm4	Isoform Rpn10A of 26S proteasome non-ATPase regulatory subunit 4	-2.861
IPI:IPI00318938.6	VALGDGVQLPPGDYSTTPG GT*LFSTT*PGGTR	1268	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.846
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1269	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.84
IPI:IPI00406741.5	AAVGTGNDITTPPNKEPPP S*PEKK	1270	Mtap4	Isoform 4 of Microtubule-associated protein 4	-2.832
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1271	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.799
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFST*TPGGTR	1272	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.799
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1273	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.794
IPI:IPI00318938.6	VALGDGVQLPPGDYSTTPG GT*LFSTT*PGGTR	1274	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.776
IPI:IPI00109318.1	NS*PMAQTTPCHLPNIPGVT SPGALIEDSK	1275	Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2	-2.763
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1276	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.762
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1277	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.756
IPI:IPI00331177.2	VSS*TPETPLTK@	1278	Pola2	DNA polymerase alpha subunit B	-2.747
IPI:IPI00109318.1	NSPMAQT*PPCHLPNIPGVT SPGALIEDSK	1279	Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2	-2.714
IPI:IPI00318938.6	VALGDGVQLPPGDYSTTPG GT*LFSTT*PGGTR	1280	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.672
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTTPGGT*R	1281	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.672
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1282	Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.672
IPI:IPI00322707.5	IK@PVTENLVLSHTGFCQ S*S*GDEALSK@	1283	Atrx	Transcriptional regulator ATRX	-2.663
IPI:IPI00322707.5	IK@PVTENLVLSHTGFCQ S*S*GDEALSK@	1284	Atrx	Transcriptional regulator ATRX	-2.663

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00918973.1	IGFPETAEELIEIASENS*D SIYSSTPEVK	1285	Strap	Serine-threonine kinase receptor-associated protein	-2.612
IPI:IPI00318938.6	VALGDGVQLPPGDYS*TTP GGTLFSTT*PGGTR	1286	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.565
IPI:IPI00125960.1	TAS*GSS*VTS*LEGTR	1287	Ndrp1	Protein NDRG1	-2.557
IPI:IPI00125960.1	TAS*GSS*VTS*LEGTR	1288	Ndrp1	Protein NDRG1	-2.557
IPI:IPI00125960.1	TAS*GSSVTS*LEGTR	1289	Ndrp1	Protein NDRG1	-2.546
IPI:IPI00323045.3	S*MDVDLNQAHMEDTPK@	1290	Melk	Maternal embryonic leucine zipper kinase	-2.53
IPI:IPI00465761.5	SQLVHGCSQDSDELNPGL GSAGGVGS*PEPPTS*PR^	1291	Arhgef1 7	Isoform 1 of Rho guanine nucleotide exchange factor 17	-2.526
IPI:IPI00465761.5	SQLVHGCSQDSDELNPGL GSAGGVGS*PEPPTS*PR^	1292	Arhgef1 7	Isoform 1 of Rho guanine nucleotide exchange factor 17	-2.513
IPI:IPI00274140.4	LSPFFTLDSPT*DDK@SSK @PSSFTEK@	1293	Grit	Isoform 2 of Rho/Cdc42/Rac GTPase-activating protein RICS	-2.507
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1294	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.506
IPI:IPI00314240.5	K@QPPVS*PGTALVGSQK @	1295	Hmga1	Isoform HMG-I of High mobility group protein HMG-I/HMG-Y	-2.493
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1296	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.484
IPI:IPI00135379.3	VSPMLPSSSLES*PKDK	1297	Myo9b	Isoform 1 of Myosin-IXb	-2.452
IPI:IPI00753701.3	SQSGS*PAAPVEQVVIHTDT SGDPTLPQR^	1298	Mdc1	mediator of DNA damage checkpoint 1	-2.44
IPI:IPI00221889.2	R^ILS*DDEDEDEDAFK@	1299	Ercc6l	DNA excision repair protein ERCC-6-like	-2.438
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1300	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.437
IPI:IPI00318938.6	RVALGDGVQLPPGDYS*TT PGGTLFSTT*PGGTR	1301	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.437
IPI:IPI00454138.4	K@QQHVISTEEGDM#M#ET *NST*DDEK@	1302	Sap130	Isoform 1 of Histone deacetylase complex subunit SAP130	-2.434
IPI:IPI00454138.4	K@QQHVISTEEGDM#M#ET *NS*TDDEK@	1303	Sap130	Isoform 1 of Histone deacetylase complex subunit SAP130	-2.434
IPI:IPI00753701.3	SQSGS*PAAPVEQVVIHTDT SGDPTLPQR^	1304	Mdc1	mediator of DNA damage checkpoint 1	-2.433
IPI:IPI00654388.2	AENQR^PAEDSALS*PGPLA GAK@	1305	Lrrfp1	Isoform 1 of Leucine-rich repeat flightless-interacting protein 1	-2.425
IPI:IPI00654388.2	AENQRPAEDSALS*PGPLA GAK	1306	Lrrfp1	Isoform 1 of Leucine-rich repeat flightless-interacting protein 1	-2.425
IPI:IPI00330121.4	GLPYADHNYGAPPPPT*PP AS*PPVQTIIPR^	1307	Setd5	Isoform 2 of SET domain-containing protein 5	-2.414
IPI:IPI00323256.3	HGS*SSYPPIYSPLMPK	1308	Zfp2	Isoform 1 of Zinc finger protein ZFPM2	-2.405
IPI:IPI00323256.3	HGSSS*YPPVIYSPLMPK	1309	Zfp2	Isoform 1 of Zinc finger protein ZFPM2	-2.405
IPI:IPI00323256.3	HGSS*SYPPVIYSPLMPK@	1310	Zfp2	Isoform 1 of Zinc finger protein ZFPM2	-2.395
IPI:IPI00123474.2	AGADIHAENEEPLCPLSPS TSGSDS*DSEGP^	1311	Nfkb2	NF-kB2 splice variant 4	-2.389
IPI:IPI00117689.1	EGDELGEGERPEDDTAAIE LS*S*DEAVEVEEVIEESR	1312	Ptf	Polymerase I and transcript release factor	-2.385

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00117689.1	EGDELGEGERPEDDTAAIE LS*S*DEAVEVEEVIEESR	1313	Ptrf	Polymerase I and transcript release factor	-2.385
IPI:IPI00127764.2	RSS*LVDEAPEDEEFQK	1314	Pcm1	Isoform 1 of Pericentriolar material 1 protein	-2.38
IPI:IPI00330121.4	GLPYADHNYGAPPPPT*PP AS*PPVQTIIPR	1315	Setd5	Isoform 2 of SET domain-containing protein 5	-2.359
IPI:IPI00121277.1	VAAAAGSGPS*PPCS*PGH DR	1316	Pi4k2a	Phosphatidylinositol 4-kinase type 2- alpha	-2.354
IPI:IPI00331361.2	SPT*KAEPATPAEAAQSDR	1317	Mybbp1 a	Myb-binding protein 1A	-2.35
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFST*PGGTR	1318	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.341
IPI:IPI00330121.4	GLPYADHNYGAPPPPT*PP AS*PPVQTIIPR^	1319	Setd5	Isoform 2 of SET domain-containing protein 5	-2.334
IPI:IPI00623284.4	IWDPTPS*HTPAGAAT*PGR GDT*PGHAT*PGHGGATSS AR	1320	Sf3b1	Splicing factor 3B subunit 1	-2.329
IPI:IPI00153715.5	TEDEEFLIQHLLQAPS*PPR	1321	Prr12	proline rich 12	-2.321
IPI:IPI00116268.3	SGS*CSS*PQPKPNY*PPLS* PPLPLPQLLPSVT*EAR	1322	N4bp1	N4bp1 protein	-2.307
IPI:IPI00322707.5	AK@QPVIGDQNS*DSDEM# LAVLK@	1323	Atrx	Transcriptional regulator ATRX	-2.262
IPI:IPI00322707.5	AKQPVIGDQNS*DSDEM#LA VLK	1324	Atrx	Transcriptional regulator ATRX	-2.262
IPI:IPI00461244.3	DTTS*FEDISPQGISDDSS GSR	1325	Ccdc88 a	Isoform 2 of Girdin	-2.242
IPI:IPI00317794.5	KEDS*DEDEDEDEDDSD* EDEDEDEEDEFEPPIVK	1326	Ncl	Nucleolin	-2.198
IPI:IPI00317794.5	K@EDS*DEDEDEDEDDSD* EDEDEDEEDEFEPPIVK@	1327	Ncl	Nucleolin	-2.198
IPI:IPI00400381.9	AHS*LLFENSDFSSEDGTG LGR^	1328	Phactr4	Isoform 1 of Phosphatase and actin regulator 4	-2.193
IPI:IPI00320208.3	YGPSSVEDTTGSGAADA KDDIDLFGS*DDEEESEEA	1329	Eef1b2	Elongation factor 1-beta	-2.192
IPI:IPI00923656.1	R^DS*SSLSSPLNPK@	1330	Baz1b	Isoform 1 of Tyrosine-protein kinase BAZ1B	-2.17
IPI:IPI00318938.6	VALGDGVQLPPGDYSTTPG GT*LFST*TPGGTR	1331	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.17
IPI:IPI00108389.5	ETVSGPLGVEDISPSMS*P DDK@	1332	Trp53b p1	Transformation related protein 53 binding protein 1	-2.161
IPI:IPI00415558.1	AASPAKPS*SLDLVPLNPR	1333	Synpo	Isoform 3 of Synaptopodin	-2.151
IPI:IPI00404545.2	SCSVT*DTVAEQAHLPPPSV AYVHTTPGLPSGWEER	1334	Nedd4l	Isoform 3 of E3 ubiquitin-protein ligase NEDD4-like	-2.113
IPI:IPI00416203.1	AVPFVPM#SYQLS*QS*Y*Y S*LGK	1335	Gtf3c1	Isoform 2 of General transcription factor 3C polypeptide 1	-2.105
IPI:IPI00355042.3	IPMPSS*PQPR	1336	Ppp1r1 3l	RelA-associated inhibitor	-2.104
IPI:IPI00320208.3	YGPSSVEDTTGSGAADA KDDIDLFGS*DDEEESEEA	1337	Eef1b2	Elongation factor 1-beta	-2.096

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
	K				
IPI:IPI00623382.2	LMKPPS*PEHQS*PDTQQE GEEEEAMVAR	1338	Morc2a	MORC family CW-type zinc finger protein 2A	-2.069
IPI:IPI00125960.1	TAS*GSS*VTSLEGTR	1339	Ndrp1	Protein NDRG1	-2.055
IPI:IPI00125960.1	TAS*GSS*VTSLEGTR	1340	Ndrp1	Protein NDRG1	-2.055
IPI:IPI00125960.1	TAS*GSS*VTSLEGTR^	1341	Ndrp1	Protein NDRG1	-2.055
IPI:IPI00330121.4	GLPYADHNYGAPPPPT*PP AS*PPVQTIIPR^	1342	Setd5	Isoform 2 of SET domain-containing protein 5	-2.045
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1343	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.035
IPI:IPI00226701.3	ILGDHLLDPAHELPPY*TPP PMLS*PVR	1344	Trerf1	Isoform 4 of Transcriptional-regulating factor 1	-2.03
IPI:IPI00348488.5	SCS*M#ELHGEGNQEPGSP AVFAHPLER^	1345	Dennd4 c	DENN/MADD domain containing 4C	-2.012
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1346	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-2.01
IPI:IPI00317794.5	K@EDS*DEDEDEDEDDDS* DEDEDEDEDEFEPPIVK@	1347	Ncl	Nucleolin	-1.999
IPI:IPI00124717.1	K@PEFS*PTLK@	1348	Orc6l	Origin recognition complex subunit 6	-1.969
IPI:IPI00380722.1	SET*PPVPPPPPYLANYPGF PENGTPGPPISR	1349	Bat2	Large proline-rich protein BAT2	-1.961
IPI:IPI00553798.2	SNSFS*DEREFSAPSTPTGT LEFAGGDAK	1350	Ahnak	AHNAK nucleoprotein isoform 1	-1.95
IPI:IPI00108389.5	LVS*PETEASEESLQFSLEK @PTTAER^	1351	Trp53b p1	Transformation related protein 53 binding protein 1	-1.94
IPI:IPI00124272.1	LTTTGQVTS*PVK@	1352	Lig3	Isoform Alpha of DNA ligase 3	-1.932
IPI:IPI00406741.5	AAVGVTGNDITTPNKEPPP S*PEKK	1353	Mtap4	Isoform 4 of Microtubule-associated protein 4	-1.932
IPI:IPI00321774.2	HLLTDLPLPELPGGDPSP DS*PEPK@	1354	Crks	Isoform 2 of Cell division cycle 2-related protein kinase 7	-1.921
IPI:IPI00321774.2	HLLTDLPLPELPGGDPSP DS*PEPK@	1355	Crks	Isoform 2 of Cell division cycle 2-related protein kinase 7	-1.921
IPI:IPI00124914.1	S*LHKPMY*FFLINLS*ALDIL FTT*TTVPK	1356	Olf521	Olfactory receptor Olf521	-1.913
IPI:IPI00123881.1	VETPDVNLDQEEIIM#ET DEGQGGVNGHADS*PAPV NR^	1357	Mcm6	DNA replication licensing factor MCM6	-1.909
IPI:IPI00123881.1	VETPDVNLDQEEIIM#ET DEGQGGVNGHADS*PAPV NR	1358	Mcm6	DNA replication licensing factor MCM6	-1.909
IPI:IPI00117932.2	S*PPVQPHTPVTISLGTAPS LQNNQPVFNHAINVVK	1359	Sin3a	Isoform 1 of Paired amphipathic helix protein Sin3a	-1.896
IPI:IPI00229571.1	ISS*K@S*PGHM#VILNQTK @	1360	Slm	Isoform 1 of SAFB-like transcription modulator	-1.88
IPI:IPI00124753.3	SLLADSNGYTNLPDVQP SHSPTENS*K	1361	Mink1	misshapen-like kinase 1 isoform 2	-1.868
IPI:IPI00117088.2	LS*VVGPPNR^	1362	Map3k2	Mitogen-activated protein kinase kinase 2	-1.86

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00127602.1	VVVAADDSEAPER*PVNGA HPALQADDD*LLDQDLPLT NSQLSLK@	1363	Slc30a4	Zinc transporter 4	-1.822
IPI:IPI00127602.1	VVVAADDSEAPER*PVNGA HPALQADDD*LLDQDLPLT NSQLSLK@	1364	Slc30a4	Zinc transporter 4	-1.822
IPI:IPI00228942.4	DLS*PGAPPAVAAAAPEER^	1365	Hectd2	Hectd2 protein	-1.792
IPI:IPI00225062.2	EMPGSNIES*S*PEVEERPA VLSALDQSQSQPSK	1366	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.785
IPI:IPI00127602.1	VVVAADDSEAPERPVNGAH PALQADDD*LLDQDLPLTN SQLSLK	1367	Slc30a4	Zinc transporter 4	-1.782
IPI:IPI00127602.1	VVVAADDSEAPERPVNGAH PALQADDD*LLDQDLPLTN SQLSLK	1368	Slc30a4	Zinc transporter 4	-1.782
IPI:IPI00551082.3	EK@PPFLPEEPSS*S*SEED DPIPELLCLICK@	1369	Rbbp6	Isoform 2 of Retinoblastoma-binding protein 6	-1.768
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1370	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.759
IPI:IPI00318938.6	RVALGDGVQLPPGDYSTT* PGGTLFSTT*PGGTR	1371	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.759
IPI:IPI00135660.5	FQHPNTDMLQEK@PSSPS PMPSS*PSPSLNLGSTEER IR^	1372	Sdpr	Serum deprivation-response protein	-1.749
IPI:IPI00131725.3	HQIVCINNDLS*EEES*DDDES *EEDEIKLCGILPAK	1373	Npm3	Nucleoplasmin-3	-1.749
IPI:IPI00320208.3	YGPSSVEDTTGSGAADA KDDIDLFGS*DDEEESEEAK K	1374	Eef1b2	Elongation factor 1-beta	-1.741
IPI:IPI00321774.2	HLLTDLPLPELPGGDPS*P PDSPEPK@	1375	Crks	Isoform 2 of Cell division cycle 2-related protein kinase 7	-1.734
IPI:IPI00420601.5	T*CDSPQNPVDFISGPVPDS PFPR^	1376	Usp10	Ubiquitin carboxyl-terminal hydrolase 10	-1.734
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK@	1377	Npm1	Nucleophosmin	-1.718
IPI:IPI00464324.2	AS*CEENLPVFIASELAK@	1378	D83003 1N03Rik	similar to mKIAA0754 protein	-1.718
IPI:IPI00318048.5	SSPKKEEVAS*EPEEAAS*PT T*PK	1379	Nop56	Nucleolar protein 56	-1.708
IPI:IPI00115257.1	QVDTEEAGMVTAA*ASN V KASPK	1380	Psip1	Isoform 1 of PC4 and SFRS1-interacting protein	-1.694
IPI:IPI00317794.5	KEDS*DEDEDEDEDDSD EDEDEDEDEFEPPIVK	1381	Ncl	Nucleolin	-1.692
IPI:IPI00125745.1	HAELSGS*PLK@	1382	Mta3	Isoform 1 of Metastasis-associated protein MTA3	-1.69
IPI:IPI00461272.6	RGS*PGGVEMNVELPQQE GDDDDDEDEEAAGR	1383	231004 7M10Rik	Putative uncharacterized protein	-1.686

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00453999.2	K@PS*VPDTASPADDSFVD PGER^	1384	Nck1	non-catalytic region of tyrosine kinase adaptor protein 1	-1.682
IPI:IPI00119442.1	M#DTGEVSDIGSQGAPIVLS *DS*EEEEMIILEPEK@NPK @	1385	Exosc9	Exosome complex exonuclease RRP45	-1.674
IPI:IPI00654388.2	AENQRPAEDSALS*PGPLA GAK	1386	Lrrfp1	Isoform 1 of Leucine-rich repeat flightless-interacting protein 1	-1.673
IPI:IPI00128975.3	DK@DDQEWEST*SPPK@P TVFISGVIAR^	1387	Dap	Death-associated protein 1	-1.669
IPI:IPI00153375.1	SACFSPVSLS*PR^PCSPFS T*PPPTS*PVALSK@	1388	Pdlim2	PDZ and LIM domain protein 2	-1.659
IPI:IPI00515576.5	LDGELAITKPNVSS*PSK	1389	Ehbp1	Isoform 2 of EH domain-binding protein 1	-1.659
IPI:IPI00169521.4	ALAEEDS*EDELPS*DVDNFN DPYFAEEVKK	1390	Esf1	ESF1 homolog	-1.656
IPI:IPI00405756.8	SISGTS*TSEK@PNSMDTA NTSPFK@	1391	Rasal2	RAS protein activator like 2	-1.654
IPI:IPI00108508.5	ET*PPTPT*S*SPAEFSPK	1392	492151 7D21Ri k	RIKEN cDNA 4921517D21 gene	-1.652
IPI:IPI00652649.1	IRPPPELETS*LTERPSS*PS LLR	1393	Als2cr4	Amyotrophic lateral sclerosis 2 chromosomal region candidate gene 4 protein homolog	-1.649
IPI:IPI00127415.1	LKCGSGPVHISGQHLVAVE EDAES*EDEDEEDVK	1394	Npm1	Nucleophosmin	-1.638
IPI:IPI00453603.1	TPVS*PVKFS*PGDFWGR	1395	Rps6kb 1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1	-1.635
IPI:IPI00313307.3	LSSS*DSIGPDVTDILSDIAE EASK@LPSTSDDCPPIGT*P VR^	1396	Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1	-1.624
IPI:IPI00379682.1	ANTLSHFVVECPAPPEPAQ SS*PGVSQR^	1397	Tbc1d1	Isoform 1 of TBC1 domain family member 1	-1.623
IPI:IPI00379682.1	ANTLSHFVVECPAPPEPAQ S*SPGVSQR^	1398	Tbc1d1	Isoform 1 of TBC1 domain family member 1	-1.623
IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR	1399	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.621
IPI:IPI00351206.5	LLK@PGEEPSEY*T*DEEDT K@	1400	Pgrmc2	Membrane-associated progesterone receptor component 2	-1.62
IPI:IPI00225062.2	NSGPVSEVNTGFS*PEVK@	1401	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.616
IPI:IPI00112339.9	R^LS*ENNCSLDDWEIGAGH LSSSAFNSEK@	1402	Lima1	LIM domain and actin binding 1 isoform a	-1.615
IPI:IPI00112339.9	R^LS*ENNCSLDDWEIGAGH LSSSAFNSEK@	1403	Lima1	LIM domain and actin binding 1 isoform a	-1.615
IPI:IPI00515576.5	LDGELAITKPNVSS*PSK	1404	Ehbp1	Isoform 2 of EH domain-binding protein 1	-1.612
IPI:IPI00229472.5	VEEQVEDS*DDEEDDDDS*H DDEEER	1405	Rbm28	RNA-binding protein 28	-1.609
IPI:IPI00229472.5	VEEQVEDS*DDEEDDDDS*H DDEEER^	1406	Rbm28	RNA-binding protein 28	-1.609

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPM#QASQSQLPS SPEDK	1407	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.6
IPI:IPI00127415.1	LKCGSGPVHISGQHLVAVE EDAES*EDEDEEDVK	1408	Npm1	Nucleophosmin	-1.599
IPI:IPI00453837.2	KLPPPPQAPPEEENES*EP EPPSGVEGAAFQSR	1409	Kdm1	Lysine-specific histone demethylase 1	-1.587
IPI:IPI00319933.4	DGTAPPPQSPSSPGSGQD EDWS*DEESPR	1410	Paccin3	Protein kinase C and casein kinase II substrate protein 3	-1.565
IPI:IPI00125662.2	S*PQVPAAQQMLNFPEK	1411	Smarcc 1	Isoform 1 of SWI/SNF complex subunit SMARCC1	-1.554
IPI:IPI00230435.1	SLTM#VEDNEDDDEDEGEEL LHHHR^VS*GSR^	1412	Lmna	Isoform C2 of Lamin-A/C	-1.546
IPI:IPI00228748.1	LDR^AS*PDLWPEQLPGVAE FAASFk@	1413	Lin52;G m7020	Protein lin-52 homolog	-1.545
IPI:IPI00622364.4	LPPFPFGMDPESEGAAGAS EPEAGDSDEGEDIFTGAA AAT*K@PQS*PK@	1414	Snx1	Sorting nexin-1	-1.535
IPI:IPI00117689.1	GEATDLLRGS*S*PDVHTLL EITEESDAVLVDK	1415	Ptrf	Polymerase I and transcript release factor	-1.532
IPI:IPI00117689.1	GEATDLLR^GS*S*PDVHTLL EITEESDAVLVDK@	1416	Ptrf	Polymerase I and transcript release factor	-1.532
IPI:IPI00606555.2	KPEPEAGQAEPLS*PRPPP CPTLSVTVEPK	1417	Rreb1	Isoform 3 of Ras-responsive element- binding protein 1	-1.526
IPI:IPI00606555.2	KPEPEAGQAEPLS*PRPPP CPTLSVTVEPK	1418	Rreb1	Isoform 3 of Ras-responsive element- binding protein 1	-1.526
IPI:IPI00380394.5	IEEPVSM#EMDNHLSKDKE SCYDNAEAAFS*DDEEDLN SK	1419	Ints3	Integrator complex subunit 3	-1.525
IPI:IPI00229571.1	IS*SK@S*PGHM#VILNQTK @	1420	Sltn	Isoform 1 of SAFB-like transcription modulator	-1.524
IPI:IPI00551082.3	EKPPFLPEEPS*S*SSEEDD PIDELCLICK	1421	Rbbp6	Isoform 2 of Retinoblastoma-binding protein 6	-1.522
IPI:IPI00468896.7	KGELMENDQDAMEYS*S*E EEEVDLQALTGYQTK	1422	Ddx46	Isoform 1 of Probable ATP-dependent RNA helicase DDX46	-1.517
IPI:IPI00280250.5	VGES*SEDVALEEETIYENE GFR^PYTEDTLSAR^	1423	Sh3pxd 2a	Isoform 1 of SH3 and PX domain- containing protein 2A	-1.513
IPI:IPI00280250.5	VGES*SEDVALEEETIYENE GFRPYTEDTLSAR	1424	Sh3pxd 2a	Isoform 1 of SH3 and PX domain- containing protein 2A	-1.513
IPI:IPI00664670.4	LGS*FGSITR	1425	Flnc	Isoform 1 of Filamin-C	-1.512
IPI:IPI00117929.1	STEESLSEDAFTESELS*PIR ^EELLSSEPR^	1426	Oxr1	Isoform 2 of Oxidation resistance protein 1	-1.51
IPI:IPI00117929.1	STEESLSEDAFTESELS*PIR ^EELLSSEPR^	1427	Oxr1	Isoform 2 of Oxidation resistance protein 1	-1.51
IPI:IPI00664670.4	LGS*FGSITR^	1428	Flnc	Isoform 1 of Filamin-C	-1.509
IPI:IPI00130920.1	AS*LS*PMDEPVPDSESPVE K@	1429	Mtap1b	Microtubule-associated protein 1B	-1.509
IPI:IPI00113362.2	NSNSYGIPEPAHAY*AQPQT TTPLPTVASTPGAAINPLPS	1430	Crkl	Crk-like protein	-1.508

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
	TQNGPVFAK				
IPI:IPI00331334.3	VSSAPIPCPS*PSPAPSAVP S*PPK	1431	Bag3	BAG family molecular chaperone regulator 3	-1.508
IPI:IPI00331209.1	NSS*FVLPK	1432	Rin2	Isoform 1 of Ras and Rab interactor 2	-1.504
IPI:IPI00225062.2	GHTQTWPDTSSEVMQT*Q VES*PLLQSK	1433	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.504
IPI:IPI00664670.4	LGS*FGSITR ^A	1434	FlnC	Isoform 1 of Filamin-C	-1.502
IPI:IPI00664670.4	LGS*FGSITR	1435	FlnC	Isoform 1 of Filamin-C	-1.502
IPI:IPI00664670.4	LGS*FGSITR	1436	FlnC	Isoform 1 of Filamin-C	-1.502
IPI:IPI00664670.4	LGS*FGSITR	1437	FlnC	Isoform 1 of Filamin-C	-1.497
IPI:IPI00126006.6	TQT*PPLGQTPQLGLK@	1438	Eif4g2	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 2	-1.492
IPI:IPI00113798.2	ATWGDGGDNS*PSNVVSK	1439	Snap23	Synaptosomal-associated protein	-1.49
IPI:IPI00664670.4	LGS*FGSITR ^A	1440	FlnC	Isoform 1 of Filamin-C	-1.483
IPI:IPI00169771.1	EDGIDAVEVAADR ^A PGS*PR ^A	1441	BC031781	UPF0667 protein C1orf55 homolog	-1.482
IPI:IPI00169806.3	GMEGLIS*PTEAVGNSCGA SSSCPGWLR ^A	1442	Nek9	Serine/threonine-protein kinase Nek9	-1.478
IPI:IPI00117932.2	S*PPVQPHTPVTISLGTAPS LQNNQPVFNHAINYVVK@	1443	Sin3a	Isoform 1 of Paired amphipathic helix protein Sin3a	-1.477
IPI:IPI00225062.2	NSGPVSEVNTGFS*PEVK@	1444	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.475
IPI:IPI00128062.1	RGQEELEVPVDPLPS*SPA QEALDLLFSCDSTEEASSSL AR	1445	Snx15	Sorting nexin-15	-1.472
IPI:IPI00224570.3	GVNFAEPMRS*DS*ENGE EEEAAEAGAFNAPVINR	1446	Prkar2b	cAMP-dependent protein kinase type II-beta regulatory subunit	-1.468
IPI:IPI00380722.1	SET*PPVPPPPPYLANYPGF PENGTPGPPISR ^A	1447	Bat2	Large proline-rich protein BAT2	-1.463
IPI:IPI00330695.5	GLLAQDLQAESSPPAS*PLL NGAPVQESSQPVAVPEAS* PPASPLR ^A	1448	Fam129b	Niban-like protein 1	-1.46
IPI:IPI00750546.1	GGGQSS*PQEEPTWK@	1449	Cwc22	Novel protein	-1.452
IPI:IPI00129356.1	SGS*GMSVISSSSVDQR	1450	Itsn1	Isoform 1 of Intersectin-1	-1.451
IPI:IPI00753701.3	SPT*LGEDS*DTEVDEDHKP GFADS*ETDVEEER	1451	Mdc1	mediator of DNA damage checkpoint 1	-1.447
IPI:IPI00137730.7	VLTPQTVMNR ^A PSS*ISWDG LDPGK@	1452	Pebp1	Phosphatidylethanolamine-binding protein 1	-1.431
IPI:IPI00123802.5	NIQQDNSEAGTQPQVQTDG QQTSQSPPS*PELTSEESK @TPDADK@	1453	Hsph1	Isoform HSP105-alpha of Heat shock protein 105 kDa	-1.428
IPI:IPI00421179.1	EATLPPVS*PPK@	1454	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	-1.421
IPI:IPI00421179.1	EATLPPVS*PPK	1455	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	-1.421
IPI:IPI00318006.5	R ^A IS*WPENSFDFVSK@	1456	Serhl	Serine hydrolase-like protein	-1.411

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00318006.5	R^IS*WPENSFDFVSK@	1457	Serhl	Serine hydrolase-like protein	-1.411
IPI:IPI00125501.1	KAEEAT*PVTALR	1458	Epb4.1l3	Isoform 1 of Band 4.1-like protein 3	-1.408
IPI:IPI00405665.6	K@IETM#SS*PK@	1459	Kif20b	Isoform 1 of M-phase phosphoprotein 1	-1.399
IPI:IPI00405665.6	KIETM#SS*PK	1460	Kif20b	Isoform 1 of M-phase phosphoprotein 1	-1.399
IPI:IPI00119442.1	M#DTGEVSDIGSQGAPIVLS *DS*EEEEMIILEPEK@NPK @	1461	Exosc9	Exosome complex exonuclease RRP45	-1.396
IPI:IPI00121760.5	LKTEEGEIVYS*AESENR	1462	Hnrpl	Isoform 1 of Heterogeneous nuclear ribonucleoprotein L-like	-1.387
IPI:IPI00320208.3	YGPSSVEDTTGSGAADA KDDIDLFGS*DDEEESEEA K	1463	Eef1b2	Elongation factor 1-beta	-1.381
IPI:IPI00664670.4	LGS*FGSITR^	1464	Flnc	Isoform 1 of Filamin-C	-1.373
IPI:IPI00664670.4	LGS*FGSITR	1465	Flnc	Isoform 1 of Filamin-C	-1.373
IPI:IPI00125348.2	AEEQLPPLLSPPS*PSTPHS R	1466	Mprip	Isoform 1 of Myosin phosphatase Rho-interacting protein	-1.371
IPI:IPI00120095.2	DFTKPQDGDIIAPLIT*PLK	1467	Samhd1	SAM domain and HD domain-containing protein 1	-1.371
IPI:IPI00756765.3	ALVIQESSEPPS*PPPS*PDR R	1468	Ehmt2	Euchromatic histone lysine N-methyltransferase 2	-1.368
IPI:IPI00135708.1	RKPVLPAITINPTIAEGPS*P TSEGASEANLVDLQK	1469	Map2k2	Dual specificity mitogen-activated protein kinase kinase 2	-1.365
IPI:IPI00317794.5	KEDS*DEDEDEDEDDSD EDEDEDEDEFEPPIVK	1470	Ncl	Nucleolin	-1.364
IPI:IPI00330695.5	GLLAQDLQAESSPPASPLL NGAPVQES*S*QPVAVPEAS *PPASPLR^	1471	Fam129b	Niban-like protein 1	-1.36
IPI:IPI00330695.5	GLLAQDLQAES*S*PPASPL LNGAPVQESSQPVAVPEAS *PPASPLR	1472	Fam129b	Niban-like protein 1	-1.36
IPI:IPI00453800.4	K@PSSS*PDLWK@VS*PDQ R^	1473	Zfp828	Zinc finger protein 828	-1.358
IPI:IPI00135443.2	AS*PITNDGEDEFVPSDGLD KDEYAFSSGK	1474	Top2b	DNA topoisomerase 2-beta	-1.357
IPI:IPI00227267.2	EVENEQTPVS*EPEEEKGS QPGPPVER	1475	Epb4.1l2	Putative uncharacterized protein	-1.357
IPI:IPI00649691.3	LASEDAALVDDDEES*DTPA QAPLAK@	1476	Cc2d1b	Coiled-coil and C2 domain-containing protein 1B	-1.353
IPI:IPI00340860.5	TAS*EGSEAETPEAPK@	1477	Larp7	Isoform 1 of La-related protein 7	-1.347
IPI:IPI00320208.3	YGPSSVEDTTGSGAADA KDDIDLFGS*DDEEESEEA K	1478	Eef1b2	Elongation factor 1-beta	-1.336
IPI:IPI00320208.3	YGPSSVEDTTGSGAADA KDDIDLFGS*DDEEESEEA K	1479	Eef1b2	Elongation factor 1-beta	-1.336
IPI:IPI00750546.1	GGGQSS*PQEEPTWK	1480	Cwc22	Novel protein	-1.327
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK	1481	Npm1	Nucleophosmin	-1.324
IPI:IPI00123871.2	VHEPPR^EDTVPPK@PVPP VPPPTQHLQPEGDVSSQSS GGG*PR^	1482	Ncor2	nuclear receptor co-repressor 2	-1.31

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00458583.3	AKS*PQPPVEEEDHFDDT VVCLDTYNCDLHFK	1483	Hnrnpu	Putative uncharacterized protein	-1.308
IPI:IPI00124959.1	GPIQTLGHTDESASDKGPT QMPCNSLQPEQVDSFQSS* PR	1484	Mki67	Ki-67 protein	-1.306
IPI:IPI00664670.4	LGS*FGSITR	1485	Finc	Isoform 1 of Filamin-C	-1.29
IPI:IPI00664670.4	LGS*FGSITR^	1486	Finc	Isoform 1 of Filamin-C	-1.289
IPI:IPI00664670.4	LGS*FGSITR^	1487	Finc	Isoform 1 of Filamin-C	-1.289
IPI:IPI00664670.4	LGS*FGSITR	1488	Finc	Isoform 1 of Filamin-C	-1.289
IPI:IPI00664670.4	LGS*FGSITR	1489	Finc	Isoform 1 of Filamin-C	-1.289
IPI:IPI00270767.3	M#K@ESETFSDSS*PIEIDE FPTFVSAK@	1490	Rtn4	Isoform 2 of Reticulon-4	-1.286
IPI:IPI00318048.5	SSPKEEVAS*EPEEAASPT* TPK	1491	Nop56	Nucleolar protein 56	-1.284
IPI:IPI00276222.1	LSIMTSENHLNNSDKEVDEV DAALS*DLEITLEGGK	1492	Fermt2	Fermitin family homolog 2	-1.279
IPI:IPI00475055.3	RCPS*T*DPEEAVEDAEGPS EASADPEELAK	1493	Zfhx3	AT motif binding factor 1	-1.274
IPI:IPI00664670.4	LGS*FGSITR^	1494	Finc	Isoform 1 of Filamin-C	-1.273
IPI:IPI00664670.4	LGS*FGSITR	1495	Finc	Isoform 1 of Filamin-C	-1.273
IPI:IPI00664670.4	LGS*FGSITR^	1496	Finc	Isoform 1 of Filamin-C	-1.273
IPI:IPI00664670.4	LGS*FGSITR	1497	Finc	Isoform 1 of Filamin-C	-1.273
IPI:IPI00664670.4	LGS*FGSITR^	1498	Finc	Isoform 1 of Filamin-C	-1.273
IPI:IPI00664670.4	LGS*FGSITR	1499	Finc	Isoform 1 of Filamin-C	-1.273
IPI:IPI00664670.4	LGS*FGSITR^	1500	Finc	Isoform 1 of Filamin-C	-1.272
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK@	1501	Npm1	Nucleophosmin	-1.271
IPI:IPI00121277.1	VAAAAGSGPS*PPCS*PGH DR	1502	Pi4k2a	Phosphatidylinositol 4-kinase type 2- alpha	-1.266
IPI:IPI00121277.1	VAAAAGSGPS*PPCS*PGH DR^	1503	Pi4k2a	Phosphatidylinositol 4-kinase type 2- alpha	-1.266
IPI:IPI00317794.5	K@EDS*DEDEDEDEDDSD* DEDEDEDEDEFEPPIVK@	1504	Ncl	Nucleolin	-1.255
IPI:IPI00270767.3	VVKEDGVM#S*PEK	1505	Rtn4	Isoform 2 of Reticulon-4	-1.252
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPM#QASQSQLPS SPEDK	1506	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.238
IPI:IPI00114352.1	VNHEPEPASGAS*PGATIPK @S*PSQLR^	1507	Bin1	Isoform 1 of Myc box-dependent- interacting protein 1	-1.237
IPI:IPI00114352.1	VNHEPEPASGAS*PGATIPK S*PSQLR	1508	Bin1	Isoform 1 of Myc box-dependent- interacting protein 1	-1.237
IPI:IPI00110435.2	TPS*PEPVDK@DFYSEFGD K@	1509	Nisch	Isoform 1 of Nischarin	-1.229
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK@	1510	Npm1	Nucleophosmin	-1.226
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK@	1511	Npm1	Nucleophosmin	-1.226

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00132386.1	ANS*TSDSMFTETPSPVLK@	1512	Cdc42e p3	Cdc42 effector protein 3	-1.225
IPI:IPI00131999.2	FELLTPPLSPS*RR	1513	Myc	myc proto-oncogene protein	-1.219
IPI:IPI00282957.4	EPAAPAS*PAPS*PVPSPT*P AQPQK	1514	Mtap7d 1	Isoform 1 of MAP7 domain-containing protein 1	-1.217
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPMQASQSQLPSS PEDK	1515	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.212
IPI:IPI00226220.2	TFS*LDAAPADHSLGPSR^	1516	Rtkn	Isoform 1 of Rhotekin	-1.207
IPI:IPI00318938.6	NS*PVAKT*PPKDLPAIPGVT SPTSDEPPM#QASQSQLPS SPEDK	1517	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	-1.203
IPI:IPI00664670.4	LGS*FGS*ITR^	1518	Finc	Isoform 1 of Filamin-C	-1.194
IPI:IPI00473912.4	NSTHSNLHTS*LGNS*VWG SINT*GPS*NQWASELVSSI WSNADTK	1519	Gigyf2	Isoform 1 of PERQ amino acid-rich with GYF domain-containing protein 2	-1.193
IPI:IPI00227380.1	TRS*EPLPPSATASPLLAPL QPR	1520	Hdac7	Isoform 4 of Histone deacetylase 7	-1.178
IPI:IPI00119442.1	M#DTGEVSDIGSQGAPIVLS *DS*EEEEMIILEPEK@NPK @	1521	Exosc9	Exosome complex exonuclease RRP45	-1.177
IPI:IPI00119442.1	M#DTGEVSDIGSQGAPIVLS *DS*EEEEMIILEPEKNPK	1522	Exosc9	Exosome complex exonuclease RRP45	-1.177
IPI:IPI00119442.1	MDTGEVSDIGSQGAPIVLS* DS*EEEEM#IILEPEKNPK	1523	Exosc9	Exosome complex exonuclease RRP45	-1.177
IPI:IPI00221882.1	DHNS*EDEDEDKYADDIDM #PGQNFDISK	1524	Slu7	Pre-mRNA-splicing factor SLU7	-1.167
IPI:IPI00675346.2	R^QSGT*DLQEDVIVR^	1525	Myo9a	Isoform 2 of Myosin-IXa	-1.166
IPI:IPI00125319.1	TTS*FAESCKPVQQPSAFG SMK	1526	Gsk3b	Glycogen synthase kinase-3 beta	-1.165
IPI:IPI00654192.2	SLS*FSEPQQPPPTVK	1527	Zfp395	zinc finger protein 395	-1.165
IPI:IPI00128975.3	DKDDQEWEST*SPPKPTVFI SGVIAR	1528	Dap	Death-associated protein 1	-1.165
IPI:IPI00330897.1	S*PVVITIDS*DS*DGSEVK @	1529	Topors	E3 ubiquitin-protein ligase Topors	-1.161
IPI:IPI00330133.2	INDELEGLGLEGGs*EGEAP R	1530	Bend3	BEN domain-containing protein 3	-1.159
IPI:IPI00330133.2	INDELEGLGLEGGs*EGEAP R	1531	Bend3	BEN domain-containing protein 3	-1.159
IPI:IPI00127415.1	CGSGPVHISGQHLLVAVEED AES*EDEDEEDVK@	1532	Npm1	Nucleophosmin	-1.157
IPI:IPI00127415.1	CGSGPVHISGQHLLVAVEED AES*EDEDEEDVK	1533	Npm1	Nucleophosmin	-1.157
IPI:IPI00314749.2	ISENYS*DKSDVENADESSS SILKPLISPAAER	1534	Slc4a4	Isoform 1 of Electrogenic sodium bicarbonate cotransporter 1	-1.156
IPI:IPI00123709.1	GPSEAPQEAEEAEEGATS*D GEK	1535	Akap12	Isoform 1 of A-kinase anchor protein 12	-1.154
IPI:IPI00321774.2	HLLTDLPLPELPGGDPS*P PDS*PEPK	1536	Crkrs	Isoform 2 of Cell division cycle 2-related protein kinase 7	-1.15

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
IPI:IPI00420601.5	SDLIEDEELEDTGKGS*EDE WEQVGPK	1537	Usp10	Ubiquitin carboxyl-terminal hydrolase 10	-1.149
IPI:IPI00421179.1	EATLPPVS*PPK@	1538	Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1	-1.146
IPI:IPI00269136.2	KGLVAASGS*DS*EDEDSDM DSPLDLSSSAASGK	1539	Tgif1	Isoform 1 of Homeobox protein TGIF1	-1.143
IPI:IPI00221581.1	TGS*ESSQTGASATSGR	1540	Eif4b	Eukaryotic translation initiation factor 4B	-1.142
IPI:IPI00756765.3	ALVIQESPPPS*PPPS*PDR ^R^	1541	Ehmt2	Euchromatic histone lysine N-methyltransferase 2	-1.141
IPI:IPI00137668.1	M#LPHAPGVQM#QAIPEDA VHEDS*GDEDEDGDPDKR	1542	Hdac2	Histone deacetylase 2	-1.123
IPI:IPI00225062.2	IHTTALTGQS*PPLASGHQG EGDAPSVEPGATNIQQPSS* PAPSTK@	1543	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.123
IPI:IPI00225062.2	IHTTALTGQS*PPLASGHQG EGDAPSVEPGATNIQQPSS* PAPSTK	1544	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.123
IPI:IPI00225062.2	IHTTALTGQSPPLASGHQG EGDAPS*VEPGATNIQQPSS *PAPSTK	1545	Srm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.123
IPI:IPI00339428.9	MSSHT*ETSSFLQTLTGR^	1546	Dock7	Isoform 2 of Dedicator of cytokinesis protein 7	-1.12
IPI:IPI00339428.9	MS*SHTETSSFLQTLTGR^	1547	Dock7	Isoform 2 of Dedicator of cytokinesis protein 7	-1.12
IPI:IPI00339428.9	MS*SHTETSSFLQTLTGR	1548	Dock7	Isoform 2 of Dedicator of cytokinesis protein 7	-1.12
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK@	1549	Npm1	Nucleophosmin	-1.119
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK@	1550	Npm1	Nucleophosmin	-1.119
IPI:IPI00331361.2	S*PSLLQSGVK	1551	Mybbp1 a	Myb-binding protein 1A	-1.116
IPI:IPI00309059.7	ST*S*PIIGSPPVR^	1552	Pat1	Protein PAT1 homolog 1	-1.115
IPI:IPI00339428.9	MSSHTETS*SFLQTLTGR^	1553	Dock7	Isoform 2 of Dedicator of cytokinesis protein 7	-1.114
IPI:IPI00123747.1	LPS*M#GDQEPPGQEK	1554	Slc7a11	Cystine/glutamate transporter	-1.114
IPI:IPI00322095.4	IDEPNTPYHNMIGDDEDAYS DS*EGNEVM#TPDILAK	1555	Ppp1r2	Putative uncharacterized protein	-1.107
IPI:IPI00135379.3	LSEGEPPVAAGEQLSEHP VEDPESLGVEAETWMNKS* PDGMS*PK	1556	Myo9b	Isoform 1 of Myosin-IXb	-1.106
IPI:IPI00125319.1	TTS*FAESCKPVQQPSAFG SMK	1557	Gsk3b	Glycogen synthase kinase-3 beta	-1.105
IPI:IPI00125319.1	TTS*FAESCK@PVQQPSAF GSMK@	1558	Gsk3b	Glycogen synthase kinase-3 beta	-1.105
IPI:IPI00125319.1	TTS*FAESCKPVQQPSAFG SMK	1559	Gsk3b	Glycogen synthase kinase-3 beta	-1.103
IPI:IPI00320208.3	YGPSSVEDTTGSGAADAAD	1560	Eef1b2	Elongation factor 1-beta	-1.102

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
	DDDIDLFGS*DDEEESEEAK K				
IPI:IPI00331361.2	SPAPSNPTLS*PS*TPAK@T PK@	1561	Mybbp1 a	Myb-binding protein 1A	-1.101
IPI:IPI00331361.2	SPAPSNPTLS*PST*PAKTP K	1562	Mybbp1 a	Myb-binding protein 1A	-1.101
IPI:IPI00668709.2	SSS*APNVHINTIEPVNIDDLI R	1563	Braf	B-Raf protein	-1.097
IPI:IPI00462466.6	K@LDES*PVLK@PEFIGHD GR^	1564	Setd2	SET domain containing 2	-1.096
IPI:IPI00462466.6	KLDES*PVLKPEFIGHDGR	1565	Setd2	SET domain containing 2	-1.096
IPI:IPI00108389.5	LLDGPTGS*S*EEEEEFLEIP PFNK	1566	Trp53b p1	Transformation related protein 53 binding protein 1	-1.094
IPI:IPI00668709.2	SSS*APNVHINTIEPVNIDDLI R	1567	Braf	B-Raf protein	-1.088
IPI:IPI00225062.2	DGSGT*PSRHSLs*GSS*PG M#KDTPQT*PSR	1568	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	-1.081
IPI:IPI00135971.1	VQIPVSHPDPEPVS*DNEDD S*YDEEVHDPR	1569	Tjp1	Tight junction protein ZO-1	-1.08
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK	1570	Npm1	Nucleophosmin	-1.077
IPI:IPI00111169.1	HIVSNDSSDS*DDEAQGPK @	1571	Pla2g4 a	Cytosolic phospholipase A2	-1.072
IPI:IPI00225670.1	EVHDELEDLPS*PPPPLSPP PT*TSPHK	1572	Gphn	Gephyrin	-1.07
IPI:IPI00225670.1	EVHDELEDLPS*PPPPLS*P PPTTSPHK@	1573	Gphn	Gephyrin	-1.07
IPI:IPI00123709.1	AEDS*GAEQLASEIEPSR	1574	Akap12	Isoform 1 of A-kinase anchor protein 12	-1.067
IPI:IPI00123709.1	AEDS*GAEQLASEIEPSR	1575	Akap12	Isoform 1 of A-kinase anchor protein 12	-1.067
IPI:IPI00454109.2	S*PPACSSSSSLFSAVWAR ^	1576	Erf	ETS domain-containing transcription factor ERF	-1.066
IPI:IPI00313517.1	GPPS*EDEGMDIHFEEGVLS PSAADMR^PEPPNSLDLNG SHPR^	1577			-1.066
IPI:IPI00313517.1	GPPS*EDEGMDIHFEEGVLS PSAADMRPEPPNSLDLNGS HPR	1578			-1.066
IPI:IPI00311375.6	S*GITSLFEGEDDLEALK	1579	Sgsm3	small G protein signaling modulator 3	-1.061
IPI:IPI00311490.4	VLS*DS*EEEEKDADVPGETS TR	1580	Phip	PH-interacting protein	-1.059
IPI:IPI00553798.2	GHYEVT*GSDDEAGKLQGS GVSLASK	1581	Ahnak	AHNAK nucleoprotein isoform 1	-1.057
IPI:IPI00553798.2	GHYEVTGS*DDEAGK@LQ GSGVSLASK@	1582	Ahnak	AHNAK nucleoprotein isoform 1	-1.057
IPI:IPI00336281.1	RDSICS*SVSMESSLAEPQD ELLQILK	1583	Golga3	Isoform 1 of Golgin subfamily A member 3	-1.056
IPI:IPI00229859.1	ALENGEADEPS*FS*DPEDF VDDVSEEELLGDVVK	1584	Eif3b	Eif3b protein	-1.053
IPI:IPI00668709.2	DRSSS*APNVHINTIEPVNID	1585	Braf	B-Raf protein	-1.048

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
	DLIR				
IPI:IPI00668709.2	DR ^A SSS*APNVHINTIEPVNI DDLIR ^A	1586	Braf	B-Raf protein	-1.048
IPI:IPI00125319.1	T*TSFAESCKPVQQPSAFG SMK	1587	Gsk3b	Glycogen synthase kinase-3 beta	-1.047
IPI:IPI00135660.5	RGNNSAVGS*NADLT*IEED EEEEPVALQQAQQVR	1588	Sdpr	Serum deprivation-response protein	-1.046
IPI:IPI00339428.9	MSS*HTETSSFLQTLTGR	1589	Dock7	Isoform 2 of Dedicator of cytokinesis protein 7	-1.042
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK	1590	Npm1	Nucleophosmin	-1.039
IPI:IPI00115660.1	GPILAT*PGK@	1591	Tcof1	Treacle protein	-1.038
IPI:IPI00115660.1	GPILAT*PGK	1592	Tcof1	Treacle protein	-1.038
IPI:IPI00115660.1	GPILAT*PGK	1593	Tcof1	Treacle protein	-1.038
IPI:IPI00115660.1	GPILAT*PGK@	1594	Tcof1	Treacle protein	-1.038
IPI:IPI00230704.4	KES*APQVLLPEEEK	1595	Arhgef7	Isoform C of Rho guanine nucleotide exchange factor 7	-1.036
IPI:IPI00320422.3	LQEEGGS*EEEEAGNPSED GM#QSGPTQAPPR	1596	Pwp1	Periodic tryptophan protein 1 homolog	-1.035
IPI:IPI00270767.3	VVKEDGVM#S*PEK	1597	Rtn4	Isoform 2 of Reticulon-4	-1.035
IPI:IPI00331306.7	ARQPSQADTGEEDSDDEDY* EKVPLPNSVFNNTTESCEV ER	1598	Sh3bp2	SH3-domain binding protein 2 isoform c	-1.034
IPI:IPI00137864.1	YDLSNQDHIMDAPPLS*PFP HIK@	1599	Rbl1	Isoform Long of Retinoblastoma-like protein 1	-1.03
IPI:IPI00137864.1	YDLSNQDHIMDAPPLS*PFP HIK	1600	Rbl1	Isoform Long of Retinoblastoma-like protein 1	-1.03
IPI:IPI00320208.3	YGPSSVEDTTGSGAADAK @DDDDIDLFGS*DDEESEE EAK@K@	1601	Eef1b2	Elongation factor 1-beta	-1.028
IPI:IPI00404545.2	SLS*S*PTVTL SAPLEGAK	1602	Nedd4l	Isoform 3 of E3 ubiquitin-protein ligase NEDD4-like	-1.027
IPI:IPI00127764.2	VIEDDGAAAAATVSNSEET PIIENHNS*PQPISDVSAVPC PR ^A	1603	Pcm1	Isoform 1 of Pericentriolar material 1 protein	-1.024
IPI:IPI00131884.1	TT*PAPS*PGS*ANESFFAPS R ^A	1604	Mid1ip1	Mid1-interacting protein 1	-1.024
IPI:IPI00131884.1	TT*PAPS*PGS*ANESFFAPS R ^A	1605	Mid1ip1	Mid1-interacting protein 1	-1.024
IPI:IPI00131884.1	TT*PAPS*PGS*ANESFFAPS R	1606	Mid1ip1	Mid1-interacting protein 1	-1.024
IPI:IPI00400381.9	LGST*GS*QPNSEAEPGPEH APK	1607	Phactr4	Isoform 1 of Phosphatase and actin regulator 4	-1.02
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK	1608	Npm1	Nucleophosmin	-1.018
IPI:IPI00756765.3	ALVIQESSEPPS*PPPS*PDR ^A R ^A	1609	Ehmt2	Euchromatic histone lysine N-methyltransferase 2	-1.017
IPI:IPI00136917.5	TDQEGLNASQPT*PPPLPK @	1610	C23008 1A13Ri	Tyrosine-protein kinase-protein kinase SgK269	-1.016

Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Log2 Area (H/L) Ratio
			k		
IPI:IPI00127415.1	CGSGPVHISGQHLVAVEED AES*EDEDEEDVK	1611	Npm1	Nucleophosmin	-1.015
IPI:IPI00453673.4	RAS*DGGANIQLHAQQLLK	1612	BC033915	serine/threonine-protein kinase QSK	-1.015
IPI:IPI00453837.2	KLPPPPQAPPEEENES*EP EETSGVEGAAFQSR	1613	Kdm1	Lysine-specific histone demethylase 1	-1.014
IPI:IPI00227900.1	FKGPGDTSNFDDYEEEEIR VS*INEK	1614	Prkaca	Isoform 2 of cAMP-dependent protein kinase catalytic subunit alpha	-1.01
IPI:IPI00125662.2	VDPTYGLESSCIAGTGPDE PEK@LEGS*EEEK@M#ETD PDGQQPEK@	1615	Smarcc1	Isoform 1 of SWI/SNF complex subunit SMARCC1	-1.007
IPI:IPI00677756.1	KLS*FSMPR	1616	Ahnak2	Putative uncharacterized protein	-1.006
IPI:IPI00395213.1	LDFLPEMMVDHCS*LNSSP VSK@K@	1617	Cugbp1	Isoform 4 of CUG-BP- and ETR-3-like factor 1	-1.002

Table 8. Gene names and sequences of the phosphopeptides whose intensities decrease after Ku-0063794 treatment. Note that the light cells were treated with rapamycin and serve as controls whereas the heavy cells were treated with a combination of rapamycin and Ku-0063794.

Table 9(a):

ID	Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Class
1	IPI:IPI00121418.1	DGEGPDNLEPACPLSLPLQ GNHTAADMYLS*PLRS*PK	1618	Rb1	Retinoblastoma-associated protein	1
2	IPI:IPI00221581.1	TGS*ESS*QTGASATSGR	1619	Eif4b	Eukaryotic translation initiation factor 4B	1
3	IPI:IPI00929786.1	T*ASISSS*PSEGTPAVGSY GCT*PQS*LPK@	1620	Larp1	Isoform 1 of La-related protein 1	1
4	IPI:IPI00929786.1	T*ASISSS*PSEGTPAVGSY* GCT*PQSLPK@	1621	Larp1	Isoform 1 of La-related protein 1	1
5	IPI:IPI00929786.1	T*ASISSS*PSEGTPAVGS*Y GCTPQSLPK@	1622	Larp1	Isoform 1 of La-related protein 1	1
6	IPI:IPI00317401.6	AES*PETSVESTQST*PQK @	1623	Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B	1
7	IPI:IPI00107958.1	TSDFGS*PVTATAPLAHPN K@PK@	1624	Hn1l	Hematological and neurological expressed 1-like protein	1
8	IPI:IPI00108454.2	R^LS*S^LR^	1625	Rps6	29 kDa protein	1
9	IPI:IPI00225062.2	R^SSS*ELS*PEVVEK@	1626	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1
10	IPI:IPI00761759.1	S*SS*GS*EHSTEGSVSLGD GPLSR^	1627	Larp4	Putative uncharacterized protein	1
11	IPI:IPI00761759.1	SSS*GSEHS*T*EGSVSLGD GPLSR^	1628	Larp4	Putative uncharacterized protein	1
12	IPI:IPI00225062.2	RSS*SELS*PEVVEK	1629	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1
13	IPI:IPI00122594.4	TTPLAS*PSLS*PGR^	1630	Ahctf1	AT-hook-containing transcription factor 1	1
14	IPI:IPI00136107.1	THS*TSS*S*IGSGESPFSR^	1631	Ndr3	Protein NDRG3	1
15	IPI:IPI00136107.1	THS*TSSS*IGSGESPFSR^	1632	Ndr3	Protein NDRG3	1
16	IPI:IPI00136107.1	THS*TSS*SIGSGESPFSR^	1633	Ndr3	Protein NDRG3	1
17	IPI:IPI00136107.1	THS*TSSSIGSGESPFSR^	1634	Ndr3	Protein NDRG3	1
18	IPI:IPI00136107.1	T*HST*SSS*IGSGESPFSR^	1635	Ndr3	Protein NDRG3	1
19	IPI:IPI00136107.1	THST*SSS*IGSGESPFSR^	1636	Ndr3	Protein NDRG3	1
20	IPI:IPI00136107.1	THSTSS*S*IGSGESPFSR^	1637	Ndr3	Protein NDRG3	1
21	IPI:IPI00136107.1	T*HSTSSSIGS*GESPFSSR^	1638	Ndr3	Protein NDRG3	1
22	IPI:IPI00136107.1	THST*SSSIGSGESPFSR^	1639	Ndr3	Protein NDRG3	1
23	IPI:IPI00551454.3	ER^QES*ESEQELVNK@	1640	Pdcd11	Protein RRP5 homolog	1
24	IPI:IPI00117229.3	TS*PAGGTWSSVVGVP	1641	Atxn2	ataxin 2	1
25	IPI:IPI00348442.1	SK@FDS*DEEDEDAENLEA VSSGK@	1642	Sfrs18	splicing factor arginine/serine-rich 18	1
26	IPI:IPI00556837.1	DTVIIVS*EPS*EDEESHDL SVTR	1643	Smarca d1	Isoform 1 of SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A containing DEAD/H box 1	1
27	IPI:IPI00153986.2	GTS*RPGT*PSAEAASTST LR	1644	Gtf2f1	General transcription factor IIF subunit 1	1

ID	Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Class
28	IPI:IPI00225062.2	GCS*PPKS*PEKPPQSTSS* ESCPPSPQPTK	1645	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1
29	IPI:IPI00128904.1	VMTIPYQMPASS*PVICAG GQDR	1646	Pcbp1	Poly(rC)-binding protein 1	1
30	IPI:IPI00121251.7	LSTTPS*PTNS*LHEDGVDD FRR	1647	Tox4	TOX high mobility group box family member 4	1
31	IPI:IPI00320594.5	SQPHSSTS*NQETS*DS*EM EMEAHYPNGVLESVSTR^	1648	Ranbp1 0	Ran-binding protein 10	1
32	IPI:IPI00808277.2	SAPAS*PNHAGVLSAHSSG AQT*PES*LSR^	1649	Foxk2	Isoform 1 of Forkhead box protein K2	1
33	IPI:IPI00137166.1	SR^DAT*PPVS*PINMEDQE R^	1650	Junb	Transcription factor jun-B	1
34	IPI:IPI00454104.1	TTEAPCSPGS*QQPPS*PD ELPANVK@	1651	Scrib	Isoform 1 of Protein LAP4	1
35	IPI:IPI00225062.2	GCS*PPK@S*PEK@PPQST SSECPPS*PQPTK@	1652	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1
36	IPI:IPI00153986.2	GTSR^PGT*PS*AEAASTSS TLR^	1653	Gtf2f1	General transcription factor IIF subunit 1	1
37	IPI:IPI00753321.2	SVSET*SEDK@K@DEES*D EEEEEEEEEEPLGATTR^	1654	Bod1l	biorientation of chromosomes in cell division 1-like	1
38	IPI:IPI00153986.2	GT*SR^PGT*PSAEAASTSS TLR^	1655	Gtf2f1	General transcription factor IIF subunit 1	1
39	IPI:IPI00153986.2	GTS*R^PGTPS*AEAASTSS TLR^	1656	Gtf2f1	General transcription factor IIF subunit 1	1
40	IPI:IPI00929786.1	TASIS*S*SPSEGTPAVGSY GCT*PQSLPK@	1657	Larp1	Isoform 1 of La-related protein 1	1
41	IPI:IPI00929786.1	TAS*ISSS*PSEGTPAVGSY GCT*PQS*LPK@	1658	Larp1	Isoform 1 of La-related protein 1	1
42	IPI:IPI00130920.1	RSES*PFEGK	1659	Mtap1b	Microtubule-associated protein 1B	1
43	IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA SK@PS*SPR^	1660	Ccnl1	Isoform 1 of Cyclin-L1	1
44	IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA S*KPSSPR	1661	Ccnl1	Isoform 1 of Cyclin-L1	1
45	IPI:IPI00336973.2	GLNLDGT*PALSTLGGFS*P ASK@PS*SPR^	1662	Ccnl1	Isoform 1 of Cyclin-L1	1
46	IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA S*K@PS*SPR^	1663	Ccnl1	Isoform 1 of Cyclin-L1	1
47	IPI:IPI00379844.4	TAS*EGDGGGAAGGAGTAG GR^PMSVAGS*PLS*PGPV R^	1664	Irs2	Insulin receptor substrate 2	1
48	IPI:IPI00336973.2	GLNLDGTPALSTLGGFS*PA SKPSS*PR	1665	Ccnl1	Isoform 1 of Cyclin-L1	1
49	IPI:IPI00336973.2	GLNLDGT*PALSTLGGFS*P ASKPSS*PR	1666	Ccnl1	Isoform 1 of Cyclin-L1	1
50	IPI:IPI00656285.2	SLVS*PIPS*PTGTISVPNSC PAS*PR^	1667	Foxk1	Forkhead box protein K1	1
51	IPI:IPI00656285.2	SLVSPIPSPT*GT*ISVPNSC	1668	Foxk1	Forkhead box protein K1	1

ID	Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Class
		PAS*PR				
52	IPI:IPI00454104.1	TTEAPCS*PGSQPPS*PD ELPANVK@	1669	Scrib	Isoform 1 of Protein LAP4	1
53	IPI:IPI00753321.2	S*VSETSEDK@K@DEES*D EEEEEEEEEEPLGATTR^	1670	Bod1l	bioorientation of chromosomes in cell division 1-like	1
54	IPI:IPI00753321.2	SVSETS*EDK@K@DEES*D EEEEEEEEEEPLGATTR^	1671	Bod1l	bioorientation of chromosomes in cell division 1-like	1
55	IPI:IPI00313307.3	SYQNS*PSS*EDGIR^PLPE YSTEK@	1672	Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1	1
56	IPI:IPI00225062.2	GCS*PPK@S*PEK@PPQS* TSSESCPPSPQPTK@	1673	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	1
57	IPI:IPI00318938.6	NS*PVAK@TPPK@DLPAIP GVTSPS*DEPPMQASQSQ LPSSPEDK@	1674	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	1
58	IPI:IPI00130920.1	SLMSS*PEDLTK@DFEELK @AEEIDVAK@	1675	Mtap1b	Microtubule-associated protein 1B	1
59	IPI:IPI00553798.2	SS*EVVLS*GDDEDYQR^	1676	Ahnak	AHNAK nucleoprotein isoform 1	1
60	IPI:IPI00129264.1	ATSR^PINLGPSS*PNTEIH WTPYR^	1677	Sorbs3	Vinexin	1
61	IPI:IPI00129264.1	ATSRPINLGPS*SPNTEIHW TPYR	1678	Sorbs3	Vinexin	1
62	IPI:IPI00123410.5	TIS*AQDTLAYATALLNEK@	1679	Usp24	Isoform 1 of Ubiquitin carboxyl-terminal hydrolase 24	1
63	IPI:IPI00226441.2	LHYT*PPLQS*PIT*DGDPLL GQS*PWR^	1680	Lin9	Isoform 2 of Lin-9 homolog	1
64	IPI:IPI00309059.7	STS*PIIGS*PPVR^	1681	Pat1	Protein PAT1 homolog 1	1
65	IPI:IPI00336713.1	CS*PVPGLSSS*PSGSPLHG K@	1682	Bcas3	Isoform 1 of Breast carcinoma-amplified sequence 3 homolog	1
66	IPI:IPI00320905.7	LGEQGPEPGPT*PPQTPT* PPS*TPPLAK	1683	Arhgap 17	Isoform 1 of Rho GTPase-activating protein 17	1
67	IPI:IPI00309059.7	R^S*TS*PIIGS*PPVR^	1684	Pat1	Protein PAT1 homolog 1	1
68	IPI:IPI00309059.7	RSTS*PIIGS*PPVR	1685	Pat1	Protein PAT1 homolog 1	1
69	IPI:IPI00309059.7	ST*S*PIIGS*PPVR^	1686	Pat1	Protein PAT1 homolog 1	1
70	IPI:IPI00317599.3	SQEDEEEIST*SPGVSEFVS DAFDTCSLNQEDLRK	1687	Syap1	Synapse-associated protein 1	1
71	IPI:IPI00317599.3	SQEDEEEISTS*PGVSEFVS DAFDTCSLNQEDLRK	1688	Syap1	Synapse-associated protein 1	1
72	IPI:IPI00656285.2	SLVS*PIPSPT*GTISVPNS* CPASPR^	1689	Foxk1	Forkhead box protein K1	1
73	IPI:IPI00676574.2	RVS*TDLPEGQDVYTAACN SVIHR	1690	Herc1	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1	1
74	IPI:IPI00458958.2	DWDK@ES*EGEEPAGGR^	1691	Rrp15	RRP15-like protein	2
75	IPI:IPI00230719.8	R^DS*SDDWEIPDGQITVGQ R^	1692	Braf	Isoform 1 of B-Raf proto-oncogene serine/threonine-protein kinase	2

ID	Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Class
76	IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTTPGGT*R	1693	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	2
77	IPI:IPI00874995.2	AS*DDLGE PDVFATAPFR	1694	Aak1	Uncharacterized protein FLJ45252 homolog	2
78	IPI:IPI00318938.6	VALGDGVQLPPGDYSTT*P GGTLFSTT*PGGTR^	1695	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	2
79	IPI:IPI00318938.6	VALGDGVQLPPGDYSTTPG GT*LFSTT*PGGTR	1696	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	2
80	IPI:IPI00318938.6	VALGDGVQLPPGDYS*TP GGTLFSTT*PGGTR^	1697	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	2
81	IPI:IPI00323045.3	S*MDVDLNQAHMEDTPK@	1698	Melk	Maternal embryonic leucine zipper kinase	2
82	IPI:IPI00623284.4	IWDPTPS*HTPAGAAT*PGR GDT*PGHAT*PGHGGATSS AR	1699	Sf3b1	Splicing factor 3B subunit 1	2
83	IPI:IPI00125960.1	TAS*GSS*VTSLEGTR	1700	Ndrp1	Protein NDRG1	2
84	IPI:IPI00318938.6	R^VALGDGVQLPPGDYSTT *PGGTLFSTT*PGGTR^	1701	Eif4ebp 1	Eukaryotic translation initiation factor 4E-binding protein 1	2
85	IPI:IPI00229571.1	IS*SK@S*PGHMVILNQTK@	1702	Sltn	Isoform 1 of SAFB-like transcription modulator	2
86	IPI:IPI00120095.2	DFTK@PQDGDIIAPLIT*PLK @	1703	Samhd 1	SAM domain and HD domain- containing protein 1	2
87	IPI:IPI00340860.5	T*AS*EGSEAETPEAPK	1704	Larp7	Isoform 1 of La-related protein 7	2
88	IPI:IPI00664670.4	LGS*FGSITR^	1705	Finc	Isoform 1 of Filamin-C	2
89	IPI:IPI00654192.2	SLS*FSEPQQPPPTVK@	1706	Zfp395	zinc finger protein 395	2
90	IPI:IPI00225062.2	IHTTALTGQS*PPLASGHQG EGDAPSVEPGATNIQQPSS *PAPSTK	1707	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	2
91	IPI:IPI00225062.2	IHTTALTGQS*PPLASGHQG EGDAPSVEPGATNIQQPSS *PAPS*TK@	1708	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	2
92	IPI:IPI00225062.2	IHTTALTGQS*PPLASGHQG EGDAPSVEPGATNIQQPSS *PAPST*K	1709	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	2
93	IPI:IPI00339428.9	MSSHT*ETSSFLQTLTGR	1710	Dock7	Isoform 2 of Dedicator of cytokinesis protein 7	2
94	IPI:IPI00225062.2	DGSGT*PSRHSLS*GS*S*P GMKDTPQT*PSR	1711	Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2	2
95	IPI:IPI00668709.2	DRSSS*APNVHINTIEPVNID DLIR	1712	Braf	B-Raf protein	2
96	IPI:IPI00135660.5	RGNNS*AVGS*NADLT*IEE DEEEEPVALQQAQQVR	1713	Sdpr	Serum deprivation-response protein	2
97	IPI:IPI00135660.5	R^GNNSAVGS*NADLT*IEE DEEEEPVALQQAQQVR^	1714	Sdpr	Serum deprivation-response protein	2
98	IPI:IPI00404545.2	SLS*S*PTVTL SAPLEGAK@	1715	Nedd4l	Isoform 3 of E3 ubiquitin-protein ligase NEDD4-like	2
99	IPI:IPI00121892.9	R^PPS*PDPNTK@	1716	Spnb2	Isoform 2 of Spectrin beta chain brain 1	2

ID	Reference	Ascore Seq	SEQ ID NO	Gene Name	Annotation	Class
100	IPI:IPI00322707.5	AKQPVIGDQNS*DSDEMLA VLK	1717	Atrx	Transcriptional regulator ATRX	2
101	IPI:IPI00929786.1	SLPT*TVPES*PNYR^	1718	Larp1	Isoform 1 of La-related protein 1	3
102	IPI:IPI00125319.1	TTS*FAESCK@PVQQPSAF GSMK@	1719	Gsk3b	Glycogen synthase kinase-3 beta	3

Table 9(b)

ID	rapa median area ratio	rapa median SN ratio	KU median area ratio	KU median SN ratio
1	-1.15E+00	-1.14E+00	-0.8183	-0.9318
2	-2.1437	-2.4238	-0.78695	-0.9492
3	-4.758	-4.9643	-0.6283	-0.5475
4	-4.62805	-4.47925	-0.6283	-0.5475
5	-3.6217	-3.885	-0.6283	-0.5475
6	-1.0246	-1.0724	-0.5666	0.1321
7	-1.881	-1.90875	-0.5354	-0.5361
8	-5.2234	-5.13485	-0.4254	-0.6826
9	-1.8021	-2.01515	-0.4151	-0.4336
10	-1.5621	-1.0464	-0.3725	-0.7405
11	-1.4347	-1.3061	-0.3725	-0.7405
12	-1.6324	-1.5779	-0.3224	-0.0637
13	-1.5511	-1.71335	-0.2831	-0.0584
14	-1.78365	-2.00075	-0.2767	0.0092
15	-1.7555	-2.0749	-0.2767	0.0092
16	-1.7499	-1.7737	-0.2767	0.0092
17	-1.5242	-1.76425	-0.2767	0.0092
18	-2.0759	-2.2586	-0.2661	-0.1505
19	-1.9707	-1.7471	-0.2661	-0.1505
20	-1.8874	-1.85315	-0.2661	-0.1505
21	-1.8106	-1.691	-0.2661	-0.1505
22	-1.6838	-1.5207	-0.2661	-0.1505
23	-2.8898	-2.7784	-0.2201	-0.1513
24	-1.0015	-0.8287	-0.2135	-0.3206
25	-3.15205	-2.9693	-0.213	0.1493
26	-1.3868	-0.6688	-0.1992	-0.1577
27	-1.1818	-1.15455	-0.1474	-0.0308
28	-1.7403	-1.8968	-0.1417	0.6197
29	-1.6267	-1.0033	-0.139	-0.2714
30	-1.0844	-1.1514	-0.106	-0.2609
31	-2.78805	-1.56635	-0.1017	-0.8833
32	-3.0877	-2.2749	-0.099	0.6127
33	-2.20425	-2.1077	-0.085	0.023
34	-1.2842	-0.6546	-0.0822	0.1059
35	-1.7868	-2.1396	-0.0816	0.1618
36	-1.2551	-1.22675	-0.0656	-0.106
37	-2.9525	-3.6913	-0.0637	0.7614

ID	rapa median area ratio	rapa median SN ratio	KU median area ratio	KU median SN ratio
38	-1.1888	-1.2446	-0.014	-0.0308
39	-1.2382	-1.25285	-0.0136	0.0107
40	-2.1557	-2.1257	-0.01	-0.0601
41	-4.4981	-3.9942	0.0259	-0.0762
42	-1.7508	-0.9897	0.0386	0.3631
43	-1.896	-2.1685	0.0563	0.2174
44	-1.89265	-2.1434	0.0563	0.1073
45	-1.40465	-1.02655	0.0563	0.2174
46	-1.896	-2.1685	0.0814	0.17005
47	-3.6492	-3.6492	0.0966	0.0223
48	-1.8973	-2.1434	0.1063	0.2306
49	-1.273	-0.7556	0.1063	0.2306
50	-2.8428	-2.9973	0.1159	0.0362
51	-2.8019	-2.9973	0.1159	0.0362
52	-1.2352	-0.0592	0.1368	0.1632
53	-3.106	-3.2482	0.1555	0.3337
54	-2.9525	-3.6913	0.1555	0.3337
55	-1.298	-1.4299	0.2219	0.413
56	-1.7403	-1.8968	0.22985	0.1085
57	-1.3906	-1.2466	0.2704	1.5615
58	-1.1401	-1.2853	0.2835	0.1358
59	-2.4187	-0.9488	0.307	0.366
60	-1.3056	-1.2452	0.3118	0.4053
61	-1.2719	-1.0234	0.3118	0.4053
62	-1.4486	-1.5455	0.3219	0.2377
63	-3.8536	-3.8536	0.3485	0.0243
64	-1.36155	-1.26665	0.3516	0.4392
65	-1.889	-1.727	0.3696	1.0368
66	-2.0572	-2.2717	0.3908	0.1481
67	-1.626	-2.0445	0.51825	0.767
68	-1.29335	-1.2722	0.51825	0.767
69	-1.9492	-2.05475	0.5526	0.865
70	-1.1567	-1.0106	0.5969	0.9976
71	-1.1567	-1.0106	0.5969	0.9976
72	-2.818	-2.9973	1.1365	1.0801
73	-3.4866	-3.4138	1.2714	1.4529
74	0.0401	-0.1138	-3.4595	-5.0415
75	0.011	-0.1502	-3.3715	-3.3715
76	-0.22145	-0.31255	-2.9948	-2.3042
77	0.2389	0.2797	-2.8989	-2.0993
78	-0.2639	-0.32955	-2.8403	-2.8893
79	-0.2514	-0.2836	-2.7755	-2.167
80	-0.2469	-0.3415	-2.5654	-2.1344
81	-0.58015	-0.1451	-2.5295	-2.6811
82	-0.1752	0.3008	-2.3289	-2.6763
83	0.2073	0.2067	-2.0546	-2.0769
84	-0.3079	-0.4553	-1.759	-1.6004
85	0.13985	0.04745	-1.5237	-1.538

ID	rapa median area ratio	rapa median SN ratio	KU median area ratio	KU median SN ratio
86	-0.1736	-0.41725	-1.3706	-0.9742
87	-0.1646	-0.2464	-1.3468	-1.5444
88	0.3745	0.3233	-1.2893	-1.2512
89	-0.5295	-0.8185	-1.1648	-1.0131
90	-0.4199	-0.3301	-1.1227	-0.4758
91	-0.2531	-0.1626	-1.1227	-0.4758
92	-0.1997	-0.1626	-1.1227	-0.4758
93	0.1923	0.3451	-1.1197	-1.2356
94	-0.0084	0.0364	-1.0814	-1.582
95	-0.3065	-0.4384	-1.0477	-1.431
96	-0.18955	-0.4136	-1.0458	-1.0184
97	-0.15495	-0.3246	-1.0458	-1.0184
98	-0.573	-0.2978	-1.0265	-0.7599
99	0.0109	-0.0378	-1.0209	-0.674
100	0.10215	0.0699	-1.011	-2.1889
101	-2.1207	-2.1939	-6.1589	-5.4183
102	-1.71915	-1.62995	-1.07715	-2.06845

Table 9. Classification of mTOR targets identified in the Rapamycin and Ku-0063794

screens. Class 1 represents downstream effectors of rapamycin-sensitive mTORC1. Class 2 represents downstream effectors of rapamycin-insensitive mTORC1 or mTORC2. Class 3 represents the proteins downstream of both mTORC1 and mTORC2. Name of the genes and the sequences of the phosphopeptides are shown. Table 9 is provided in two parts because the columns span more than a single page. Table 9(a) contains columns 1-6 of Table 9 and Table 9(b) contains columns 7-10, wherein corresponding entries are identified in an ID column in each section. Information provided in (a) for ID 1 relates to the information provided in (b) for ID 1 and vice versa, information provided in (a) for ID 2 relates to the information provided in (b) for ID 2 and vice versa, and so on.

Table 10:

Rapa BP GO pathways (a):

ID	Term	Count	%	PValue
1	GO:0010605~negative regulation of macromolecule metabolic process	20	10.41666667	4.18E-07
2	GO:0031327~negative regulation of cellular biosynthetic process	17	8.854166667	4.17E-06
3	GO:0010558~negative regulation of macromolecule biosynthetic process	16	8.333333333	1.31E-05
4	GO:0045934~negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	15	7.8125	0.0000314
5	GO:0032868~response to insulin stimulus	6	3.125	0.000264
6	GO:0016481~negative regulation of transcription	13	6.770833333	0.000271
7	GO:0016192~vesicle-mediated transport	14	7.291666667	0.000603
8	GO:0032869~cellular response to insulin stimulus	5	2.604166667	0.000783
9	GO:0051253~negative regulation of RNA metabolic process	11	5.729166667	0.000886
10	GO:0051248~negative regulation of protein metabolic process	6	3.125	0.00096
11	GO:0006898~receptor-mediated endocytosis	4	2.083333333	0.001048574
12	GO:0006468~protein amino acid phosphorylation	16	8.333333333	0.00137311
13	GO:0051276~chromosome organization	12	6.25	0.001936745
14	GO:0016568~chromatin modification	9	4.6875	0.002136023
15	GO:0043434~response to peptide hormone stimulus	6	3.125	0.002310739
16	GO:0032870~cellular response to hormone stimulus	5	2.604166667	0.002406516
17	GO:0008286~insulin receptor signaling pathway	4	2.083333333	0.002457872
18	GO:0045892~negative regulation of transcription, DNA-dependent	10	5.208333333	0.003123471
19	GO:0006325~chromatin organization	10	5.208333333	0.003622675
20	GO:0046777~protein amino acid autophosphorylation	5	2.604166667	0.003851564
21	GO:0010627~regulation of protein kinase cascade	7	3.645833333	0.004027038
22	GO:0016310~phosphorylation	16	8.333333333	0.004128421
23	GO:0051656~establishment of organelle localization	4	2.083333333	0.004303328
24	GO:0007010~cytoskeleton organization	10	5.208333333	0.004531801
25	GO:0032535~regulation of cellular component size	7	3.645833333	0.004843432
26	GO:0022402~cell cycle process	11	5.729166667	0.00498568
27	GO:0045926~negative regulation of growth	5	2.604166667	0.005003024
28	GO:0032269~negative regulation of cellular protein metabolic process	5	2.604166667	0.005258125
29	GO:0065003~macromolecular complex assembly	10	5.208333333	0.005717288
30	GO:0032268~regulation of cellular protein metabolic process	9	4.6875	0.006003754
31	GO:0000122~negative regulation of transcription from RNA polymerase II promoter	8	4.166666667	0.007342706
32	GO:0032319~regulation of Rho GTPase activity	3	1.5625	0.007895767
33	GO:0046578~regulation of Ras protein signal transduction	7	3.645833333	0.008452332
34	GO:0043933~macromolecular complex subunit organization	10	5.208333333	0.009572997
35	GO:0006793~phosphorus metabolic process	17	8.854166667	0.009756342

ID	Term	Count	%	PValue
36	GO:0006796~phosphate metabolic process	17	8.854166667	0.009756342
37	GO:0006897~endocytosis	7	3.645833333	0.010081394
38	GO:0010324~membrane invagination	7	3.645833333	0.010081394
39	GO:0006396~RNA processing	11	5.729166667	0.01020022
40	GO:0007169~transmembrane receptor protein tyrosine kinase signaling pathway	7	3.645833333	0.01110676
41	GO:0010608~posttranscriptional regulation of gene expression	6	3.125	0.01469374
42	GO:0045792~negative regulation of cell size	4	2.083333333	0.014742447
43	GO:0001701~in utero embryonic development	8	4.166666667	0.015417559
44	GO:0051640~organelle localization	4	2.083333333	0.015500935
45	GO:0051493~regulation of cytoskeleton organization	5	2.604166667	0.015757695
46	GO:0007049~cell cycle	13	6.770833333	0.015795779
47	GO:0006417~regulation of translation	5	2.604166667	0.016293879
48	GO:0017148~negative regulation of translation	3	1.5625	0.019054263
49	GO:0034622~cellular macromolecular complex assembly	7	3.645833333	0.019238583
50	GO:0008361~regulation of cell size	5	2.604166667	0.020996944
51	GO:0009725~response to hormone stimulus	6	3.125	0.022401918
52	GO:0051056~regulation of small GTPase mediated signal transduction	7	3.645833333	0.023850905
53	GO:0030029~actin filament-based process	6	3.125	0.028573614
54	GO:0048729~tissue morphogenesis	7	3.645833333	0.028642761
55	GO:0001932~regulation of protein amino acid phosphorylation	5	2.604166667	0.030261806
56	GO:0008104~protein localization	14	7.291666667	0.031319732
57	GO:0000278~mitotic cell cycle	7	3.645833333	0.031803074
58	GO:0034621~cellular macromolecular complex subunit organization	7	3.645833333	0.032351058
59	GO:0009719~response to endogenous stimulus	6	3.125	0.03367924
60	GO:0045449~regulation of transcription	31	16.14583333	0.03551581
61	GO:0007163~establishment or maintenance of cell polarity	3	1.5625	0.036247509
62	GO:0080135~regulation of cellular response to stress	4	2.083333333	0.036466875
63	GO:0006357~regulation of transcription from RNA polymerase II promoter	12	6.25	0.037453702
64	GO:0032314~regulation of Rac GTPase activity	2	1.041666667	0.038299417
65	GO:0040007~growth	6	3.125	0.040063168
66	GO:0022403~cell cycle phase	8	4.166666667	0.040932988
67	GO:0031328~positive regulation of cellular biosynthetic process	11	5.729166667	0.042602185
68	GO:0032318~regulation of Ras GTPase activity	4	2.083333333	0.042864282
69	GO:0010604~positive regulation of macromolecule metabolic process	12	6.25	0.044146336
70	GO:0022613~ribonucleoprotein complex biogenesis	5	2.604166667	0.044519805
71	GO:0009891~positive regulation of biosynthetic process	11	5.729166667	0.044819532
72	GO:0046822~regulation of nucleocytoplasmic transport	3	1.5625	0.045236118
73	GO:0006346~methylation-dependent chromatin silencing	2	1.041666667	0.047644564
74	GO:0016044~membrane organization	7	3.645833333	0.049524346
75	GO:0007167~enzyme linked receptor protein signaling pathway	7	3.645833333	0.05025049

ID	Term	Count	%	PValue
76	GO:0035023~regulation of Rho protein signal transduction	4	2.083333333	0.051230918
77	GO:0043009~chordate embryonic development	9	4.6875	0.052874272
78	GO:0006916~anti-apoptosis	4	2.083333333	0.054183284
79	GO:0009792~embryonic development ending in birth or egg hatching	9	4.6875	0.055294577
80	GO:0044087~regulation of cellular component biogenesis	4	2.083333333	0.055689578
81	GO:0006350~transcription	25	13.02083333	0.055970599
82	GO:0043062~extracellular structure organization	5	2.604166667	0.057303217
83	GO:0043122~regulation of I-kappaB kinase/NF-kappaB cascade	3	1.5625	0.057483236
84	GO:0051726~regulation of cell cycle	6	3.125	0.057658627
85	GO:0046907~intracellular transport	9	4.6875	0.059056688
86	GO:0006260~DNA replication	5	2.604166667	0.060776557
87	GO:0048598~embryonic morphogenesis	8	4.166666667	0.060833555
88	GO:0043087~regulation of GTPase activity	4	2.083333333	0.061912428
89	GO:0051129~negative regulation of cellular component organization	4	2.083333333	0.061912428
90	GO:0032386~regulation of intracellular transport	3	1.5625	0.062669535
91	GO:0033043~regulation of organelle organization	5	2.604166667	0.063153096
92	GO:0042325~regulation of phosphorylation	7	3.645833333	0.063602017
93	GO:0045786~negative regulation of cell cycle	3	1.5625	0.065320236
94	GO:0001570~vasculogenesis	3	1.5625	0.065320236
95	GO:0045947~negative regulation of translational initiation	2	1.041666667	0.066065335
96	GO:0006461~protein complex assembly	6	3.125	0.070461851
97	GO:0070271~protein complex biogenesis	6	3.125	0.070461851
98	GO:0030833~regulation of actin filament polymerization	3	1.5625	0.070731878
99	GO:0010557~positive regulation of macromolecule biosynthetic process	10	5.208333333	0.073220823
100	GO:0019220~regulation of phosphate metabolic process	7	3.645833333	0.073259901
101	GO:0051174~regulation of phosphorus metabolic process	7	3.645833333	0.073259901
102	GO:0048589~developmental growth	4	2.083333333	0.073541659
103	GO:0030838~positive regulation of actin filament polymerization	2	1.041666667	0.075142677
104	GO:0030308~negative regulation of cell growth	3	1.5625	0.076284196
105	GO:0030036~actin cytoskeleton organization	5	2.604166667	0.077082848
106	GO:0031399~regulation of protein modification process	5	2.604166667	0.077082848
107	GO:0000902~cell morphogenesis	7	3.645833333	0.080785789
108	GO:0016477~cell migration	6	3.125	0.08471051
109	GO:0008064~regulation of actin polymerization or depolymerization	3	1.5625	0.084860387
110	GO:0030832~regulation of actin filament length	3	1.5625	0.08778162
111	GO:0002009~morphogenesis of an epithelium	5	2.604166667	0.088103636
112	GO:0006333~chromatin assembly or disassembly	4	2.083333333	0.089801855
113	GO:0010638~positive regulation of organelle organization	3	1.5625	0.090732662
114	GO:0045941~positive regulation of transcription	9	4.6875	0.091555467
115	GO:0006887~exocytosis	4	2.083333333	0.091694717
116	GO:0008283~cell proliferation	6	3.125	0.092969193
117	GO:0035020~regulation of Rac protein signal transduction	2	1.041666667	0.093035503

ID	Term	Count	%	PValue
118	GO:0000226~microtubule cytoskeleton organization	4	2.083333333	0.093604179
119	GO:0060562~epithelial tube morphogenesis	4	2.083333333	0.093604179

Rapa BP GO pathways (b):

ID	Genes
1	BCLAF1,FOXK1,GM5611,ZEB2,SAP30,EIF4EBP1,SORBS3,EIF4EBP2,NPM1,GM7289,FAM129A,HELLS,IBTK,LOC100046628,NACC1,GM9118,TRIM28,RB1,EHMT2,FLNA,FXR1,GM6477,NFIC,CUX1,LOC633387,SMARCA4
2	PALM,BCLAF1,NACC1,FOXK1,TRIM28,ZEB2,RB1,EHMT2,FXR1,SAP30,EIF4EBP1,SORBS3,EIF4EBP2,CUX1,NFIC,HELLS,SMARCA4
3	BCLAF1,NACC1,FOXK1,TRIM28,ZEB2,RB1,EHMT2,FXR1,SAP30,EIF4EBP1,SORBS3,EIF4EBP2,CUX1,NFIC,HELLS,SMARCA4
4	PALM,LOC100046628,BCLAF1,NACC1,FOXK1,GM9118,TRIM28,GM5611,ZEB2,RB1,EHMT2,GM6477,SAP30,SORBS3,NPM1,GM7289,CUX1,NFIC,LOC633387,HELLS,SMARCA4
5	ZFP106,IRS2,EIF4EBP1,EIF4EBP2,LOC100048123,LOC544757,MTOR,AKT2
6	NACC1,BCLAF1,FOXK1,TRIM28,ZEB2,RB1,EHMT2,SAP30,SORBS3,NFIC,CUX1,HELLS,SMARCA4
7	MYO5A,GM8786,LOC100048600,SNX17,ARHGAP17,LLGL1,SCRIB,FLNA,DAB2,CTTN,ULK1,RAB1,FKBP15,CUX1,ERC1,TRIP10
8	ZFP106,IRS2,EIF4EBP1,EIF4EBP2,LOC100048123,LOC544757,AKT2
9	LOC100046628,FOXK1,GM9118,TRIM28,GM5611,RB1,EHMT2,GM6477,SAP30,SORBS3,NPM1,GM7289,CUX1,NFIC,LOC633387,HELLS,SMARCA4
10	IBTK,EIF4EBP1,EIF4EBP2,FAM129A,FLNA,FXR1
11	DAB2,CTTN,GM8786,ULK1,SNX17
12	SRPK2,GM4521,BCR,TRIM28,LOC544757,PKN2,WNK1,RPS6KB1,PRKD2,PTK2,LOC100048123,ULK1,AAK1,GSK3B,EEF2K,BMP2K,CDK12,MTOR,AKT2
13	KDM6A,PDS5B,ARID1A,RB1,EHMT2,1600027N09RIK,SMARCC2,LOC675933,CHD1,KDM3B,TINF2,HELLS,SMARCA4
14	KDM6A,SMARCC2,CHD1,KDM3B,RB1,1600027N09RIK,EHMT2,HELLS,SMARCA4
15	ZFP106,IRS2,EIF4EBP1,EIF4EBP2,LOC100048123,LOC544757,MTOR,AKT2
16	ZFP106,IRS2,EIF4EBP1,EIF4EBP2,LOC100048123,LOC544757,AKT2
17	ZFP106,IRS2,EIF4EBP1,EIF4EBP2
18	SAP30,SORBS3,FOXK1,TRIM28,RB1,CUX1,EHMT2,NFIC,HELLS,SMARCA4
19	KDM6A,SMARCC2,LOC675933,CHD1,ARID1A,KDM3B,RB1,1600027N09RIK,EHMT2,HELLS,SMARCA4
20	PTK2,ULK1,TRIM28,CDK12,MTOR
21	PDCD11,SORBS3,LOC100048123,SQSTM1,LOC544757,ZEB2,RICTOR,FLNA,AKT2
22	SRPK2,GM4521,BCR,TRIM28,LOC544757,PKN2,WNK1,RPS6KB1,PRKD2,PTK2,LOC100048123,ULK1,AAK1,GSK3B,EEF2K,BMP2K,CDK12,MTOR,AKT2
23	MYO5A,LOC100046628,PTK2,GM9118,NPM1,GM5611,GM7289,SCRIB,LOC633387,GM6477
24	INF2,PALM,LOC100046628,FMNL3,GM9118,GM5611,ARHGAP17,RICTOR,INF2Q,FLNA,GM6477,PTK2,NPM1,MTAP1B,GM7289,LOC633387,RANBP10
25	LOC100046628,GM9118,FOXK1,GM5611,RICTOR,GM6477,ULK1,NPM1,GM7289,SPNA2,MTOR,DNAJC2,LOC633387
26	LOC100046628,PDS5B,ZC3HC1,GM9118,AHCTF1,GM5611,RB1,EHMT2,CD2AP,GM6477,MACF1,GSK3B,NPM1,GM7289,DNAJC2,LOC633387,HELLS
27	ATXN2,PTK2,FOXK1,ULK1,DNAJC2
28	IBTK,EIF4EBP1,EIF4EBP2,FAM129A,FXR1
29	SRPK2,LOC100046628,NACC1,GM9118,AHCTF1,GM5611,FLNA,GM6477,EIF3A,PTK2,GTF2F1,NPM1,GM7289,LOC633387,HELLS,SMARCA4

ID	Genes
30	IBTK, EIF4G1, EIF4EBP1, EIF4EBP2, ZEB2, MTOR, RICTOR, FAM129A, FXR1
31	SAP30, SORBS3, TRIM28, RB1, CUX1, EHMT2, NFIC, SMARCA4
32	MTOR, RICTOR, SCRIB
33	BCR, GBF1, TBC1D4, MTOR, RICTOR, SCRIB, IQSEC1
34	SRPK2, LOC100046628, NACC1, GM9118, AHCTF1, GM5611, FLNA, GM6477, EIF3A, PTK2, GTF2F1, NPM1, GM7289, LOC633387, HELLS, SMARCA4
35	SRPK2, GM4521, BCR, TRIM28, LOC544757, PKN2, WNK1, RPS6KB1, PRKD2, PTK2, LOC100048123, ULK1, AAK1, GSK3B, CDK12, EEK2K, BMP2K, PPP1R12A, MTOR, AKT2
36	SRPK2, GM4521, BCR, TRIM28, LOC544757, PKN2, WNK1, RPS6KB1, PRKD2, PTK2, LOC100048123, ULK1, AAK1, GSK3B, CDK12, EEK2K, BMP2K, PPP1R12A, MTOR, AKT2
37	DAB2, CTTN, GM8786, ULK1, SNX17, FKBP15, TRIP10, SCRIB
38	DAB2, CTTN, GM8786, ULK1, SNX17, FKBP15, TRIP10, SCRIB
39	LOC100046766, SRPK2, PDCD11, LOC100046744, EMG1, SFRS1, LOC100047322, RSL1D1, SFRS8, PCB P1, SRRM2, LARP7, LOC100046735, DHX15, SRRM1, LOC100048559
40	ZFP106, GRB10, PTK2, IRS2, EIF4EBP1, EIF4EBP2, FLNA
41	EIF4G1, EIF4EBP1, EIF4EBP2, FAM129A, FLNA, FXR1
42	FOXK1, ULK1, MTOR, DNAJC2
43	MIB1, DAB2, SFRS1, TCFEB, JUNB, LOC100048559, MLL2, MED1, SMARCA4
44	MYO5A, LOC100046628, PTK2, GM9118, NPM1, GM5611, GM7289, SCRIB, LOC633387, GM6477
45	LOC100046628, GM9118, MTAP1B, NPM1, GM5611, SPNA2, GM7289, MTOR, RICTOR, LOC633387, GM6477
46	LOC100046628, ZC3HC1, PDS5B, GM9118, LIN9, GM5611, AHCTF1, RB1, EHMT2, CD2AP, GM6477, NUMA1, MACF1, GSK3B, NPM1, GM7289, DNAJC2, HELLS, LOC633387
47	EIF4G1, EIF4EBP1, EIF4EBP2, FAM129A, FXR1
48	EIF4EBP1, EIF4EBP2, FXR1
49	SRPK2, PTK2, EIF3A, AHCTF1, HELLS, FLNA, SMARCA4
50	LOC100046628, FOXK1, GM9118, ULK1, NPM1, GM5611, GM7289, MTOR, DNAJC2, LOC633387, GM6477
51	ZFP106, IRS2, EIF4EBP1, EIF4EBP2, LOC100048123, LOC544757, MTOR, AKT2
52	BCR, GBF1, TBC1D4, MTOR, RICTOR, SCRIB, IQSEC1
53	MYO5A, INF2, FMNL3, ARHGAP17, RICTOR, INF2Q, FLNA
54	MIB1, MACF1, TNC, ZEB2, SCRIB, MED1, SMARCA4
55	IBTK, ZEB2, MTOR, RICTOR, FAM129A
56	PALM, LOC100046628, LOC100048600, GM9118, SNX17, GM5611, AHCTF1, FLNA, SCRIB, GM6477, POM121, ERBB2IP, MACF1, ULK1, RAB1, GSK3B, NPM1, GM7289, SNX30, ERC1, LOC633387
57	ZC3HC1, PDS5B, AHCTF1, RB1, CD2AP, DNAJC2, HELLS
58	SRPK2, PTK2, EIF3A, AHCTF1, HELLS, FLNA, SMARCA4
59	ZFP106, IRS2, EIF4EBP1, EIF4EBP2, LOC100048123, LOC544757, MTOR, AKT2
60	BCLAF1, CARHSP1, FOXK1, FOXK2, AHCTF1, ZEB2, 1600027N09RIK, SAP30, SORBS3, GM9791, KDM3B, TCFEB, DNAJC2, HELLS, NACC1, PDCD11, TRIM28, CCNL1, RB1, EHMT2, JUNB, FLNA, RFC1, GTF2F1, SMARCC2, TMPO, ZFP516, CUX1, NFIC, PBX2, SMARCA4, MED1
61	MACF1, SCRIB, LLGL1
62	LOC100046628, LOC100048123, GM9118, NPM1, LOC544757, GM5611, ZEB2, GM7289, MTOR, LOC633387, AKT2, GM6477
63	SAP30, SORBS3, FOXK1, TRIM28, RB1, CUX1, TCFEB, EHMT2, NFIC, PBX2, MED1, SMARCA4
64	MTOR, RICTOR
65	MYO5A, LOC100046628, GM9118, ULK1, NPM1, GM5611, GM7289, EHMT2, LOC633387, MED1, GM6477, SMARCA4
66	ZC3HC1, PDS5B, AHCTF1, RB1, EHMT2, CD2AP, DNAJC2, HELLS
67	LOC100046628, GM9118, FOXK1, TRIM28, AHCTF1, GM5611, RB1, GM6477, GTF2F1, NPM1, GM7289, TCFEB, FAM129A, NFIC, PBX2, LOC633387, MED1

ID	Genes
68	TBC1D4,MTOR,RICTOR,SCRIB
69	FOXK1,GTF2F1,TRIM28,AHCTF1,MTOR,RB1,RICTOR,TCFEB,FAM129A,NFIC,PBX2,MED1
70	SRPK2,LOC100046628,PDCD11,EIF3A,GM9118,EMG1,NPM1,GM5611,GM7289,LOC633387,GM6477
71	LOC100046628,GM9118,FOXK1,TRIM28,AHCTF1,GM5611,RB1,GM6477,GTF2F1,NPM1,GM7289,TCFEB,FAM129A,NFIC,PBX2,LOC633387,MED1
72	GSK3B,PPP1R12A,FLNA
73	HELLS,SMARCA4
74	DAB2,CTTN,GM8786,ULK1,SNX17,FKBP15,TRIP10,SCRIB
75	ZFP106,GRB10,PTK2,IRS2,EIF4EBP1,EIF4EBP2,FLNA
76	BCR,MTOR,RICTOR,SCRIB
77	MIB1,DAB2,ZEB2,SFRS1,TCFEB,JUNB,LOC100048559,MLL2,MED1,SMARCA4
78	AKT1S1,ZC3HC1,GSK3B,HELLS
79	MIB1,DAB2,ZEB2,SFRS1,TCFEB,JUNB,LOC100048559,MLL2,MED1,SMARCA4
80	PTK2,SPNA2,MTOR,RICTOR
81	BCLAF1,FOXK1,FOXK2,MYEF2,AHCTF1,ZEB2,1600027N09RIK,SAP30,KDM3B,TCFEB,HELLS,NACC1,TRIM28,CCNL1,RB1,JUNB,PHF3,RFC1,GTF2F1,SMARCC2,ZFP516,NFIC,CUX1,PBX2,MED1
82	MYO5A,PTK2,TNC,LOC100048740,ADAMTS2,SMARCA4
83	PDCD11,SQSTM1,FLNA
84	LOC100046628,BCR,FOXK1,GM9118,NPM1,GM5611,GM7289,RB1,SCRIB,JUNB,LOC633387,GM6477
85	MYO5A,LOC100046628,LOC100048600,GM9118,GM5611,FLNA,GM6477,MACF1,ERBB2IP,GSK3B,RAB1,NPM1,GM7289,CUX1,ERC1,LOC633387
86	RFC1,LIN9,NFIC,DNAJC2,MED1
87	MIB1,MACF1,ZEB2,EXT1,PBX2,SCRIB,MED1,SMARCA4
88	TBC1D4,MTOR,RICTOR,SCRIB
89	PTK2,ULK1,MTAP1B,SPNA2
90	GSK3B,PPP1R12A,FLNA
91	LOC100046628,GM9118,MTAP1B,NPM1,GM5611,SPNA2,GM7289,MTOR,RICTOR,LOC633387,GM6477
92	IBTK,LOC100046628,GM9118,GM5611,ZEB2,RICTOR,RB1,GM6477,NPM1,GM7289,MTOR,FAM129A,LOC633387
93	FOXK1,RB1,SCRIB
94	PTK2,JUNB,SMARCA4
95	EIF4EBP1,EIF4EBP2
96	LOC100046628,PTK2,NACC1,GM9118,GTF2F1,NPM1,AHCTF1,GM5611,GM7289,LOC633387,FLNA,GM6477
97	LOC100046628,PTK2,NACC1,GM9118,GTF2F1,NPM1,AHCTF1,GM5611,GM7289,LOC633387,FLNA,GM6477
98	SPNA2,MTOR,RICTOR
99	FOXK1,GTF2F1,TRIM28,AHCTF1,RB1,TCFEB,FAM129A,NFIC,PBX2,MED1
100	IBTK,LOC100046628,GM9118,GM5611,ZEB2,RICTOR,RB1,GM6477,NPM1,GM7289,MTOR,FAM129A,LOC633387
101	IBTK,LOC100046628,GM9118,GM5611,ZEB2,RICTOR,RB1,GM6477,NPM1,GM7289,MTOR,FAM129A,LOC633387
102	MYO5A,ULK1,MED1,SMARCA4
103	MTOR,RICTOR
104	FOXK1,ULK1,DNAJC2
105	INF2,FMNL3,ARHGAP17,RICTOR,INF2Q,FLNA
106	IBTK,ZEB2,MTOR,RICTOR,FAM129A
107	DAB2,PTK2,MACF1,ULK1,TRIM28,SCRIB,LLGL1

ID	Genes
108	PTK2,TNS1,ULK1,ZEB2,CD2AP,SCRIB
109	SPNA2,MTOR,RICTOR
110	SPNA2,MTOR,RICTOR
111	MIB1,TNC,ZEB2,SCRIB,MED1
112	SMARCC2,CHD1,HELLS,SMARCA4
113	LOC100046628,GM9118,NPM1,GM5611,GM7289,MTOR,RICTOR,LOC633387,GM6477
114	FOXK1,GTF2F1,TRIM28,AHCTF1,RB1,TCFEB,NFIC,PBX2,MED1
115	MYO5A,ARHGAP17,SCRIB,LLGL1
116	IRS2,GSK3B,ZEB2,SCRIB,HELLS,MED1
117	MTOR,RICTOR
118	LOC100046628,PTK2,GM9118,MTAP1B,NPM1,GM5611,GM7289,LOC633387,RANBP10,GM6477
119	MIB1,ZEB2,SCRIB,MED1

Rapa BP GO pathways (c):

ID	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
1	133	506	13588	4.038158638	0.000424	4.24E-04	6.62E-04
2	133	430	13588	4.039097744	0.00422262	0.002113544	0.006599221
3	133	418	13588	3.910637839	0.013202715	0.003317148	0.020725619
4	133	397	13588	3.860154164	0.031339368	0.006347957	0.049646045
5	133	59	13588	10.38970307	0.234820063	0.037513168	0.4165415
6	133	372	13588	3.57029671	0.240156236	0.033747706	0.427409635
7	133	466	13588	3.069347188	0.458108033	0.065811007	0.950983483
8	133	43	13588	11.87969925	0.548457185	0.069730046	1.232339007
9	133	310	13588	3.625224351	0.593238056	0.072219958	1.393086083
10	133	78	13588	7.858877964	0.622688909	0.072234052	1.508600184
11	133	21	13588	19.46007877	0.655224183	0.073240783	1.647016896
12	133	640	13588	2.554135338	0.752083804	0.08878612	2.151600307
13	133	404	13588	3.034616244	0.860222342	0.115719883	3.022171324
14	133	236	13588	3.896138652	0.885866021	0.119855821	3.328229194
15	133	95	13588	6.452552434	0.904450787	0.122300298	3.595818606
16	133	58	13588	8.807363236	0.913322224	0.120774231	3.742213886
17	133	28	13588	14.59505908	0.917735112	0.117406498	3.820625016
18	133	308	13588	3.317058881	0.958217785	0.140327713	4.831479072
19	133	315	13588	3.243346461	0.974869971	0.154173087	5.583086162
20	133	66	13588	7.739804056	0.980097008	0.156587702	5.925840566
21	133	155	13588	4.613921902	0.983355842	0.15688676	6.187818747
22	133	718	13588	2.276666597	0.984989728	0.154613045	6.33886821
23	133	34	13588	12.01946042	0.987440816	0.154948588	6.59892672
24	133	326	13588	3.133908391	0.990050495	0.156967149	6.937610234
25	133	161	13588	4.441974501	0.992759227	0.161382833	7.397709501
26	133	393	13588	2.859591727	0.993737166	0.16048863	7.607019539
27	133	71	13588	7.194747432	0.993846998	0.156076846	7.632510001
28	133	72	13588	7.094820384	0.995256964	0.158538831	8.006669044
29	133	338	13588	3.022645371	0.997031505	0.166286638	8.676553117
30	133	280	13588	3.283888292	0.997784278	0.169076444	9.092166954
31	133	231	13588	3.53819614	0.999435936	0.197489303	11.01137247
32	133	14	13588	21.89258861	0.999679622	0.205375826	11.79297815

ID	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
33	133	181	13588	3.95114859	0.99981874	0.212838341	12.57303844
34	133	367	13588	2.783798734	0.999942481	0.231930955	14.12415408
35	133	866	13588	2.005556617	0.999952335	0.230394008	14.37545544
36	133	866	13588	2.005556617	0.999952335	0.230394008	14.37545544
37	133	188	13588	3.804031355	0.999965843	0.231800837	14.81929399
38	133	188	13588	3.804031355	0.999965843	0.231800837	14.81929399
39	133	437	13588	2.571669448	0.999969761	0.229071539	14.98100495
40	133	192	13588	3.724780702	0.99998807	0.241565162	16.20528578
41	133	148	13588	4.141841089	0.99999702	0.300740537	20.88938812
42	133	53	13588	7.710597248	0.99999716	0.295721164	20.95127119
43	133	267	13588	3.061135986	0.99999858	0.301224134	21.80434851
44	133	54	13588	7.56780841	0.9999987	0.296980281	21.90910181
45	133	99	13588	5.15986937	0.999999	0.295639893	22.230872
46	133	611	13588	2.173732203	0.99999904	0.290960801	22.27849302
47	133	100	13588	5.108270677	0.99999943	0.293467107	22.89881268
48	133	22	13588	13.9316473	0.99999997	0.328676558	26.2532865
49	133	217	13588	3.295658501	0.99999997	0.325881168	26.47233348
50	133	108	13588	4.729880256	1	0.344482216	28.53155823
51	133	165	13588	3.715105947	1	0.357404888	30.13796653
52	133	228	13588	3.136657433	1	0.370168333	31.75922119
53	133	176	13588	3.482911825	1	0.420100589	36.80211781
54	133	238	13588	3.004865104	1	0.41509568	36.87329018
55	133	121	13588	4.221711303	1	0.427055137	38.51844258
56	133	753	13588	1.89948976	1	0.432566345	39.57163653
57	133	244	13588	2.930974978	1	0.431978548	40.04717075
58	133	245	13588	2.919011815	1	0.432065576	40.58206094
59	133	184	13588	3.331480876	1	0.439852811	41.86001448
60	133	2227	13588	1.422149897	1	0.452125635	43.58475519
61	133	31	13588	9.886975503	1	0.453613528	44.25845315
62	133	75	13588	5.448822055	1	0.450365735	44.4589569
63	133	616	13588	1.990235329	1	0.454144887	45.35260328
64	133	4	13588	51.08270677	1	0.456547995	46.10772521
65	133	193	13588	3.176126846	1	0.466771241	47.65120316
66	133	328	13588	2.491839354	1	0.469084762	48.39705082
67	133	552	13588	2.03590498	1	0.477872288	49.80054252
68	133	80	13588	5.108270677	1	0.475050206	50.01764292
69	133	633	13588	1.936785091	1	0.480392471	51.06697676
70	133	137	13588	3.728664728	1	0.478500703	51.36875
71	133	557	13588	2.017629352	1	0.476086095	51.60967499
72	133	35	13588	8.757035446	1	0.474622436	51.94267678
73	133	5	13588	40.86616541	1	0.488078471	53.82618784
74	133	272	13588	2.629256966	1	0.497115601	55.24796589
75	133	273	13588	2.619625988	1	0.497699806	55.7861226
76	133	86	13588	4.751879699	1	0.50004125	56.50311848
77	133	421	13588	2.184058722	1	0.506829853	57.6805401
78	133	88	13588	4.643882433	1	0.511161168	58.59697919
79	133	425	13588	2.163502875	1	0.514070595	59.36036942
80	133	89	13588	4.591703979	1	0.512284313	59.62851936

ID	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
81	133	1772	13588	1.441385631	1	0.509804241	59.81828305
82	133	149	13588	3.428369582	1	0.51404321	60.70683174
83	133	40	13588	7.662406015	1	0.510980221	60.82544158
84	133	214	13588	2.864450847	1	0.507942029	60.94067925
85	133	431	13588	2.133384505	1	0.512485719	61.84796511
86	133	152	13588	3.360704393	1	0.518823826	62.93700974
87	133	359	13588	2.276666597	1	0.515146769	62.97259844
88	133	93	13588	4.394211335	1	0.51755278	63.64021648
89	133	93	13588	4.394211335	1	0.51755278	63.64021648
90	133	42	13588	7.297529538	1	0.518038348	64.10197022
91	133	154	13588	3.317058881	1	0.516945411	64.39400928
92	133	290	13588	2.466061706	1	0.515677628	64.66313432
93	133	43	13588	7.127819549	1	0.521573895	65.67569163
94	133	43	13588	7.127819549	1	0.521573895	65.67569163
95	133	7	13588	29.19011815	1	0.521941211	66.10627789
96	133	227	13588	2.700407406	1	0.541900011	68.54571328
97	133	227	13588	2.700407406	1	0.541900011	68.54571328
98	133	45	13588	6.811027569	1	0.539576096	68.69004358
99	133	530	13588	1.927649312	1	0.548723845	69.99148633
100	133	301	13588	2.37593985	1	0.545243603	70.01150996
101	133	301	13588	2.37593985	1	0.545243603	70.01150996
102	133	100	13588	4.086616541	1	0.543036347	70.15551118
103	133	8	13588	25.54135338	1	0.547458295	70.9615401
104	133	47	13588	6.521196609	1	0.549517711	71.52373165
105	133	165	13588	3.095921622	1	0.549873189	71.91098296
106	133	165	13588	3.095921622	1	0.549873189	71.91098296
107	133	309	13588	2.314426844	1	0.563991497	73.64287114
108	133	240	13588	2.554135338	1	0.578472896	75.36897392
109	133	50	13588	6.129924812	1	0.575662811	75.43274213
110	133	51	13588	6.009730208	1	0.58511535	76.64517662
111	133	173	13588	2.952757617	1	0.583088756	76.77534105
112	133	109	13588	3.749189487	1	0.586996658	77.45061982
113	133	52	13588	5.894158473	1	0.587580562	77.81289666
114	133	475	13588	1.93576573	1	0.58770496	78.12859078
115	133	110	13588	3.715105947	1	0.584982961	78.1816002
116	133	247	13588	2.481750936	1	0.587000314	78.66120379
117	133	10	13588	20.43308271	1	0.584028864	78.68588514
118	133	111	13588	3.681636524	1	0.583150293	78.89645491
119	133	111	13588	3.681636524	1	0.583150293	78.89645491

Rapa KEGG pathways (a):

ID	Term	Count	%	PValue	minuslog10 P
1	mmu04150:mTOR signaling pathway	7	3.51758794	1.57E-06	5.8
2	mmu04012:ErbB signaling pathway	6	3.015075377	3.09E-04	3.51
3	mmu04910:Insulin signaling pathway	7	3.51758794	3.40E-04	3.47
4	mmu05221:Acute myeloid leukemia	4	2.010050251	0.007078848	2.15
5	mmu04510:Focal adhesion	6	3.015075377	0.011465215	1.94
6	mmu04530:Tight junction	5	2.512562814	0.013906132	1.86
7	mmu05200:Pathways in cancer	7	3.51758794	0.02305239	1.64
8	mmu05215:Prostate cancer	4	2.010050251	0.024273508	1.61
9	mmu03018:RNA degradation	3	1.507537688	0.065096102	1.19
10	mmu05214:Glioma	3	1.507537688	0.072876584	1.14
11	mmu04920:Adipocytokine signaling pathway	3	1.507537688	0.078901015	1.1
12	mmu04370:VEGF signaling pathway	3	1.507537688	0.097853719	1.01
13	mmu05220:Chronic myeloid leukemia	3	1.507537688	0.097853719	1.01

Rapa KEGG pathways (b):

ID	Genes
1	IPI00453603,IPI00318938,IPI00399440,IPI00268673,IPI00467843,IPI00221581,IPI00121335
2	IPI00125319,IPI00453603,IPI00318938,IPI00113563,IPI00268673,IPI00121335
3	IPI00125319,IPI00453603,IPI00116923,IPI00318938,IPI00268673,IPI00379844,IPI00121335
4	IPI00453603,IPI00318938,IPI00268673,IPI00121335
5	IPI00403938,IPI00125319,IPI00131138,IPI00113563,IPI00671847,IPI00121335
6	IPI00118143,IPI00380354,IPI00323349,IPI00845596,IPI00121335
7	IPI00125319,IPI00121418,IPI00381495,IPI00113563,IPI00268673,IPI00380817,IPI00121335
8	IPI00125319,IPI00121418,IPI00268673,IPI00121335
9	IPI00169888,IPI00309059,IPI00330066
10	IPI00121418,IPI00268673,IPI00121335
11	IPI00268673,IPI00379844,IPI00121335
12	IPI00111169,IPI00113563,IPI00121335
13	IPI00121418,IPI00380817,IPI00121335

5 Rapa KEGG pathways (c):

ID	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
1	41	54	5738	18.14182475	1.10E-04	1.10E-04	0.001624292
2	41	87	5738	9.651808242	0.02142063	0.010768293	0.319622391
3	41	138	5738	7.098974903	0.023507108	0.007897915	0.35107298
4	41	57	5738	9.821138211	0.391818277	0.116903139	7.088295684
5	41	198	5738	4.240946046	0.553895165	0.149082636	11.24945571
6	41	135	5738	5.1833785	0.624786839	0.150728903	13.49142317
7	41	323	5738	3.032998565	0.804570905	0.208022678	21.44454537
8	41	90	5738	6.220054201	0.820953112	0.193469404	22.45479997
9	41	60	5738	6.997560976	0.991011485	0.407576887	50.1731853
10	41	64	5738	6.560213415	0.994992413	0.411206711	54.30152323
11	41	67	5738	6.266472515	0.99682721	0.407268104	57.28300003
12	41	76	5738	5.524390244	0.999259735	0.451577052	65.55273205

13	41	76	5738	5.524390244	0.999259735	0.451577052	65.55273205
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Ku BP GO (a):

ID	Term	Count	%	PValue
1	GO:0030032~lamellipodium assembly	3	3.092783505	3.25E-03
2	GO:0006468~protein amino acid phosphorylation	10	10.30927835	7.09E-03
3	GO:0008286~insulin receptor signaling pathway	3	3.092783505	9.83E-03
4	GO:0030029~actin filament-based process	5	5.154639175	0.014807537
5	GO:0006913~nucleocytoplasmic transport	4	4.12371134	0.014880914
6	GO:0051493~regulation of cytoskeleton organization	4	4.12371134	0.016150894
7	GO:0006796~phosphate metabolic process	11	11.34020619	0.016942852
8	GO:0006259~DNA metabolic process	7	7.216494845	0.025415897
9	GO:0045947~negative regulation of translational initiation	2	2.06185567	0.037014038
10	GO:0007049~cell cycle	8	8.24742268	0.04530749
11	GO:0033043~regulation of organelle organization	4	4.12371134	0.049959502
12	GO:0043484~regulation of RNA splicing	2	2.06185567	0.052460451
13	GO:0010605~negative regulation of macromolecule metabolic process	7	7.216494845	0.05420299
14	GO:0030031~cell projection assembly	3	3.092783505	0.054397233
15	GO:0022402~cell cycle process	6	6.18556701	0.059968997
16	GO:0033554~cellular response to stress	6	6.18556701	0.065899107
17	GO:0045884~regulation of survival gene product expression	2	2.06185567	0.072676117
18	GO:0010558~negative regulation of macromolecule biosynthetic process	6	6.18556701	0.073909203
19	GO:0006916~anti-apoptosis	3	3.092783505	0.081129603
20	GO:0031327~negative regulation of cellular biosynthetic process	6	6.18556701	0.081184023
21	GO:0046907~intracellular transport	6	6.18556701	0.081807159
22	GO:0009890~negative regulation of biosynthetic process	6	6.18556701	0.083692072
23	GO:0006396~RNA processing	6	6.18556701	0.085600178
24	GO:0051129~negative regulation of cellular component organization	3	3.092783505	0.089153114
25	GO:0006325~chromatin organization	5	5.154639175	0.08921682
26	GO:0030030~cell projection organization	5	5.154639175	0.092408475
27	GO:0043434~response to peptide hormone stimulus	3	3.092783505	0.092426596
28	GO:0016569~covalent chromatin modification	3	3.092783505	0.094076504
29	GO:0043271~negative regulation of ion transport	2	2.06185567	0.097348357
30	GO:0007010~cytoskeleton organization	5	5.154639175	0.098124703

Ku BP GO (b):

ID	Genes
1	CCDC88A,NCK1,VCL
2	ALPK3,BAZ1B,BRAF,MAP3K2,SPNB2,GSK3B,NEK9,RPS6KB1,C230081A13RIK,MELK
3	PHIP,EIF4EBP1,EIF4EBP2
4	EPB4.1L3,NCK1,ARHGEF17,MYO9B,FLNC
5	LOC100046628,GM9118,SPNB2,GSK3B,NPM1,GM5611,GM7289,MYBBP1A,LOC633387,GM6477
6	LOC100046628,CCDC88A,GM9118,SPNB2,MTAP1B,NPM1,GM5611,GM7289,LOC633387,GM6477
7	ALPK3,BAZ1B,BRAF,MAP3K2,SPNB2,GSK3B,SYNJ1,NEK9,RPS6KB1,C230081A13RIK,MELK
8	ATRX,TRP53BP1,CCDC88A,MDC1,ORC6L,TOP2B,MYC
9	EIF4EBP1,EIF4EBP2

ID	Genes
10	LOC100046628,GM9118,RBL1,GM5611,ZFP318,GM6477,MDC1,GSK3B,NPM1,KIF20B,NEK9,GM7289,LOC633387,ERCC6L
11	LOC100046628,CCDC88A,GM9118,SPNB2,MTAP1B,NPM1,GM5611,GM7289,LOC633387,GM6477
12	LOC100046628,GM9118,GPX4,NPM1,GM5611,GM7289,HNRPLL,LOC633387,GM6477
13	LOC100046628,GM9118,RBL1,GM5611,GM6477,EIF4EBP1,EIF4EBP2,NPM1,GM7289,MYC,MYBBP1A,LOC633387,SMARCA4
14	CCDC88A,NCK1,VCL
15	LOC100046628,GM9118,GSK3B,NPM1,KIF20B,NEK9,GM5611,GM7289,ZFP318,LOC633387,GM6477,ERCC6L
16	ATRX,TRP53BP1,BAZ1B,MDC1,GPX4,GSK3B,HNRPLL
17	AKT1S1,MYC
18	EIF4EBP1,EIF4EBP2,RBL1,MYBBP1A,MYC,SMARCA4
19	AKT1S1,GSK3B,MYC
20	EIF4EBP1,EIF4EBP2,RBL1,MYBBP1A,MYC,SMARCA4
21	LOC100046628,GM9118,SPNB2,GSK3B,NPM1,AKAP12,GM5611,MYO9B,GM7289,MYBBP1A,LOC633387,GM6477
22	EIF4EBP1,EIF4EBP2,RBL1,MYBBP1A,MYC,SMARCA4
23	LOC100046766,SF3B1,EXOSC9,LOC100046744,GPX4,LARP7,SRRM2,LOC100046735,POP1,LOC675032,LOC100047322,HNRPLL
24	RTN4,SPNB2,MTAP1B
25	BAZ1B,GPX4,RBL1,SETD2,HNRPLL,SMARCA4
26	CCDC88A,NCK1,MTAP1B,TOP2B,VCL
27	PHIP,EIF4EBP1,EIF4EBP2
28	BAZ1B,SETD2,SMARCA4
29	BEST3,NEDD4L
30	EPB4.1L3,LOC100046628,GM9118,NCK1,MTAP1B,NPM1,ARHGEF17,GM5611,GM7289,LOC633387,GM6477

Ku BP GO (c):

ID	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
1	74	16	13588	34.42905405	0.882872164	8.83E-01	4.76E+00
2	74	640	13588	2.869087838	0.990722194	0.903678632	10.0912277
3	74	28	13588	19.67374517	0.998498942	0.885501679	13.73744045
4	74	176	13588	5.216523342	0.99994544	0.859597701	19.99753834
5	74	96	13588	7.650900901	0.99994805	0.806833826	20.08660666
6	74	99	13588	7.419055419	0.999977769	0.737959309	21.61357964
7	74	866	13588	2.332376256	0.999986913	0.713301589	22.55196875
8	74	421	13588	3.053091096	0.999999956	0.785616066	31.95670058
9	74	7	13588	52.46332046	1	0.87357656	43.11139373
10	74	611	13588	2.404211085	1	0.869178376	50.01437111
11	74	154	13588	4.769392769	1	0.878480874	53.53582478
12	74	10	13588	36.72432432	1	0.875783402	55.33191067
13	74	506	13588	2.540220062	1	0.869599238	56.5448088
14	74	70	13588	7.869498069	1	0.855869756	56.678091
15	74	393	13588	2.803383536	1	0.869269287	60.34271545
16	74	404	13588	2.727053786	1	0.881875859	63.92395423
17	74	14	13588	26.23166023	1	0.895305874	67.64630011
18	74	418	13588	2.635717057	1	0.888826293	68.28378078

19	74	88	13588	6.25982801	1	0.901699824	71.78744367
20	74	430	13588	2.562162162	1	0.892310062	71.81242243
21	74	431	13588	2.55621747	1	0.884669916	72.09697589
22	74	434	13588	2.538547764	1	0.881167309	72.94148547
23	74	437	13588	2.521120663	1	0.877904651	73.77204657
24	74	93	13588	5.923278117	1	0.879820716	75.2555379
25	74	315	13588	2.914628915	1	0.871223772	75.28140884
26	74	319	13588	2.878081844	1	0.872300131	76.54568607
27	74	95	13588	5.798577525	1	0.863873178	76.55268842
28	74	96	13588	5.738175676	1	0.860545996	77.18216045
29	74	19	13588	19.32859175	1	0.862220501	78.38406819
30	74	326	13588	2.81628254	1	0.856532331	78.66045069

Ku KEGG pathways (a):

ID	Term	Count	%	PValue	minuslogP
1	mmu04012:ErbB signaling pathway	6	6.060606061	2.42E-05	4.62
2	mmu04150:mTOR signaling pathway	4	4.04040404	1.39E-03	2.86
3	mmu05221:Acute myeloid leukemia	4	4.04040404	1.62E-03	2.79
4	mmu04110:Cell cycle	4	4.04040404	0.015586032	1.81
5	mmu04910:Insulin signaling pathway	4	4.04040404	0.01903863	1.72
6	mmu05213:Endometrial cancer	3	3.03030303	0.019575313	1.71
7	mmu04010:MAPK signaling pathway	5	5.050505051	0.022772811	1.64
8	mmu03018:RNA degradation	3	3.03030303	0.025605774	1.59
9	mmu04510:Focal adhesion	4	4.04040404	0.048078613	1.32
10	mmu05210:Colorectal cancer	3	3.03030303	0.049516956	1.31
11	mmu04350:TGF-beta signaling pathway	3	3.03030303	0.050554685	1.3

Ku KEGG pathways (b):

ID	Genes
1	IPi00453999,IPi00125319,IPi00453603,IPi00230719,IPi00318938,IPi00668709,IPi00131999
2	IPi00453603,IPi00230719,IPi00318938,IPi00668709,IPi00221581
3	IPi00453603,IPi00230719,IPi00318938,IPi00668709,IPi00131999
4	IPi00125319,IPi00124717,IPi00137864,IPi00131999
5	IPi00125319,IPi00453603,IPi00230719,IPi00318938,IPi00668709
6	IPi00125319,IPi00230719,IPi00668709,IPi00131999
7	IPi00230719,IPi00117088,IPi00123474,IPi00668709,IPi00664670,IPi00131999
8	IPi00309059,IPi00119442,IPi00330066
9	IPi00125319,IPi00230719,IPi00405227,IPi00668709,IPi00664670
10	IPi00125319,IPi00230719,IPi00668709,IPi00131999
11	IPi00453603,IPi00137864,IPi00131999

5 Ku KEGG pathways (c):

ID	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
1	25	87	5738	15.82896552	1.38E-03	1.38E-03	0.023962829
2	25	54	5738	17.00148148	0.076050732	0.038777202	1.366086094
3	25	57	5738	16.10666667	0.088400206	0.030380355	1.596618843
4	25	128	5738	7.1725	0.591555799	0.200564953	14.41914204
5	25	138	5738	6.652753623	0.6656829	0.196785171	17.34826426
6	25	52	5738	13.24153846	0.675950335	0.171227632	17.79538958
7	25	265	5738	4.330566038	0.731003969	0.171037042	20.41453368
8	25	60	5738	11.476	0.772029847	0.168744085	22.67212753
9	25	198	5738	4.636767677	0.939707705	0.268063281	38.63940264
10	25	86	5738	8.006511628	0.944686732	0.251342928	39.55225136
11	25	87	5738	7.914482759	0.948025839	0.235718393	40.20324697

Table 10. Gene ontology analysis of the hits identified in the rapamycin and Ku-0063794 screens. The Table contains four subsections: Biological processes that the rapamycin-sensitive and Ku-0063794-sensitive hits overrepresented are identified in the “Rapa BP GO” and “Ku BP GO” subsection, respectively. Pathways that the Rapamycin-sensitive and Ku-0063794-sensitive hits overrepresented are shown under “Rapa KEGG pathways” and “Ku KEGG pathways,” respectively. Subsections are displayed in three parts, (a), (b), and (c), because the Table columns span more than one page. Corresponding entries are identified by an ID number. For example, entries under ID number 1 in Rapa BP GO (a), (b), and (c) refer to the same entry, entries under ID number 2 in Rapa BP GO (a), (b), and (c) refer to the same entry, entries under ID number 1 in Rapa KEGG pathways (a), (b), and (c) refer to the same entry, and so forth.

Table 11:

Gene Symbol	Annotation
Rapa replicate 1	
1600027N09Rik	RIKEN cDNA 1600027N09 gene
Ahctf1	AT-hook-containing transcription factor 1
Ahnak	AHNAK nucleoprotein isoform 1
Akt1s1	Proline-rich AKT1 substrate 1
Bat2l	Isoform 1 of Protein BAT2-like
Bclaf1	Isoform 2 of Bcl-2-associated transcription factor 1
Bmp2k	Isoform 1 of BMP-2-inducible protein kinase
C130092O11Rik	Isoform 1 of Uncharacterized protein KIAA1680
Carhsp1	Calcium-regulated heat stable protein 1
Ccnl1	Isoform 1 of Cyclin-L1
Chd1	Chromodomain-helicase-DNA-binding protein 1
Cttn	Src substrate cortactin
D6Wsu116e	Isoform 1 of Protein FAM21
Dab2	Isoform p93 of Disabled homolog 2
Dock11	Dedicator of cytokinesis protein 11
Edc4	Isoform 1 of Enhancer of mRNA-decapping protein 4
Eif3a	Eukaryotic translation initiation factor 3 subunit A
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2
Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1
Eif5;LOC100047658	Eukaryotic translation initiation factor 5
Epyc	Epiphycan
Fkbp15	Isoform B of FK506-binding protein 15
Foxk1	Forkhead box protein K1
Gm13697	Novel protein containing MIF4G and MA3 domains
Grb10	Isoform 3 of Growth factor receptor-bound protein 10
Gtf2f1	General transcription factor IIF subunit 1
Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2
Hisppd1	140 kDa protein
Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase
Inf2	Isoform 1 of Inverted formin-2
Iqsec1	IQ motif and Sec7 domain 1 isoform b
Irs2	Insulin receptor substrate 2
Iws1	Isoform 1 of Protein IWS1 homolog
Kdm3b	Isoform 2 of Lysine-specific demethylase 3B
Larp1	Isoform 1 of La-related protein 1
Larp4	Putative uncharacterized protein
Ldhd	22 kDa protein
Luc7l2	Isoform 1 of Putative RNA-binding protein Luc7-like 2
Macf1	Isoform 3 of Microtubule-actin cross-linking factor 1
Mett10d	Isoform 1 of Putative methyltransferase METT10D
Mtap1b	Microtubule-associated protein 1B
Myef2	Isoform 2 of Myelin expression factor 2
Myo5a	Myosin-Va
Ndr3	Protein NDRG3
Nfic	Isoform 1 of Nuclear factor 1 C-type
Npm1	Nucleophosmin

Gene Symbol	Annotation
Numa1	Nuclear mitotic apparatus protein 1
Pat11	Protein PAT1 homolog 1
Pcbp2	Isoform 1 of Poly(rC)-binding protein 2
Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B
Peg3	Isoform 1 of Paternally-expressed gene 3 protein
Phf3	PHD finger protein 3
Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1
Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2
Pi4k2a	Phosphatidylinositol 4-kinase type 2-alpha
Pkn2	Isoform 1 of Serine/threonine-protein kinase N2
Pla2g4a	Cytosolic phospholipase A2
Plekhm1	Pleckstrin homology domain-containing family M member 1
Ppp1r12a	MCG122391 isoform CRA_e
Rab1	Ras-related protein Rab-1A
Rps6	29 kDa protein
Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1
Rsl1d1	Putative uncharacterized protein
Sap30	Histone deacetylase complex subunit SAP30
Serbp1	Isoform 1 of Plasminogen activator inhibitor 1 RNA-binding protein
Sfrs8	splicing factor arginine/serine-rich 8
Sgta	Isoform 1 of Small glutamine-rich tetratricopeptide repeat-containing protein alpha
Smarca4	Putative uncharacterized protein
Snx17	Sorting nexin-17
Srpk2	serine/arginine-rich protein-specific kinase 2
Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2
Syap1	Synapse-associated protein 1
Tbc1d4	140 kDa protein
Tcfef	Transcription factor EB
Tjp2	Tight junction protein ZO-2
Tmem106b	Transmembrane protein 106B isoform CRA_b
Tmpo	Isoform Beta of Lamina-associated polypeptide 2 isoforms beta/delta/epsilon/gamma
Trim28	Isoform 1 of Transcription intermediary factor 1-beta
Ubxn7	UBX domain-containing protein 7
Usp24	Isoform 1 of Ubiquitin carboxyl-terminal hydrolase 24
Uvrug	UV radiation resistance associated
Wnk1	Serine/threonine-protein kinase WNK1
Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK
Zfp516	Zinc finger protein 516

Rapa Replicate 2	
Mib1	E3 ubiquitin-protein ligase MIB1
rsp6	29 kDa protein
Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2
Gm13099	Novel protein similar to preferentially expressed antigen in melanoma-like family
Rnf19b	IBR domain containing 3
Rps6	29 kDa protein

Gene Symbol	Annotation
Carhsp1	Calcium-regulated heat stable protein 1
Pgrmc2	Membrane-associated progesterone receptor component 2
FLNA	Filamin-A
Ext1	Exostosin-1
Gm14085	Novel protein similar to solute carrier family 28 (Sodium-coupled nucleoside transporter) member 2
Akt1s1	Proline-rich AKT1 substrate 1
Gm9757	Putative uncharacterized protein
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2
Gon4l	RIKEN cDNA 5830417110 gene
Mogat1	2-acylglycerol O-acyltransferase 1
Eef2k	Elongation factor 2 kinase
Dhx15	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15
Srrm1	Isoform 2 of Serine/arginine repetitive matrix protein 1
Setd1a	SET domain containing 1A
D830015G02Rik	Putative uncharacterized protein
Vwa5b1	von Willebrand factor A domain-containing protein 5B1
Ibtk	Isoform 2 of Inhibitor of Bruton tyrosine kinase
Erc1;LOC100048600	Isoform 1 of ELKS/RAB6-interacting/CAST family member 1
Adams2	A disintegrin and metalloproteinase with thrombospondin motifs 2
Grb10	Isoform 3 of Growth factor receptor-bound protein 10
Foxk1	Forkhead box protein K1
Gm6988	similar to hCG1640785
Tnc	Isoform 1 of Tenascin
Larp1	Isoform 1 of La-related protein 1
Alkbh6	24 kDa protein
Larp7	Isoform 1 of La-related protein 7
Ahnak	AHNAK nucleoprotein isoform 1
Qsox2	Isoform 3 of Sulfhydryl oxidase 2
Wnk1	Serine/threonine-protein kinase WNK1
Megf11	Isoform 4 of Multiple epidermal growth factor-like domains 11
Ahctf1	AT-hook-containing transcription factor 1
Fxr1	Isoform E of Fragile X mental retardation syndrome-related protein 1
Ddx21	Nucleolar RNA helicase 2
Lin9	Isoform 2 of Lin-9 homolog
D6Wsu116e	Isoform 1 of Protein FAM21
Sfrs8	splicing factor arginine/serine-rich 8
Ppfibp2	Isoform 4 of Liprin-beta-2
Hdgfrp2	Isoform 3 of Hepatoma-derived growth factor-related protein 2
Irs2	Insulin receptor substrate 2
Tinf2	Putative uncharacterized protein
Hisppd1	140 kDa protein
Edc3	Enhancer of mRNA-decapping protein 3
Aim1l	Absent in melanoma 1-like
Herc1	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1
Fbxw9	F-box and WD-40 domain protein 9

Gene Symbol	Annotation
Sfrs18	splicing factor arginine/serine-rich 18
Dnajc2	DnaJ homolog subfamily C member 2
Cux1	cut-like homeobox 1 isoform a
Ranbp10	Ran-binding protein 10
Foxk2	Isoform 1 of Forkhead box protein K2
Bod1l	biorientation of chromosomes in cell division 1-like
Zeb2	Zinc finger E-box-binding homeobox 2
Bcr	Breakpoint cluster region protein
Pdcd11	Protein RRP5 homolog
Hn1l	Hematological and neurological expressed 1-like protein
Palm	Isoform 1 of Paralemmin
Phf3	PHD finger protein 3
Ptk2	Isoform 1 of Focal adhesion kinase 1
1110013L07Rik	Putative uncharacterized protein
Tcfef	Transcription factor EB
Ehmt2	Isoform 1 of Histone-lysine N-methyltransferase H3 lysine-9 specific 3
Zc3h4	Isoform 2 of Zinc finger CCCH domain-containing protein 4
Ktn1	Isoform 1 of Kinetin
Pbx2	Pre-B-cell leukemia transcription factor 2
Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1
Cdgap	Cdc42 GTPase-activating protein
Eif3a	Eukaryotic translation initiation factor 3 subunit A
Tbc1d4	140 kDa protein
Dennd4a	hypothetical protein LOC102442
Wdr91	WD repeat-containing protein 91
Junb	Transcription factor jun-B
Srpk2	serine/arginine-rich protein-specific kinase 2
Eif4b	Eukaryotic translation initiation factor 4B
Gbf1	Golgi-specific brefeldin A-resistance factor 1
Cd2ap	CD2-associated protein
LOC100048559;Sfrs1	Isoform 1 of Splicing factor arginine/serine-rich 1
Ccdc6	coiled-coil domain containing 6
Ndrp3	Protein NDRG3
Ulk1	Putative uncharacterized protein
Arhgap17	Isoform 1 of Rho GTPase-activating protein 17
Spna2	Isoform 2 of Spectrin alpha chain brain
Patl1	Protein PAT1 homolog 1
Bcas3	Isoform 1 of Breast carcinoma-amplified sequence 3 homolog
Atg2a	Autophagy-related protein 2 homolog A
Ccnl1	Isoform 1 of Cyclin-L1
Znrf2	E3 ubiquitin-protein ligase ZNRF2
Larp4	Putative uncharacterized protein
Mtor	Isoform 1 of FKBP12-rapamycin complex-associated protein
Gsk3b	Glycogen synthase kinase-3 beta
Ranbp9	RAN binding protein 9
Kdm6a	Isoform 1 of Lysine-specific demethylase 6A
C130092O11Rik	Isoform 1 of Uncharacterized protein KIAA1680
Mtap1b	Microtubule-associated protein 1B

Gene Symbol	Annotation
Prkd2	Serine/threonine-protein kinase D2
Usp36	Ubiquitin specific peptidase 36
Slc4a1ap	solute carrier family 4 (anion exchanger) member 1 adaptor protein
Llg1l	lethal giant larvae homolog 1 isoform 1
Cabin1	calcineurin binding protein 1
Pcbp1	Poly(rC)-binding protein 1
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1
Rfc1	Rfc1 protein
Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B
St5	Isoform 1 of Suppression of tumorigenicity 5
Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1
Pom121	Nuclear envelope pore membrane protein POM 121
Smarcc2	Isoform 2 of SWI/SNF complex subunit SMARCC2
Eps8l2	Isoform 1 of Epidermal growth factor receptor kinase substrate 8-like protein 2
Plekhm1	Pleckstrin homology domain-containing family M member 1
B230208H17Rik	Putative GTP-binding protein Parf
Mll2	similar to myeloid/lymphoid or mixed-lineage leukemia 2
Snx30	Sorting nexin-30
Rps6kb1	Isoform Alpha 1 of Ribosomal protein S6 kinase beta-1
Usp24	Isoform 1 of Ubiquitin carboxyl-terminal hydrolase 24
Micall1	Isoform 1 of MICAL-like protein 1
Med1	Isoform 4 of Mediator of RNA polymerase II transcription subunit 1
Sorbs3	Vinexin
Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2
Smarcad1	Isoform 1 of SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A containing DEAD/H box 1
Crkrs	Isoform 2 of Cell division cycle 2-related protein kinase 7
Gtf2f1	General transcription factor IIF subunit 1
Scrib	Isoform 1 of Protein LAP4
2610110G12Rik	Isoform 1 of UPF0635 protein C6orf134 homolog
Mllt4	Isoform 3 of Afadin
Nacc1	Nucleus accumbens-associated protein 1
Zfp106	Isoform 1 of Zinc finger protein 106
Rictor	Isoform 1 of Rapamycin-insensitive companion of mTOR
Tns1	tensin 1
Cttn	Src substrate cortactin
Sbno1	Isoform 2 of Protein strawberry notch homolog 1
Fmn13	Isoform 1 of Formin-like protein 3
Syap1	Synapse-associated protein 1
Strn3	Striatin-3
Rb1	Retinoblastoma-associated protein
Ehbp1	Isoform 2 of EH domain-binding protein 1
Sqstm1	Isoform 1 of Sequestosome-1
Zc3hc1	Isoform 1 of Nuclear-interacting partner of ALK
Tox4	TOX high mobility group box family member 4
Emg1	Probable ribosome biogenesis protein NEP1
Pcm1	Isoform 1 of Pericentriolar material 1 protein

Gene Symbol	Annotation
Trip10	Isoform 3 of Cdc42-interacting protein 4
LOC100048123;Akt2	RAC-beta serine/threonine-protein kinase
Aak1	Isoform 2 of AP2-associated protein kinase 1
Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2
Phldb2	Isoform 1 of Pleckstrin homology-like domain family B member 2
Phldb1	Isoform 2 of Pleckstrin homology-like domain family B member 1
Ahctf1	AT-hook-containing transcription factor 1
Ahctf1	AT-hook-containing transcription factor 1
Ahctf1	AT-hook-containing transcription factor 1
Arhgap17	Isoform 1 of Rho GTPase-activating protein 17
Rb1	Retinoblastoma-associated protein
Rb1	Retinoblastoma-associated protein
Tox4	TOX high mobility group box family member 4
Tox4	TOX high mobility group box family member 4
Hells	Isoform 1 of Lymphocyte-specific helicase
Hells	Isoform 1 of Lymphocyte-specific helicase
Hells	Isoform 1 of Lymphocyte-specific helicase
ErbB2ip	Isoform 1 of Protein LAP2
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2
Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B
Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B
Pds5b	Isoform 1 of Sister chromatid cohesion protein PDS5 homolog B
Fam129a	Protein Niban
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1
Ahnak	AHNAK nucleoprotein isoform 1
Ahnak	AHNAK nucleoprotein isoform 1
Ahnak	AHNAK nucleoprotein isoform 1
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1
Arid1a	AT rich interactive domain 1A
Fam129a	Protein Niban
Fam129a	Protein Niban
Atxn2	ataxin 2
Atxn2	ataxin 2
Ranbp10	Ran-binding protein 10
Ranbp10	Ran-binding protein 10
Ranbp10	Ran-binding protein 10
Ranbp10	Ran-binding protein 10
Ranbp10	Ran-binding protein 10
Tox4	TOX high mobility group box family member 4
Tox4	TOX high mobility group box family member 4

Ku	
Myo18a	Isoform 4 of Myosin-XVIIIa
Brd2	Isoform 2 of Bromodomain-containing protein 2
6330577E15Rik	Uncharacterized protein C10orf78 homolog
Best3	Bestrophin-3
Larp1	Isoform 1 of La-related protein 1
Fam62c	Isoform 1 of Extended synaptotagmin-3

Gene Symbol	Annotation
Mdn1	Midasin homolog
Rtn4	Isoform 2 of Reticulon-4
Pcdh24	Pcdh24 protein
Synj1	similar to mKIAA0910 protein
Zfp318	zinc finger protein 318 isoform 1
Akt1s1	Proline-rich AKT1 substrate 1
Alpk3	myocyte induction differentiation originator
Zc3h14	Isoform 2 of Zinc finger CCCH domain-containing protein 14
Edc4	Isoform 1 of Enhancer of mRNA-decapping protein 4
Srrm2	Isoform 3 of Serine/arginine repetitive matrix protein 2
Kif20b	Isoform 1 of M-phase phosphoprotein 1
1110007A13Rik	UPF0557 protein C10orf119 homolog
Pi4k2a	Phosphatidylinositol 4-kinase type 2-alpha
Top2b	DNA topoisomerase 2-beta
BC021381	Isoform 2 of Uncharacterized protein KIAA1931
Bbx	Isoform 1 of HMG box transcription factor BBX
Vcl	Vinculin
Eif4ebp1	Eukaryotic translation initiation factor 4E-binding protein 1
Rrp15	RRP15-like protein
D10Wsu102e	Uncharacterized protein C12orf45 homolog
Braf	Isoform 1 of B-Raf proto-oncogene serine/threonine-protein kinase
Atg2b	Isoform 1 of Autophagy-related protein 2 homolog B
Npm1	Nucleophosmin
Pcsk5	proprotein convertase subtilisin/kexin type 5
Mtap1b	Microtubule-associated protein 1B
Ercc6l	DNA excision repair protein ERCC-6-like
Serinc1	Serine incorporator 1
Klf3;LOC100046855	Krueppel-like factor 3
Smarca4	Putative uncharacterized protein
Aak1	Uncharacterized protein FLJ45252 homolog
Eif4ebp2	Eukaryotic translation initiation factor 4E-binding protein 2
Ndrp1	Protein NDRG1
Mek	Maternal embryonic leucine zipper kinase
Arhgef17	Isoform 1 of Rho guanine nucleotide exchange factor 17
Grit	Isoform 2 of Rho/Cdc42/Rac GTPase-activating protein RICS
Mdc1	mediator of DNA damage checkpoint 1
Nfkb2	NF-kB2 splice variant 4
Pcm1	Isoform 1 of Pericentriolar material 1 protein
Mybbp1a	Myb-binding protein 1A
Sf3b1	Splicing factor 3B subunit 1
Atrx	Transcriptional regulator ATRX
Ccdc88a	Isoform 2 of Girdin
Baz1b	Isoform 1 of Tyrosine-protein kinase BAZ1B
Nedd4l	Isoform 3 of E3 ubiquitin-protein ligase NEDD4-like
Orc6l	Origin recognition complex subunit 6
Trp53bp1	Transformation related protein 53 binding protein 1
Map3k2	Mitogen-activated protein kinase kinase kinase 2
Hectd2	Hectd2 protein
Usp10	Ubiquitin carboxyl-terminal hydrolase 10

Gene Symbol	Annotation
D830031N03Rik	similar to mKIAA0754 protein
Nck1	non-catalytic region of tyrosine kinase adaptor protein 1
Exosc9	Exosome complex exonuclease RRP45
Dap	Death-associated protein 1
Rps6kb1	Isoform Alpha I of Ribosomal protein S6 kinase beta-1
Lmna	Isoform C2 of Lamin-A/C
Sltm	Isoform 1 of SAFB-like transcription modulator
Sh3pxd2a	Isoform 1 of SH3 and PX domain-containing protein 2A
Flnc	Isoform 1 of Filamin-C
Oxr1	Isoform 2 of Oxidation resistance protein 1
Rin2	Isoform 1 of Ras and Rab interactor 2
Nek9	Serine/threonine-protein kinase Nek9
Pebp1	Phosphatidylethanolamine-binding protein 1
Pop1	Processing of 1 ribonuclease P/MRP family
Serhl	Serine hydrolase-like protein
Epb4.113	Isoform 1 of Band 4.1-like protein 3
Hnrpll	Isoform 1 of Heterogeneous nuclear ribonucleoprotein L-like
Samhd1	SAM domain and HD domain-containing protein 1
Zfp828	Zinc finger protein 828
Larp7	Isoform 1 of La-related protein 7
Myc	myc proto-oncogene protein
Myo9a	Isoform 2 of Myosin-IXa
Gsk3b	Glycogen synthase kinase-3 beta
Zfp395	zinc finger protein 395
Bend3	BEN domain-containing protein 3
Akap12	Isoform 1 of A-kinase anchor protein 12
Eif4g1	Isoform 1 of Eukaryotic translation initiation factor 4 gamma 1
Eif4b	Eukaryotic translation initiation factor 4B
Dock7	Isoform 2 of Dedicator of cytokinesis protein 7
Pat1	Protein PAT1 homolog 1
Slc7a11	Cystine/glutamate transporter
Myo9b	Isoform 1 of Myosin-IXb
Setd2	SET domain containing 2
Gphn	Gephyrin
Erf	ETS domain-containing transcription factor ERF
Spnb2	Isoform 2 of Spectrin beta chain brain 1
Phip	PH-interacting protein
Sdpr	Serum deprivation-response protein
Tcof1	Treacle protein
Pwp1	Periodic tryptophan protein 1 homolog
Rbl1	Isoform Long of Retinoblastoma-like protein 1
Eef1b2	Elongation factor 1-beta
Phactr4	Isoform 1 of Phosphatase and actin regulator 4
C230081A13Rik	Tyrosine-protein kinase-protein kinase Sgk269
Ahnak2	Putative uncharacterized protein

Table 11. Proteins with downregulated phosphorylation identified in the rapamycin and Ku-0063794 screen.

CLAIMS

1. A method for determining mTOR kinase activity in a cancer cell, the method comprising

(a) obtaining a cancer cell from a subject diagnosed to have a cancer,

(b) determining the level of Grb10 phosphorylation in the cell, and

(c) comparing the level of Grb10 phosphorylation to a reference level, wherein if the level of Grb10 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

2. The method of claim 1, further comprising selecting a method of treatment based on the cell exhibiting an elevated level of mTOR kinase activity.

3. The method of claim 2, wherein if the cell is determined to exhibit an elevated level of mTOR kinase activity, then the selected method of treatment comprises administering an effective amount of an mTOR kinase inhibitor to the subject.

4. The method of claim 3, wherein the method of treatment further comprises administering an effective amount of a compound that stabilizes Grb10 or that inhibits the degradation of Grb10 and/or an effective amount of a PI3K inhibitor to the subject.

5. The method of claim 3 or 4, wherein the mTOR inhibitor is an allosteric mTOR kinase inhibitor or a catalytic mTOR kinase inhibitor.

6. The method of claim 5, wherein the allosteric mTOR kinase inhibitor is rapamycin or a rapamycin analog, or wherein the catalytic mTOR kinase inhibitor is an ATP-competitive mTOR kinase inhibitor.

7. The method of any of claims 3-6, wherein the mTOR inhibitor is an mTORC1 inhibitor.

8. The method of any of claims 3-6, wherein the mTOR inhibitor is an mTORC1/2 inhibitor.

9. The method of claim 6, wherein the rapamycin analog is Ridaforolimus, Sirolimus or Everolimus.

10. The method of any of claims 3-4, wherein the mTOR kinase inhibitor is PP242,
5 PP30, AZD8055, OSI-027, WYE354, INK-128, XL388, or torin1.

11. The method of any of claims 3-4, wherein the mTOR inhibitor is a dual PI3K/mTOR kinase inhibitor.

10 12. The method of claim 11, wherein the dual PI3K/mTOR kinase inhibitor is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126.

13. The method of any of claims 4-12, wherein the PI3K inhibitor is ZSTK474, TGX221, GDC0941, or LY294002, XL147, PX147, BKM120, GSK 615, CAL101, or PX-
15 866.

14. The method of any of claims 4-12, wherein the PI3K inhibitor is a dual PI3K/mTOR kinase inhibitor.

20 15. The method of claim 14, wherein the dual PI3K/mTOR kinase inhibitor is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126.

16. The method of any of claims 3-5, wherein the method of treatment further comprises administering an effective amount of an Akt inhibitor to the subject.
25

17. The method of claim 16, wherein the Akt inhibitor is perifosine, GSK690693, A443654 or MK2206.

18. The method of any of claims 4-17, wherein the compound that inhibits the
30 degradation of Grb10 is a ubiquitin ligase inhibitor.

19. The method of claim 18, wherein the ubiquitin ligase inhibitor is an E3 ubiquitin ligase inhibitor.

20. The method of any of claims 2-19, further comprising carrying out the selected method of treatment.

21. A method for selecting a treatment of a cancer, the method comprising,

- 5 (a) obtaining a cancer cell from a subject diagnosed to have a cancer exhibiting an elevated level of mTOR activity,
- (b) determining the level of Grb10 expression in the cell, and
- 10 (c) comparing the level of Grb10 expression to a reference level, wherein if the level of Grb10 expression in the cell is higher than the reference level, then the cell is determined to exhibit a high risk of expressing an elevated level of PI3K, Akt, and/or MAPK activity upon being contacted with an mTORC1 inhibitor.

22. The method of claim 21, the method further comprising selecting a method of treatment based on the cell exhibiting a high risk of expressing an elevated level of PI3K, Akt, and/or MAPK activity upon being contacted with an mTORC1 inhibitor.

23. The method of claim 22, wherein the method of treatment comprises administering (i) an effective amount of an mTOR kinase inhibitor and/or (ii) an effective amount of an IGF1R, EGFR, PI3K, Akt, MEK, and/or RSK inhibitors and/or of a compound stabilizing Grb10 to the subject, or

20 administering an effective amount of a dual or multi-target inhibitor that inhibits mTOR and inhibits IGFR, EGFR, PI3K, Akt, MEK, and/or RSK and/or of a compound stabilizing Grb10 to the subject.

24. The method of claim 23, wherein the mTOR inhibitor is an allosteric mTOR kinase inhibitor or a catalytic mTOR kinase inhibitor.

25. The method of claim 24, wherein the allosteric mTOR kinase inhibitor is rapamycin or a rapamycin analog, or wherein the catalytic mTOR kinase inhibitor is an ATP-competitive mTOR kinase inhibitor.

26. The method of any of claims 23-25, wherein the mTOR inhibitor is an mTORC1 inhibitor.

27. The method of any of claims 23-25, wherein the mTOR inhibitor is an mTORC1/2 inhibitor.

28. The method of any of claims 23-24, wherein the mTOR inhibitor is rapamycin, a rapamycin analog, Ku0063794, or AZD8055.

29. The method of claim 28, wherein the rapamycin analog is Ridaforolimus, Sirolimus or Everolimus.

30. The method of any of claims 23-24, wherein the mTOR kinase inhibitor is PP242, PP30, AZD8055, OSI-027, WYE354, INK-128, XL388, or torin1.

31. The method of any of claims 23-24, wherein the mTOR inhibitor is a dual PI3K/mTOR kinase inhibitor.

32. The method of claim 31, wherein the dual PI3K/mTOR kinase inhibitor is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126.

33. The method of any of claims 24-32, wherein the PI3K inhibitor is ZSTK474, TGX221, GDC0941, or LY294002, XL147, PX147, BKM120, GSK 615, CAL101, or PX-866.

34. The method of any of claims 24-32, wherein the PI3K inhibitor is a dual PI3K/mTOR kinase inhibitor.

35. The method of claim 34, wherein the dual PI3K/mTOR kinase inhibitor is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126.

36. The method of any of claims 23-35, wherein the method of treatment further comprises administering an effective amount of an Akt inhibitor to the subject.

37. The method of claim 36, wherein the Akt inhibitor is perifosine, GSK690693, A443654 or MK2206.

38. The method of any of claims 23-37, wherein the compound stabilizing Grb10 is an ubiquitin ligase inhibitor.

39. The method of claim 38, wherein the ubiquitin ligase inhibitor is an E3 ubiquitin
5 ligase inhibitor.

40. The method of any of claims 22-39, further comprising carrying out the selected method of treatment.

10 41. A method for determining mTOR kinase activity in a cell, the method comprising
(a) determining the level of phosphorylation of a plurality of phosphorylation sites disclosed in Table 1, 2, 3, 7, or 8, or 11 in the cell; and

(b) comparing the level of phosphorylation determined in step (a) to a reference level, wherein

15 (i) if the level of phosphorylation determined in step (b) is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity, or

(ii) if the level of phosphorylation determined in step (b) is equal or lower than the reference level, then the cell is determined to not exhibit an elevated level of mTOR kinase activity.

20

42. The method of claim 41, wherein the method further comprises determining whether the cell carries a mutation in a gene involved in an mTOR signaling pathway.

43. The method of claim 42, wherein the gene involved in an mTOR signaling
25 pathway is a gene involved in IGF signaling, PI3K signaling, AKT signaling, Ras signaling, or Rb signaling.

44. The method of claim 43, wherein the gene involved in an mTOR signaling
30 pathway is TSC1/2, a receptor tyrosine kinases (RTK), PI3K, PTEN, Akt, Ras, Raf, MEK, LKB, or NF2.

45. The method of any of claims 41-44, wherein the plurality of phosphorylation sites is selected from the list consisting of a Grb10 phosphorylation site, a pNDRG3 phosphorylation site, a CDK12 phosphorylation site, and a SRPK2 phosphorylation site.

46. The method of claim 45, wherein the Grb10 phosphorylation site is comprised in the amino acid sequence MNILSS*QS*PLHPSTLNAVIHR (SEQ ID NO: 28), the amino acid sequence MNILGS*QS*PLHPSTLSTVIHR (SEQ ID NO: 29), or a homologous Grb10 sequence, wherein * denotes the preceding amino acid residue as a phosphorylation site.

47. The method of claim 45, wherein the GRb10 phosphorylation site comprises an S421 phosphorylation site and/or an S423 phosphorylation site of mouse Grb10 isoform 3, an S501 phosphorylation site and/or an S503 phosphorylation site of mouse Grb10 isoform 1, or an S474 phosphorylation site and/or an S476 in human isoform 3, or a homologous Grb10 phosphorylation site.

48. The method of any of claims 41-47, wherein the method comprises determining the level of phosphorylation 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, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 1, 2, 3, 7, 8, or 11.

49. The method of any of claims 41-48, wherein

(iii) if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class I phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTORC1 activity,

(iv) if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class II phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity, or

(vi) if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class III phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR activity, or an elevated level of rapamycin-insensitive mTOR activity, or both.

50. The method of any of claims 41-49, wherein the method further comprises selecting a method of treatment of the subject based on the level of phosphorylation of the plurality of phosphorylation sites.

51. The method of claim 50, wherein

if the cell is determined to exhibit an elevated level of mTOR kinase activity, then a method of treatment is selected that comprises administering an effective amount of an mTOR kinase inhibitor to the subject, or

if the cell is determined to not exhibit an elevated level of mTOR kinase activity, then a method of treatment is selected that does not comprise administering an mTOR kinase inhibitor.

52. The method of claim 50, wherein

if the cell is determined to exhibit an elevated level of rapamycin-sensitive mTORC1 activity, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-sensitive mTORC1 kinase activity to the subject,

if the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-insensitive mTORC1 kinase activity to the subject, or

if the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR kinase activity, or an elevated level of rapamycin-insensitive mTOR kinase activity, or both, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-sensitive and rapamycin-insensitive mTOR kinase activity or a combination of an inhibitor of rapamycin-sensitive mTOR kinase activity and an inhibitor of rapamycin-insensitive mTOR kinase activity to the subject.

53. The method of any of claims 41-52, wherein the method further comprises determining the level of expression of Grb10 in the cell.

54. The method of any of claims 41-52, wherein the method further comprises determining the level of expression of PTEN in the cell.

55. The method of any of claims 41-52, wherein the method further comprises determining the level of expression of Grb10 and of PTEN in the cell.

56. The method of any of claims 53-55, wherein determining the level of expression comprises determining a level of protein, a level of mRNA, or a level of protein phosphorylation in the cell.

5 57. The method of any of claims 53-56, wherein the method further comprises comparing the level of expression determined in the cell to a reference level, and if the level of expression in the cell is lower than the reference level, then the cell is determined to exhibit an elevated level of PI3K activity.

10 58. The method of any of claims 50-57, wherein the method of treatment further comprises administering an effective amount of a compound that stabilizes Grb10 or that inhibits degradation of Grb10 to the subject.

15 59. The method of claim 58, wherein the compound that inhibits degradation of Grb10 is a ubiquitin ligase inhibitor.

60. The method of claim 59, wherein the ubiquitin ligase inhibitor is an E3 ubiquitin ligase inhibitor.

20 61. The method of any of claims 50-60, wherein the method of treatment further comprises administering an effective amount of a PI3K inhibitor to the subject.

25 62. The method of any of claims 51-61, wherein the mTOR inhibitor is an allosteric mTOR kinase inhibitor or a catalytic mTOR kinase inhibitor.

63. The method of claim 62, wherein the allosteric mTOR kinase inhibitor is rapamycin or a rapamycin analog, or wherein the catalytic mTOR kinase inhibitor is an ATP-competitive mTOR kinase inhibitor.

30 64. The method of any of claims 51-63, wherein the mTOR inhibitor is an mTORC1 inhibitor.

65. The method of any of claims 51-63, wherein the mTOR inhibitor is an mTORC1/2 inhibitor.

66. The method of claim 63, wherein the rapamycin analog is Ridaforolimus, Sirolimus or Everolimus.

5 67. The method of any of claims 51-62, wherein the mTOR kinase inhibitor is PP242, PP30, AZD8055, OSI-027, WYE354, INK-128, XL388, or torin1.

68. The method of any of claims 51-62, wherein the mTOR inhibitor is a dual PI3K/mTOR kinase inhibitor.

10

69. The method of claim 68, wherein the dual PI3K/mTOR kinase inhibitor is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126.

70. The method of any of claims 51-69, wherein the PI3K inhibitor is ZSTK474, 15 TGX221, GDC0941, or LY294002, XL147, PX147, BKM120, GSK 615, CAL101, or PX-866.

71. The method of any of claims 51-70, wherein the PI3K inhibitor is a dual PI3K/mTOR kinase inhibitor.

20

72. The method of claim 71, wherein the dual PI3K/mTOR kinase inhibitor is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126.

73. The method of any of claims 51-72, wherein the method of treatment further 25 comprises administering an effective amount of an Akt inhibitor to the subject.

74. The method of claim 73, wherein the Akt inhibitor is perifosine, GSK690693, A443654 or MK2206.

30 75. The method of any of claims 51-74, wherein the method further comprises carrying out the selected method of treatment.

76. The method of any of claims 41-75, wherein the cell is a cancer cell.

77. The method of any of claims 41-76, wherein the cell is a cell obtained from a tumor in a subject.

78. The method of any of claims 41-76, wherein the method further comprises
5 obtaining the cell from a subject.

79. A method for determining mTOR kinase activity in a cell, the method comprising
(a) determining the level of phosphorylation of a phosphorylation site disclosed in
Table 1, 2, 3, 7, 8, or 11 in the cell; and

10 (b) comparing the level of phosphorylation determined in step (a) to a reference level,
and

(i) if the level of phosphorylation determined in step (b) is higher than the reference
level, then the cell is determined to exhibit an elevated level of mTOR kinase activity, or

15 (ii) if the level of phosphorylation determined in step (b) is equal or lower than the
reference level, then the cell is determined to not exhibit an elevated level of mTOR kinase
activity.

80. The method of claim 79, wherein the method further comprises determining
whether the cell carries a mutation in a gene involved in an mTOR signaling pathway.

20

81. The method of claim 80, wherein the gene involved in an mTOR signaling
pathway is a gene involved in IGF signaling, PI3K signaling, AKT signaling, EGF receptor
signaling, GF receptor signaling, Ras signaling, Raf signaling, or Rb signaling.

25 82. The method of claim 81, wherein the gene involved in an mTOR signaling
pathway is TSC1/2.

83. The method of any of claims 79-82, wherein

30 the phosphorylation site is a phosphorylation site not previously known to be a
phosphorylation site targeted by mTOR; or

wherein the phosphorylation site is selected from the list consisting of a Grb10
phosphorylation site, a pNDRG3 phosphorylation site, a CDK12 phosphorylation site,
and a SRPK2 phosphorylation site.

84. The method of claim 83, wherein the Grb10 phosphorylation site is an S421 phosphorylation site.

85. The method of claim 83, wherein the Grb10 phosphorylation site is an S423 phosphorylation site.

86. The method of any of claims 79-85, wherein

(iii) if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class I phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTORC1 activity,

(iv) if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class II phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity, or

(vi) if a phosphorylation site determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class III phosphorylation site, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR activity, or an elevated level of rapamycin-insensitive mTOR activity, or both.

87. The method of any of claims 79-86, wherein the method further comprises selecting a method of treatment of the subject based on the level of phosphorylation of the phosphorylation site.

88. The method of claim 87, wherein

if the cell is determined to exhibit an elevated level of mTOR kinase activity, then a method of treatment is selected that comprises administering an effective amount of an mTOR kinase inhibitor to the subject, or

if the cell is determined to not exhibit an elevated level of mTOR kinase activity, then a method of treatment is selected that does not comprise administering an mTOR kinase inhibitor.

89. The method of claim 87, wherein

if the cell is determined to exhibit an elevated level of rapamycin-sensitive mTORC1 activity, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-sensitive mTORC1 kinase activity to the subject,

if the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-insensitive mTORC1 kinase activity to the subject, or

if the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR kinase activity, or an elevated level of rapamycin-insensitive mTOR kinase activity, or both, then a method of treatment is selected that comprises administering an effective amount of an inhibitor of rapamycin-sensitive and rapamycin-insensitive mTOR kinase activity or a combination of an inhibitor of rapamycin-sensitive mTOR kinase activity and an inhibitor of rapamycin-insensitive mTOR kinase activity to the subject.

90. The method of any of claims 79-89, wherein the method further comprises determining the level of expression of Grb10 in the cell.

91. The method of any of claims 79-89, wherein the method further comprises determining the level of expression of PTEN in the cell.

92. The method of any of claims 79-89, wherein the method further comprises determining the level of expression of Grb10 and of PTEN in the cell.

93. The method of any of claims 90-92, wherein determining the level of expression comprises determining a level of protein, a level of mRNA, or a level of protein phosphorylation in the cell.

94. The method of any of claims 90-93, wherein the method further comprises comparing the level of expression determined in the cell to a reference level, and

if the level of expression in the cell is lower than the reference level, then the cell is determined to exhibit an elevated level of PI3K activity.

95. The method of any of claims 87-94, wherein the method of treatment further comprises administering an effective amount of a compound that stabilizes Grb10 or that inhibits degradation of Grb10 to the subject.

5 96. The method of claim 95, wherein the compound that inhibits degradation of Grb10 is a ubiquitin ligase inhibitor.

97. The method of claim 96, wherein the ubiquitin ligase inhibitor is an E3 ubiquitin ligase inhibitor.

10 98. The method of any of claims 87-97, wherein the method of treatment further comprises administering an effective amount of a PI3K inhibitor to the subject.

99. The method of any of claims 88-98, wherein the mTOR inhibitor is an allosteric mTOR kinase inhibitor or a catalytic mTOR kinase inhibitor.

15 100. The method of claim 99, wherein the allosteric mTOR kinase inhibitor is rapamycin or a rapamycin analog, or wherein the catalytic mTOR kinase inhibitor is an ATP-competitive mTOR kinase inhibitor.

20 101. The method of any of claims 88-98, wherein the mTOR inhibitor is an mTORC1 inhibitor.

102. The method of any of claims 88-98, wherein the mTOR inhibitor is an mTORC1/2 inhibitor.

25 103. The method of claim 100, wherein the rapamycin analog is Ridaforolimus, Sirolimus or Everolimus.

30 104. The method of any of claims 88-98, wherein the mTOR kinase inhibitor is PP242, PP30, AZD8055, OSI-027, WYE354, INK-128, XL388, or torin1.

105 The method of any of claims 88-98, wherein the mTOR inhibitor is a dual PI3K/mTOR kinase inhibitor.

106. The method of claim 105, wherein the dual PI3K/mTOR kinase inhibitor is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126.

5 107. The method of any of claims 98-106, wherein the PI3K inhibitor is ZSTK474, TGX221, GDC0941, or LY294002, XL147, PX147, BKM120, GSK 615, CAL101, or PX-866.

108. The method of any of claims 98-106, wherein the PI3K inhibitor is a dual
10 PI3K/mTOR kinase inhibitor.

109. The method of claim 108, wherein the dual PI3K/mTOR kinase inhibitor is NVP-BEZ235, BGT-226, XL-765, GSK2126458 or SF1126.

15 110. The method of any of claims 88-109, wherein the method of treatment further comprises administering an effective amount of an Akt inhibitor to the subject.

111. The method of claim 110, wherein the Akt inhibitor is perifosine, GSK690693, A443654 or MK2206.
20

112. The method of any of claims 88-111, wherein the method further comprises carrying out the selected method of treatment.

113. The method of any of claims 79-112, wherein the cell is a cancer cell.
25

114. The method of any of claims 79-113, wherein the cell is a cell obtained from a tumor in a subject.

115. A phosphoproteomics array, comprising a plurality of phosphosensitive
30 antibodies or antibody fragments specifically binding to a plurality of phosphorylation sites disclosed in Table 1, 2, 3, 7, 8, or 11.

116. The phosphoproteomics array of claim 115, wherein the antibodies or antibody fragments are immobilized on a solid substrate.

117. The phosphoproteomics array of claim 115 or 116, wherein the plurality of phosphosensitive antibodies or antibody fragments comprises antibodies or antibody fragments specifically binding to at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, or at least 100 phosphorylation sites disclosed in Table 1, 2, 3, 7, 8, or 11.

118. The phosphoproteomics array of claim 115 or 116, wherein the plurality of phosphosensitive antibodies or antibody fragments comprises antibodies or antibody fragments selected from the group comprising anti-phospho-S501/503-Grb10, anti-mTOR, anti-phospho-mTOR (S2481), anti-Grb10 (human), anti-phospho-Akt (Ser473), anti-Akt, anti-S6K, anti-phospho-S6K (T389), anti-IRS2, anti-PARP, anti-caspase 3, anti-4EBP, anti-4EBP (Ser37/46), anti-phospho-ribosomal protein S6 (Ser235/236), anti-ribosomal protein S6, anti-phospho-ERK1/2, anti-phospho-IRS (Y612), anti-p85 and anti-p110 of PI3K, anti ERK1/2, and anti-HA antibodies and antibody fragments.

119. A method of using a phosphoproteomics array to determine mTOR activity in a cancer cell, the method comprising

(a) contacting a proteinaceous sample derived from a cancer cell with the phosphoproteomics array of any of claims E1-E4 under conditions suitable for a protein expressed in the cell to bind to an antibody or antibody fragment of the array,

(b) determining the level of phosphorylated protein bound to an antibody or antibody fragment of the array,

(c) comparing the level of phosphorylated protein bound to an antibody or antibody fragment of the array to a reference level, wherein if the level phosphorylated protein in the sample derived from the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

120. The method of claim 119, the method further comprising generating a phosphoproteomic profile of the cell, wherein the profile comprises phosphorylation values of a plurality of proteins expressed in the cell.

121. The method of claim 120, wherein the method further comprises comparing the phosphoproteomic profile of the cell with a phosphoproteomic profile of a control cell, wherein, if the phosphoproteomic profile of the cell is substantially similar to that of the control cell, then the cell is determined to exhibit a level of mTOR kinase activity similar to that of the control cell.

122. The method of claim 121, wherein the control cell is a cancer cell.

123. The method of claim 122, wherein the control cell is a rapamycin-sensitive cancer cell.

124. The method of claim 122, wherein the control cell is a rapamycin insensitive cancer cell.

125. The method of claim 124, wherein the control cell is a cell exhibiting normal mTOR kinase activity.

126. The method of claim 119-125, wherein the method further comprises classifying a cell that is determined to exhibit an elevated level of mTOR kinase activity, wherein if a protein determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class I protein, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTORC1 activity,

if a protein determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class II protein, then the cell is determined to exhibit an elevated level of rapamycin-insensitive mTORC1 and/or mTORC2 activity, or

if a protein determined to exhibit a higher level of phosphorylation in the cell as compared to the reference level is a class III protein, then the cell is determined to exhibit an elevated level of rapamycin-sensitive mTOR activity, or an elevated level of rapamycin-insensitive mTOR activity, or both.

127. A method of identifying an mTOR kinase inhibitor, the method comprising

(a) contacting an mTOR kinase with a polypeptide comprising a phosphorylation site disclosed in Table 1, 2, 3, 7, 8, or 11 under conditions suitable

for the mTOR kinase to phosphorylate the phosphorylation site in the presence of a candidate agent,

(b) determining the level of phosphorylation at the phosphorylation site,

(c) comparing the level of phosphorylation determined in step (b) to a
5 reference level, wherein if the level determined in step (b) is lower than the reference level,
then the candidate agent is identified as an mTOR kinase inhibitor.

128. The method of claim 127, wherein the phosphorylation site is a Grb10
phosphorylation site.

10

129. The method of claim 127 or 128, wherein the candidate agent is a polypeptide,
an aptamer, an adnectin, or a small molecule compound.

130. The method of any of claims 127-129, wherein the reference level is a level of
15 phosphorylation at the phosphorylation site determined in the absence of the candidate agent.

131. The method of any of claims 127-130, wherein the level determined in step (b)
is lower than the reference level, if the level determined in step (b) is less than 75%, less than
50%, less than 40%, less than 30%, less than 25%, less than 20%, less than 10%, less than
20 5%, less than 2.5%, or less than 1% of the reference level.

132. The method of any of claims 127-131, wherein the contacting is performed in
vitro.

25 133. The method of any of claims 127-131, wherein the contacting is performed in
vivo.

134. An antibody or antibody fragment, wherein the antibody or antibody fragment
specifically binds to a phosphorylation site described in Table 1, 2, 3, 7, 8, or 11.

30

135. The antibody or antibody fragment of claim 134, wherein the antibody or
antibody fragment is a phospho-sensitive antibody or antibody fragment.

136. The antibody or antibody fragment of claim 134 or 135, wherein the antibody or antibody fragment specifically binds to a phosphorylation site of a protein described in Table 1, 2, or 3.

5 137. The antibody or antibody fragment of any of claims 134-136, wherein the antibody or antibody fragment is an anti-phospho-NDRG3 (Ser331) antibody or antibody fragment.

10 138. The antibody or antibody fragment of any of claims 134-136, wherein the antibody or antibody fragment is an anti-phospho-S501/503-Grb10 antibody or antibody fragment.

15 139. The antibody or antibody fragment of any of claims 134-136, wherein the antibody or antibody fragment is an Anti-CDC2-related Kinase, Arg/Ser-Rich (Ser437) antibody or antibody fragment.

140. A method for determining mTOR kinase activity in a cell, the method comprising

- 20 (a) obtaining a cell from a subject,
(b) determining the level of Grb10 phosphorylation in the cell, and
(c) comparing the level of Grb10 phosphorylation to a reference level, wherein if the level of Grb10 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

25 141. A method for determining mTOR kinase activity in a cell, the method comprising

- (a) obtaining a cell from a subject,
(b) determining the level of FOXK1 phosphorylation in the cell, and
30 (c) comparing the level of FOXK1 phosphorylation to a reference level, wherein if the level of FOXK1 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

142. A method for determining mTOR kinase activity in a cell, the method comprising

- (a) obtaining a cell from a subject,
- (b) determining the level of ZEB2 phosphorylation in the cell, and
- (c) comparing the level of ZEB2 phosphorylation to a reference level, wherein if the level of ZEB2 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

143. A method for determining mTOR kinase activity in a cell, the method comprising

- (a) obtaining a cell from a subject,
- (b) determining the level of NDRG3 phosphorylation in the cell, and
- (c) comparing the level of NDRG3 phosphorylation to a reference level, wherein if the level of NDRG3 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

144. A method for determining mTOR kinase activity in a cell, the method comprising

- (a) obtaining a cell from a subject,
- (b) determining the level of LARP1 phosphorylation in the cell, and
- (c) comparing the level of LARP1 phosphorylation to a reference level, wherein if the level of LARP1 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

145. A method for determining mTOR kinase activity in a cell, the method comprising

- (a) obtaining a cell from a subject,
- (b) determining the level of SRPK2 phosphorylation in the cell, and
- (c) comparing the level of SRPK2 phosphorylation to a reference level, wherein if the level of SRPK2 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

146. A method for determining mTOR kinase activity in a cell, the method comprising

- (a) obtaining a cell from a subject,
- (b) determining the level of CDK12 phosphorylation in the cell, and

(c) comparing the level of CDK12 phosphorylation to a reference level, wherein if the level of CDK12 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

- 5 147. A method for determining mTOR kinase activity in a cell, the method comprising
- (a) obtaining a cell from a subject,
- (b) determining the level of MIB1 phosphorylation in the cell, and
- (c) comparing the level of MIB1 phosphorylation to a reference level, wherein if the level of
- 10 MIB1 phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

148. A method for determining mTOR kinase activity in a cell, the method comprising
- 15 (a) obtaining a cell from a subject,
- (b) determining the level of IBTK phosphorylation in the cell, and
- (c) comparing the level of IBTK phosphorylation to a reference level, wherein if the level of IBTK phosphorylation in the cell is higher than the reference level, then the cell is determined to exhibit an elevated level of mTOR kinase activity.

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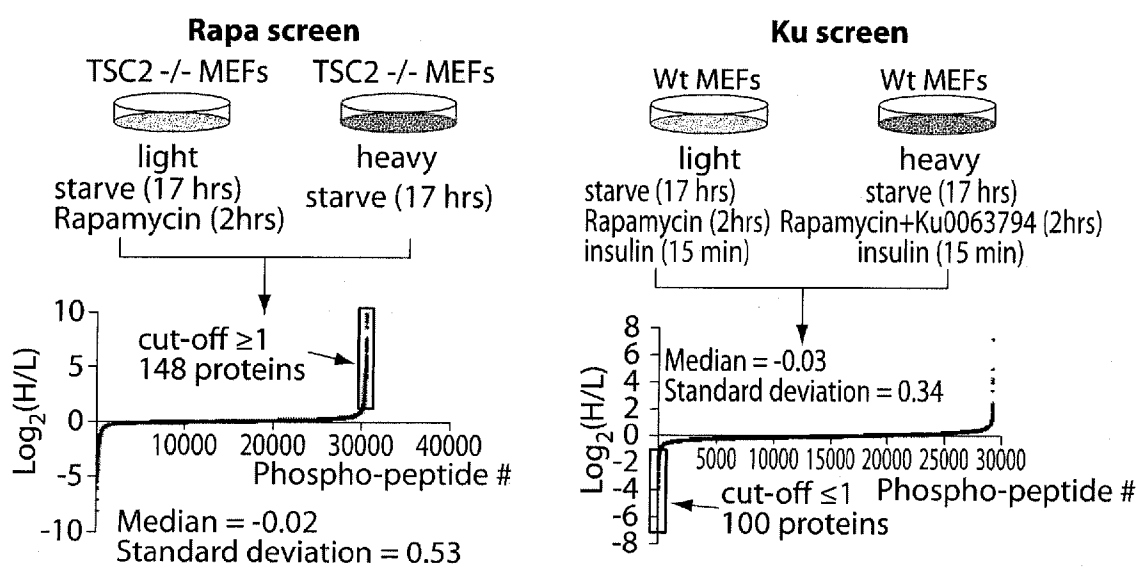
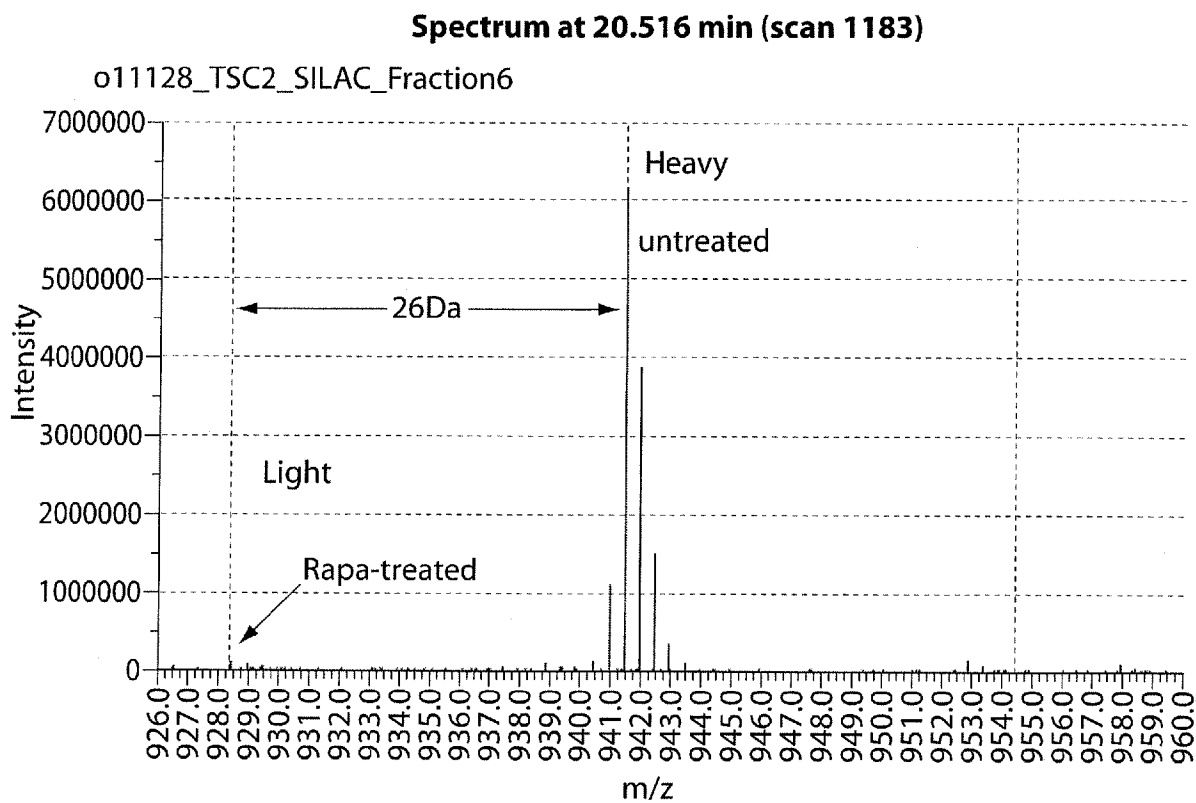


Fig. 1A

2/30



MS/MS

 $[MH_2-H_3PO_4]^{2+}$

Ribosomal protein S6

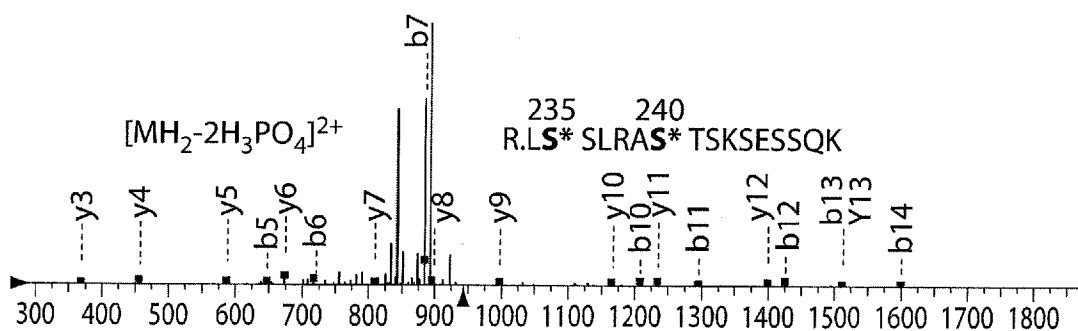


Fig. 1B

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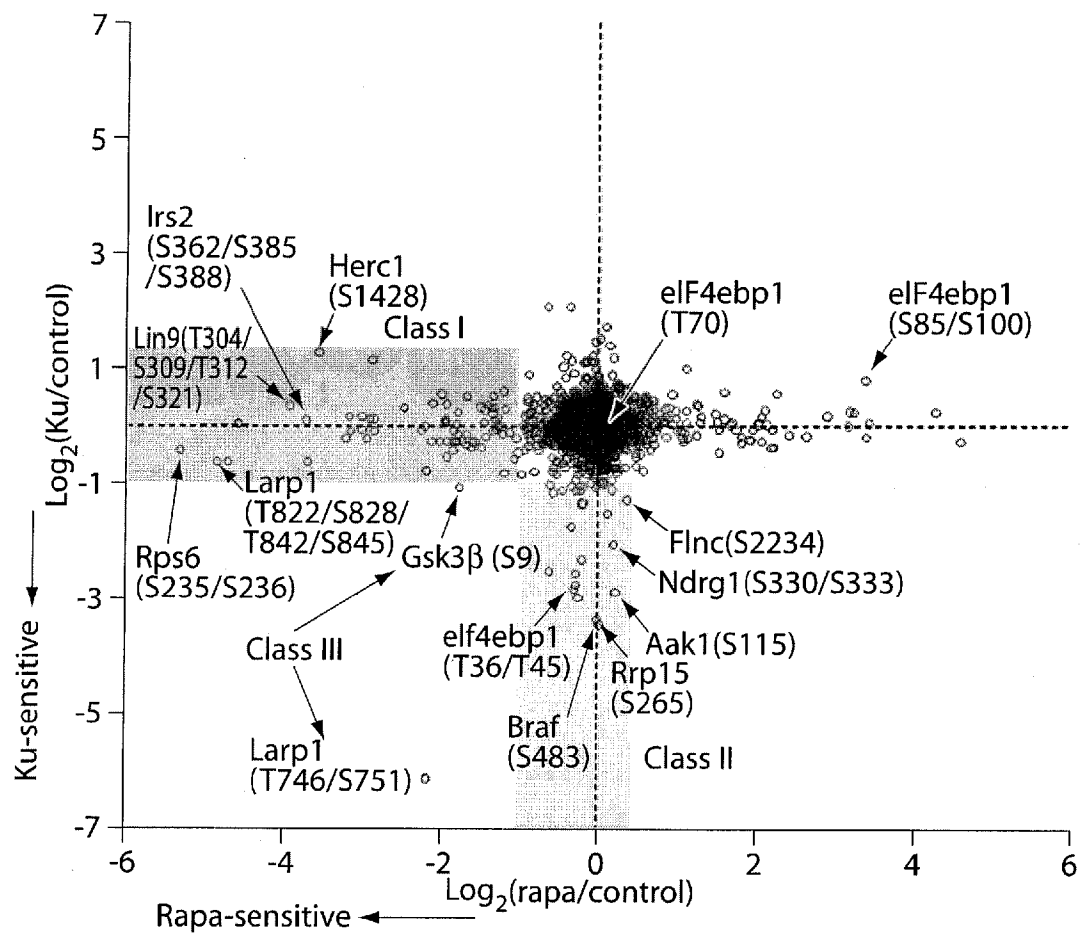


Fig. 1C

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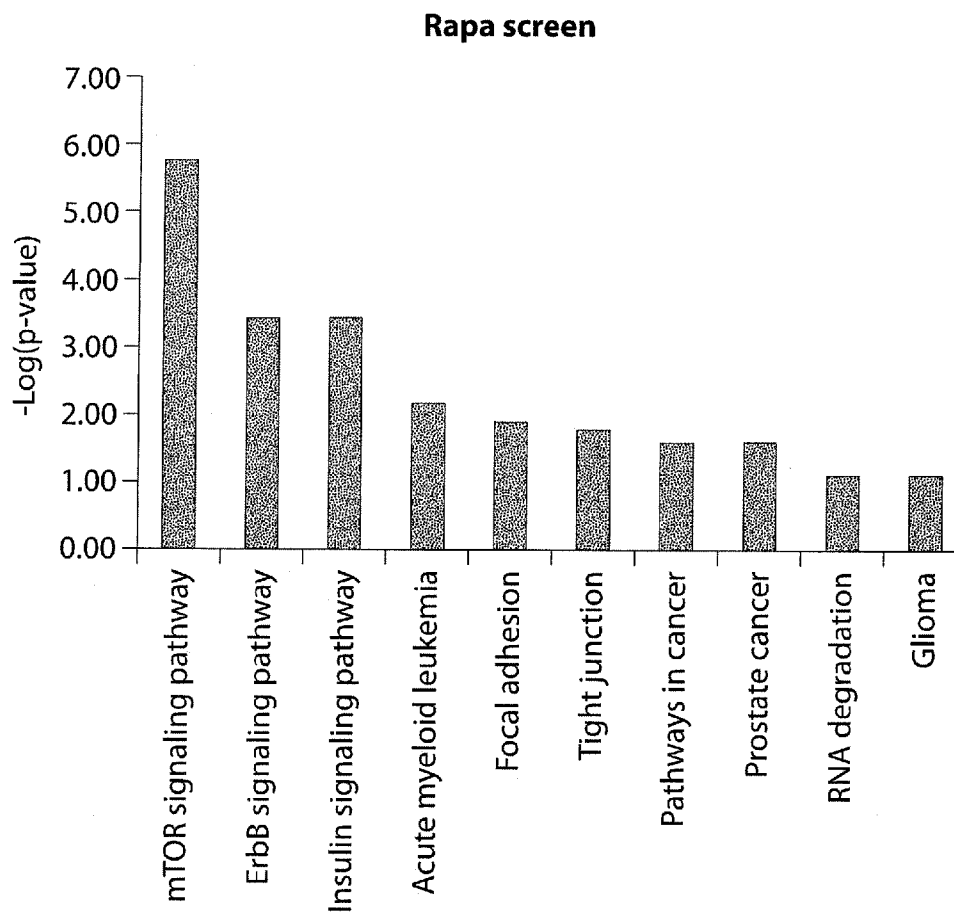
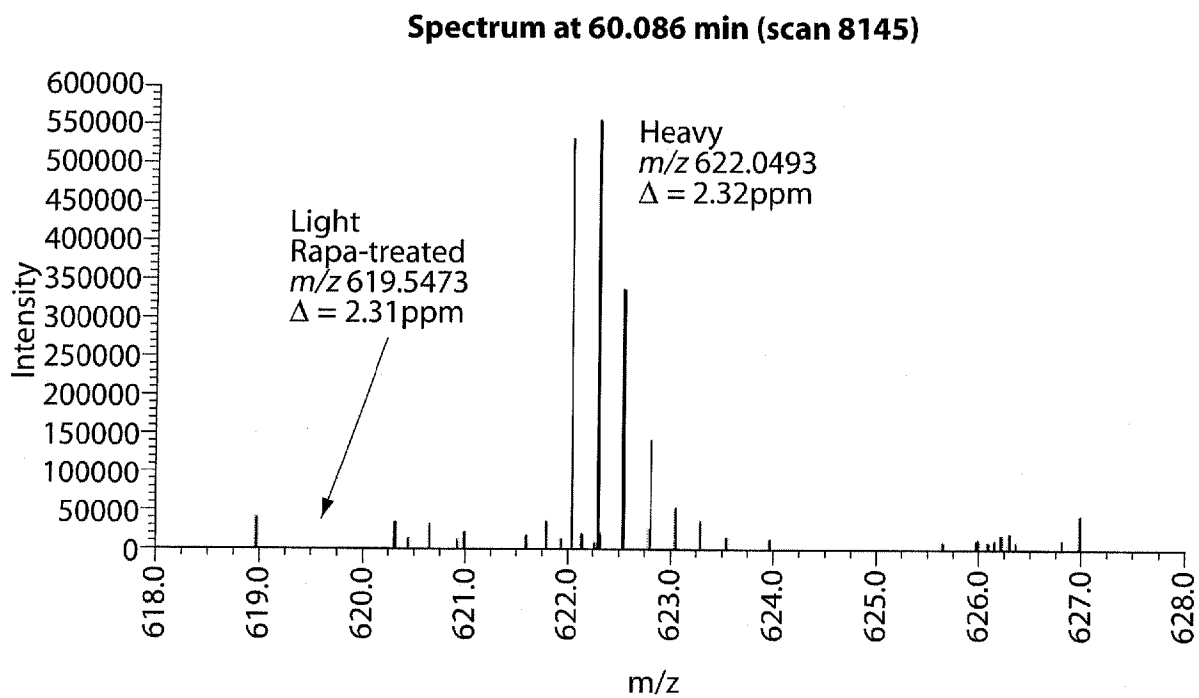


Fig. 1D

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**Fig. 2A**

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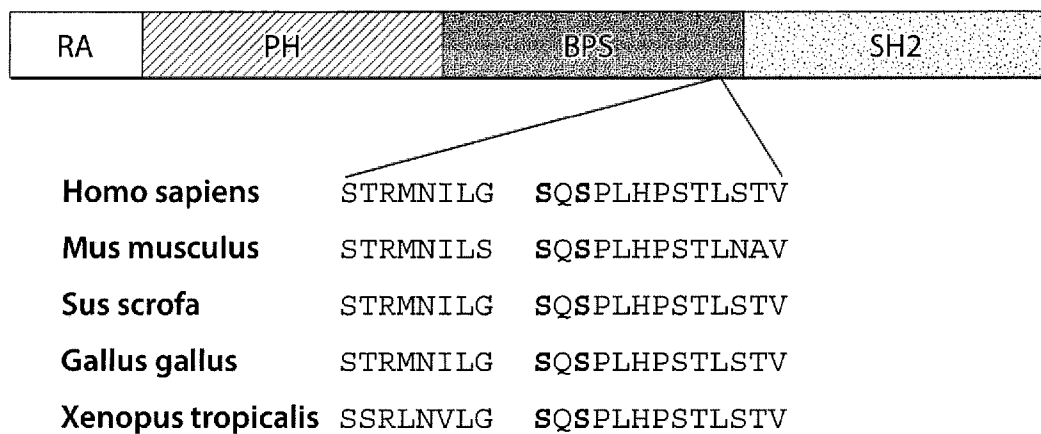


Fig. 2B

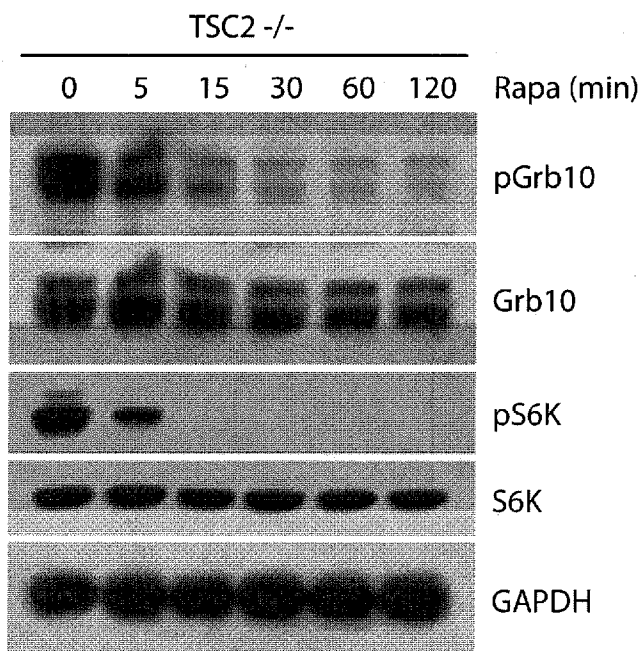


Fig. 2C

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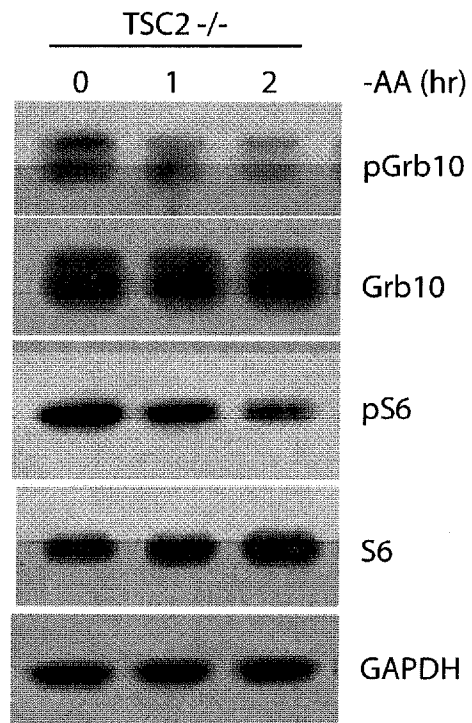


Fig. 2D

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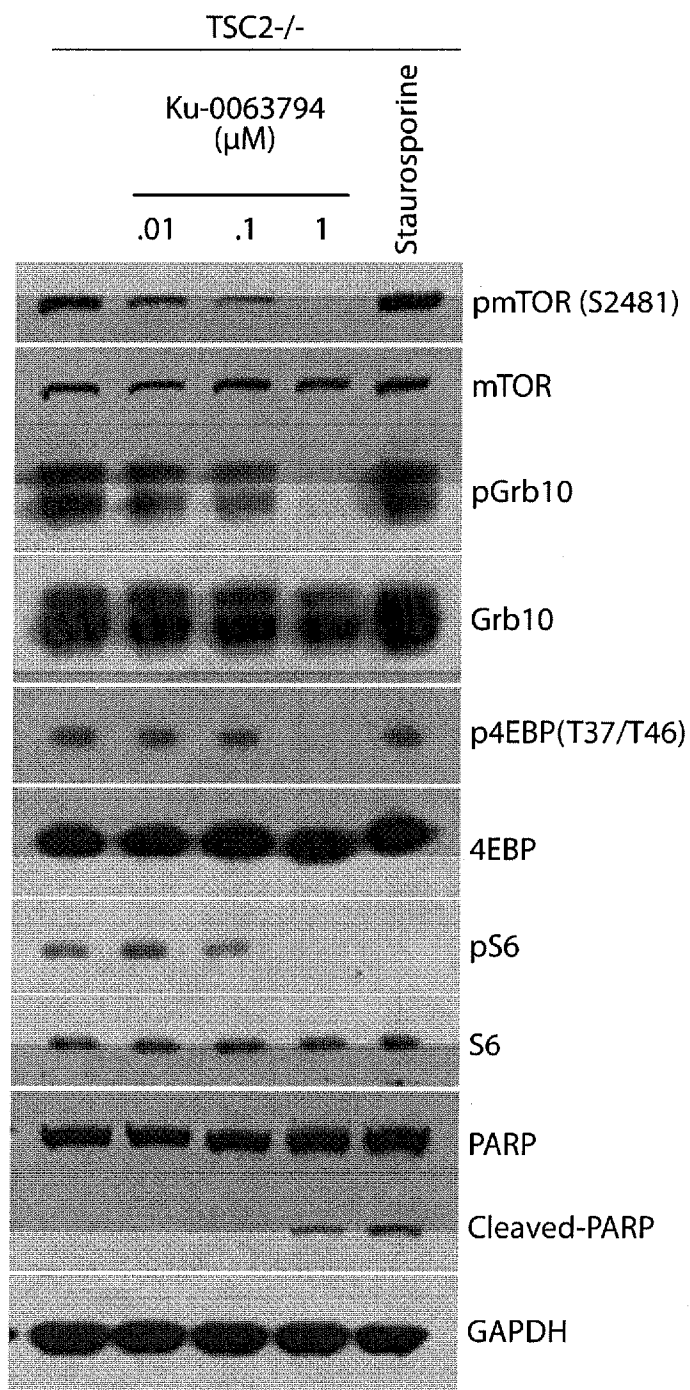


Fig. 2E

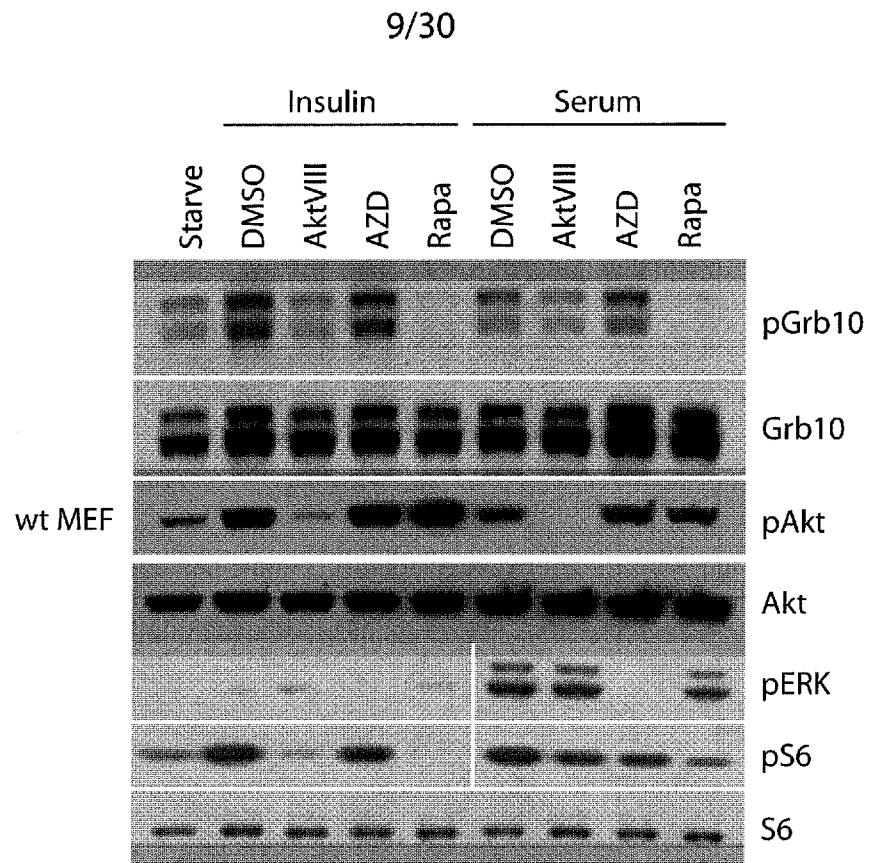


Fig. 2F

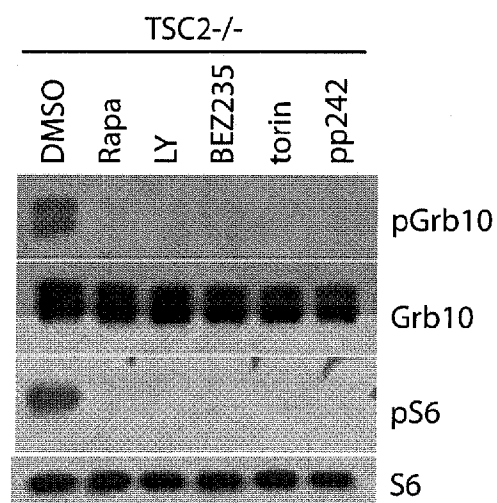


Fig. 2G

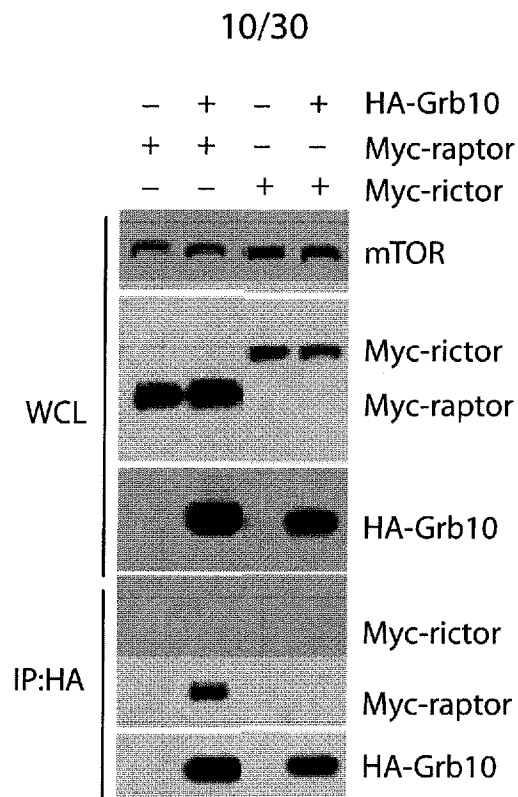


Fig. 3A

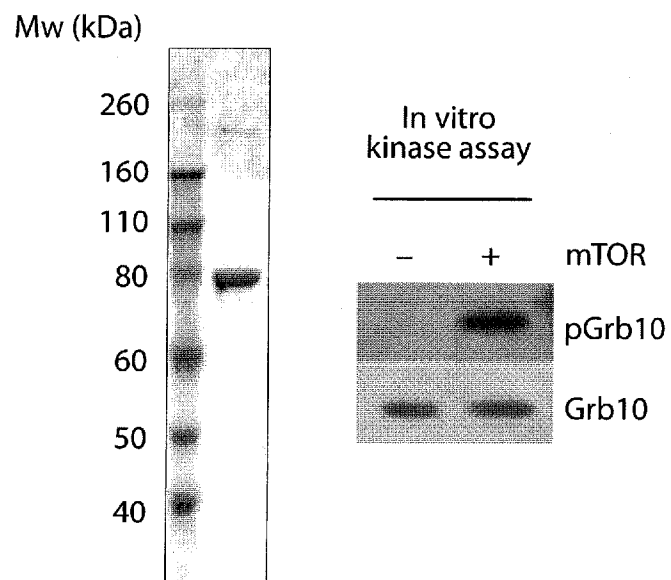


Fig. 3B

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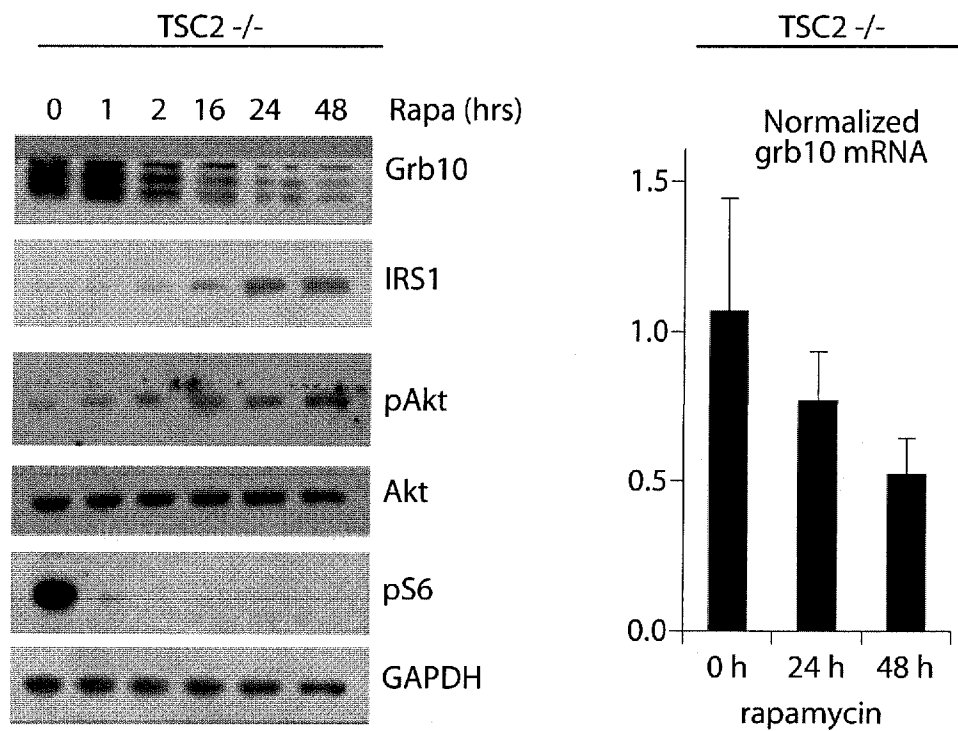


Fig. 3C

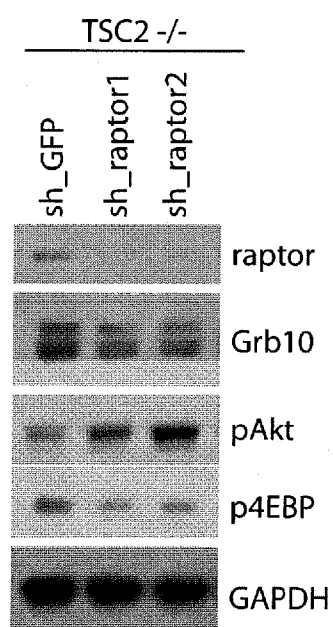


Fig. 3D

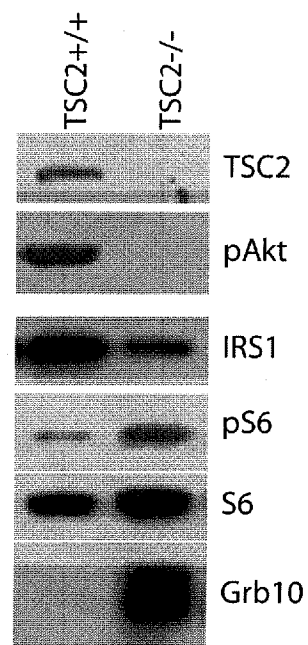


Fig. 3E

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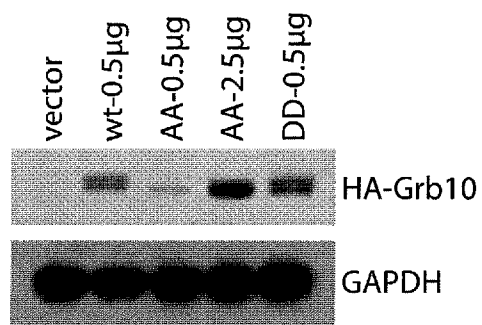


Fig. 3F

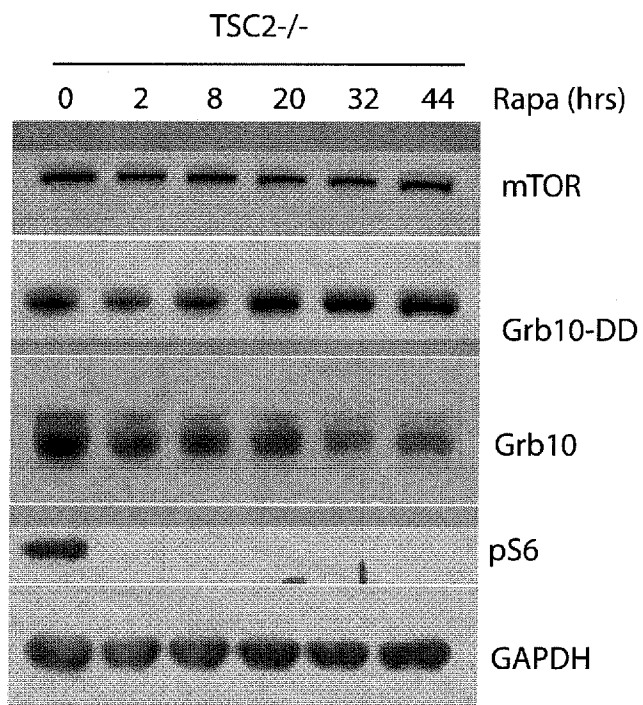


Fig. 3G

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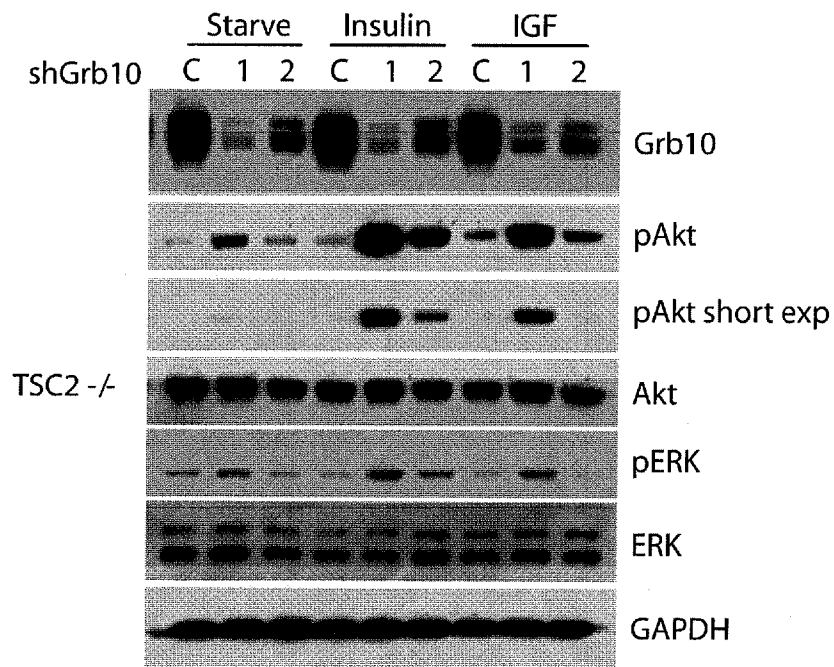


Fig. 4A

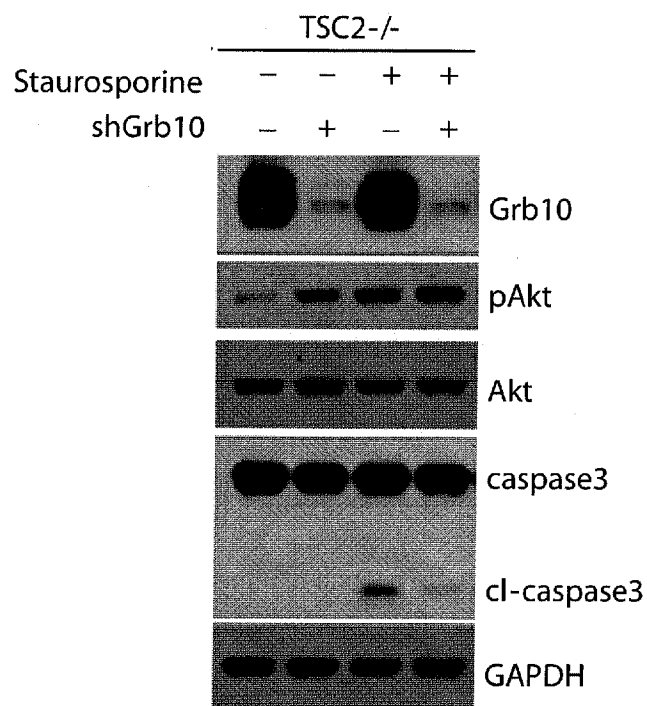


Fig. 4B

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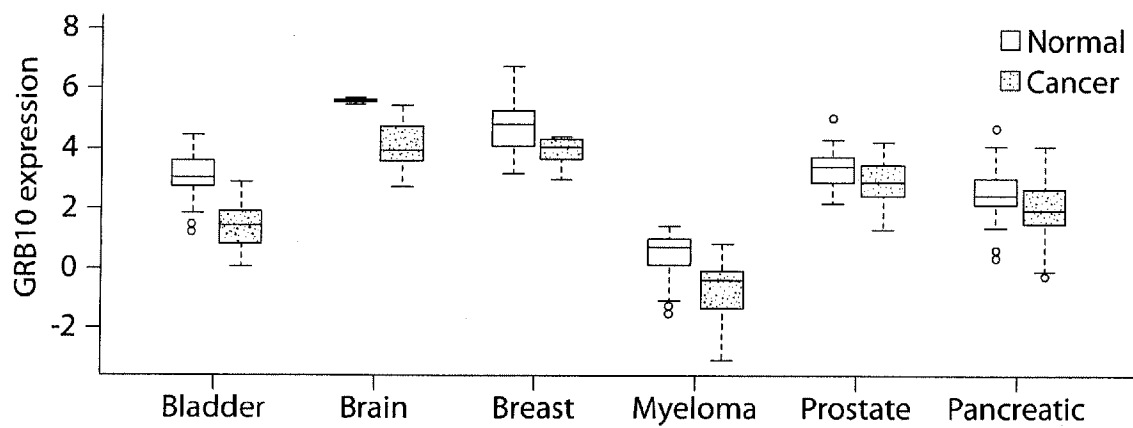


Fig. 4C

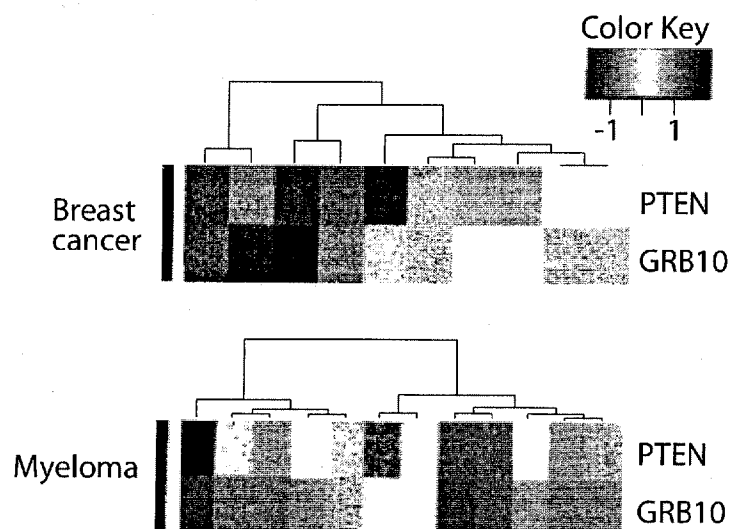


Fig. 4D

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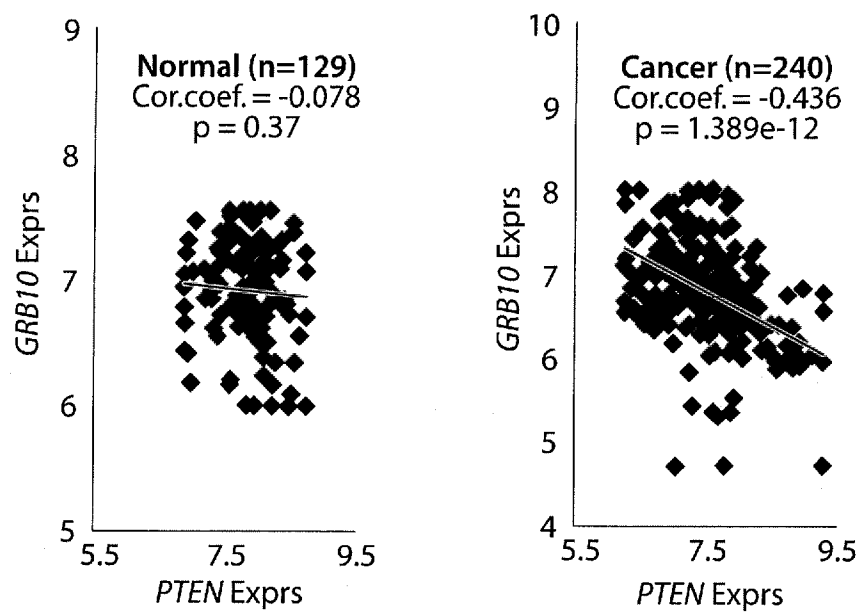


Fig. 4E

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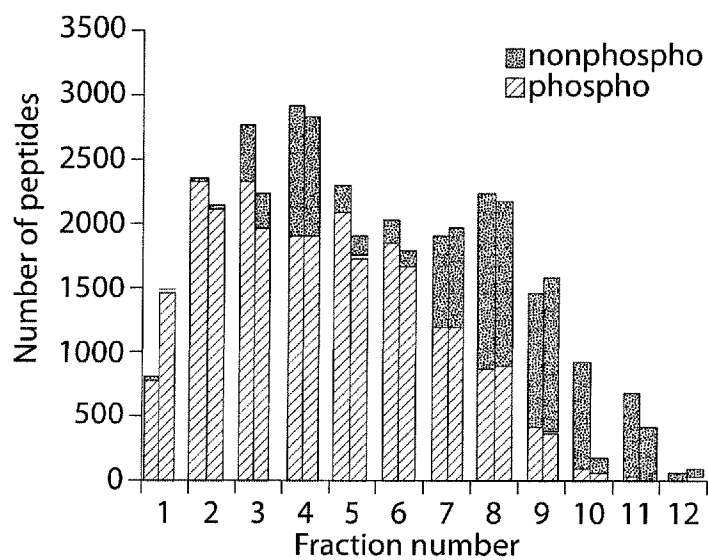


Fig. 5A

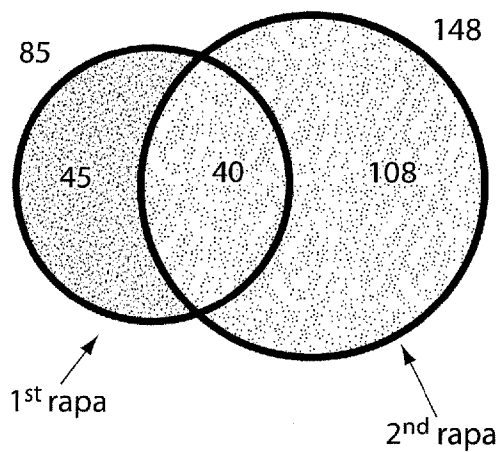


Fig. 5B

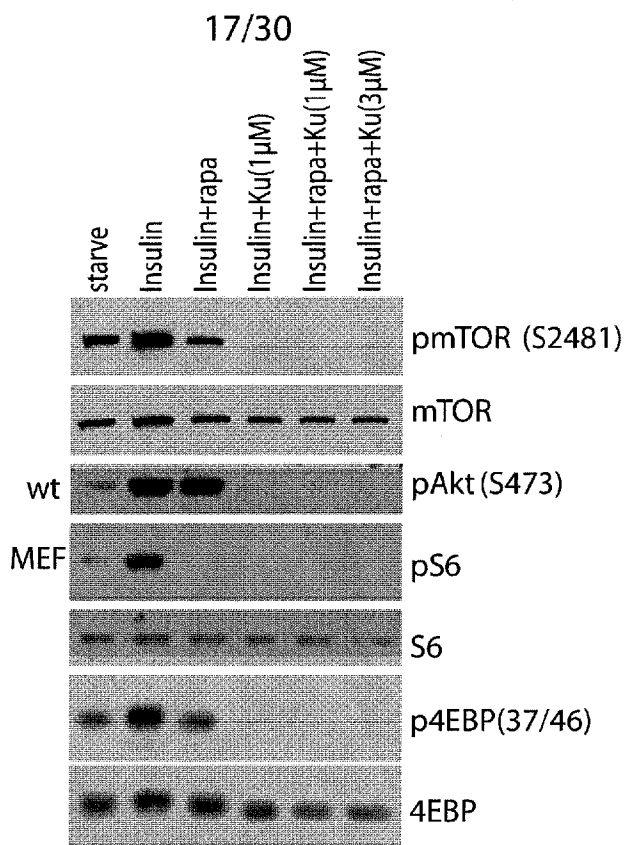


Fig. 5C

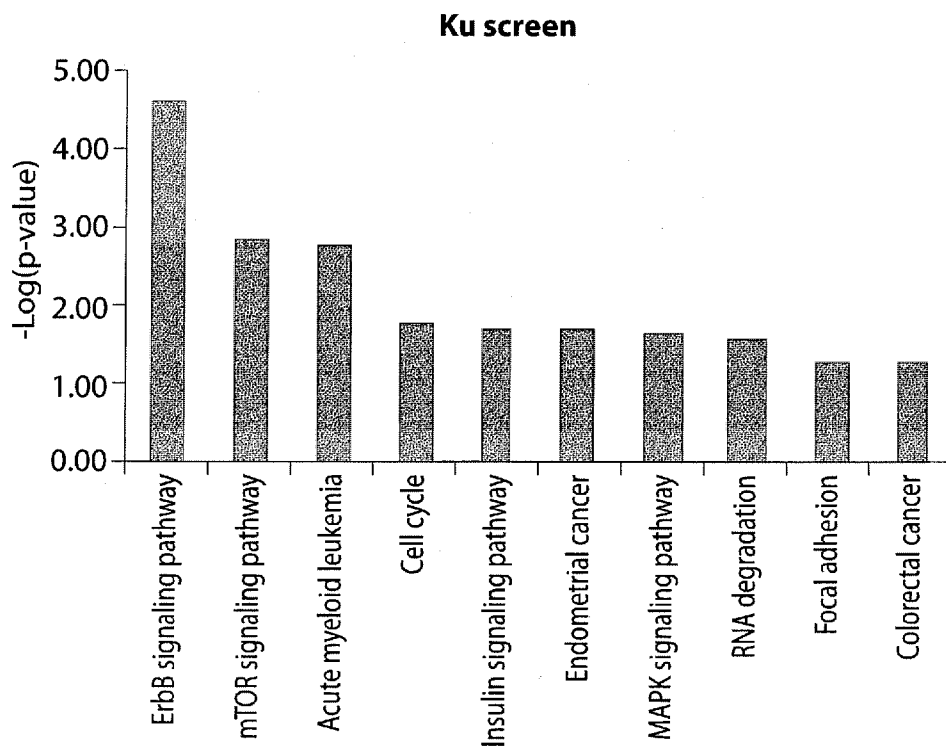
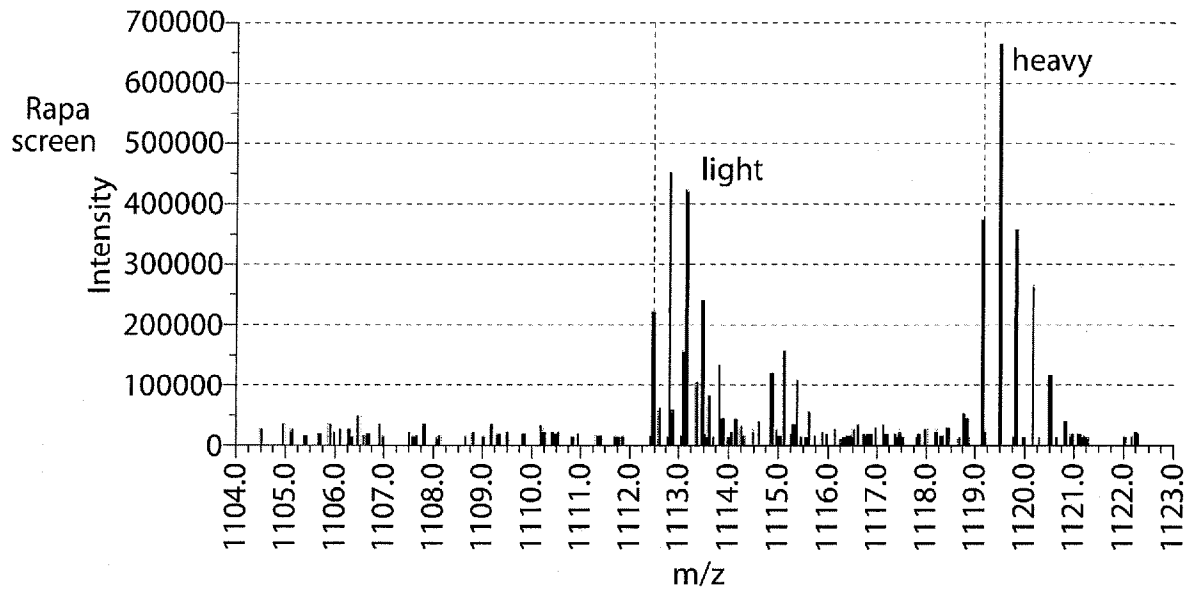


Fig. 5D

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4EBP T36/T45

Spectrum at 54.859 min (scan 7513)



Spectrum at 87.937 min (scan 19890)

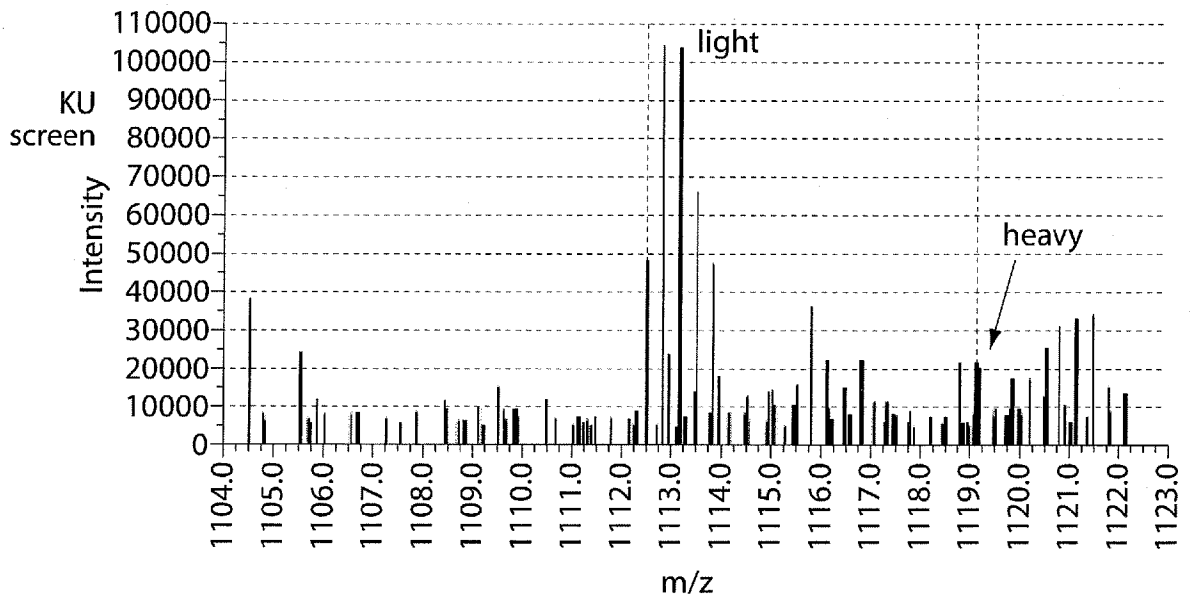


Fig. 6A-1

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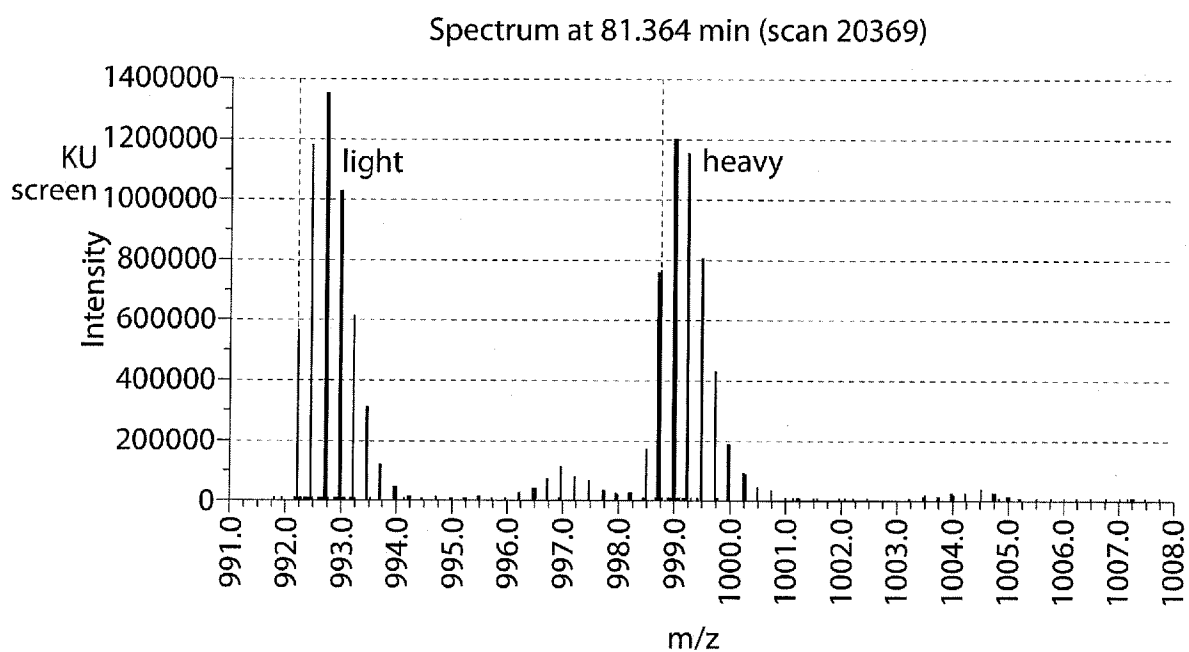
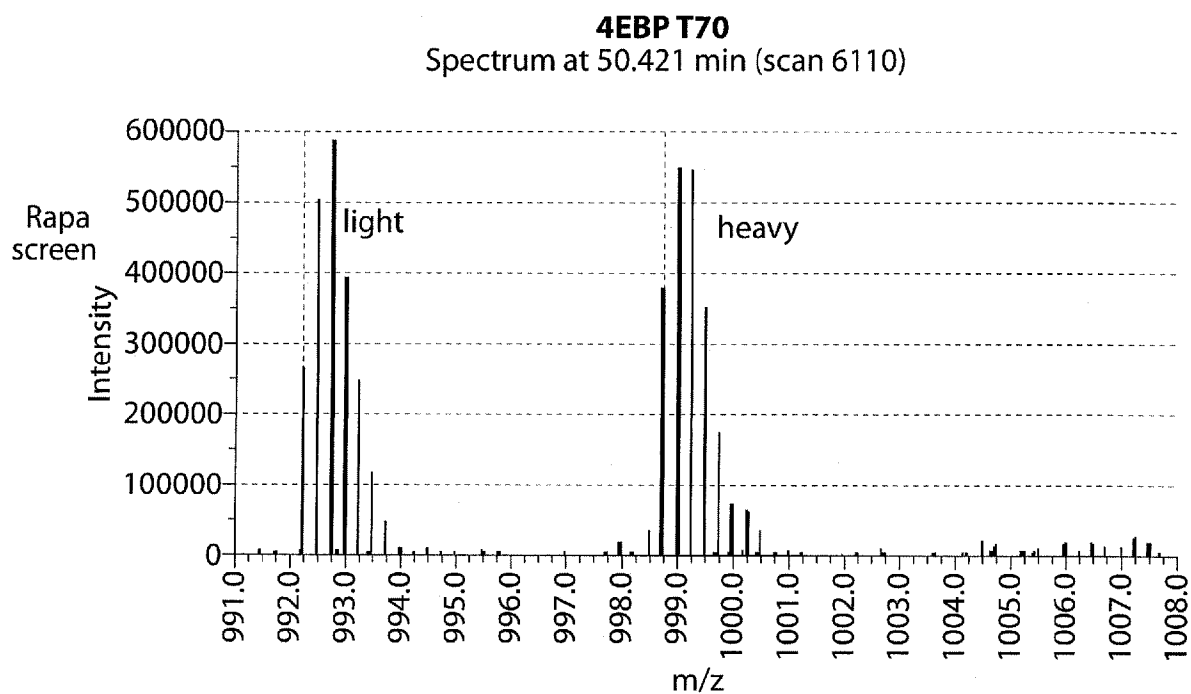
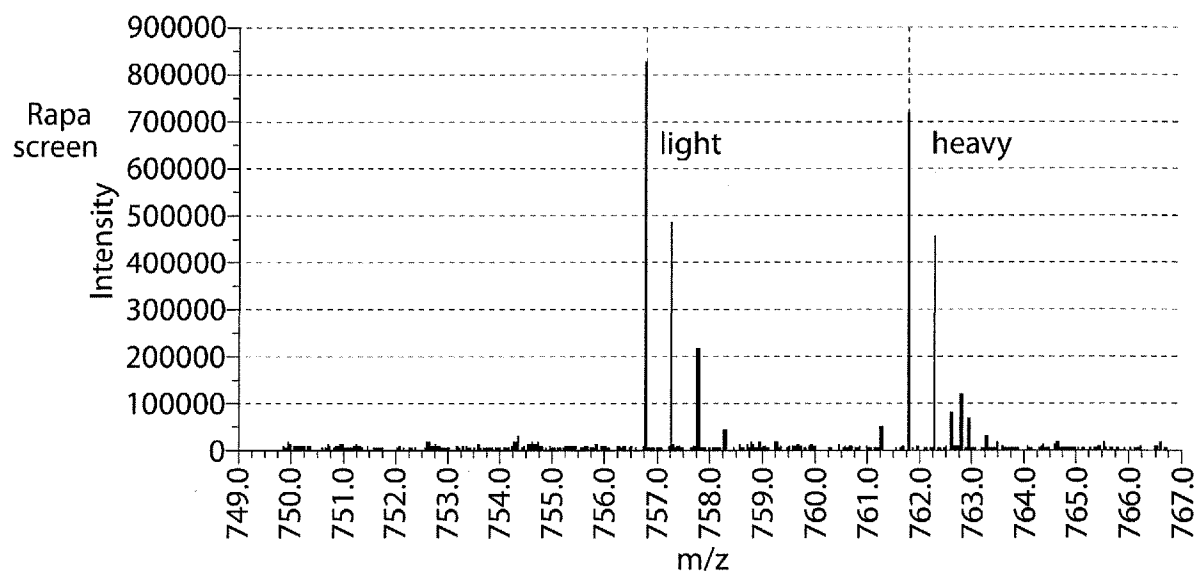


Fig. 6A-2

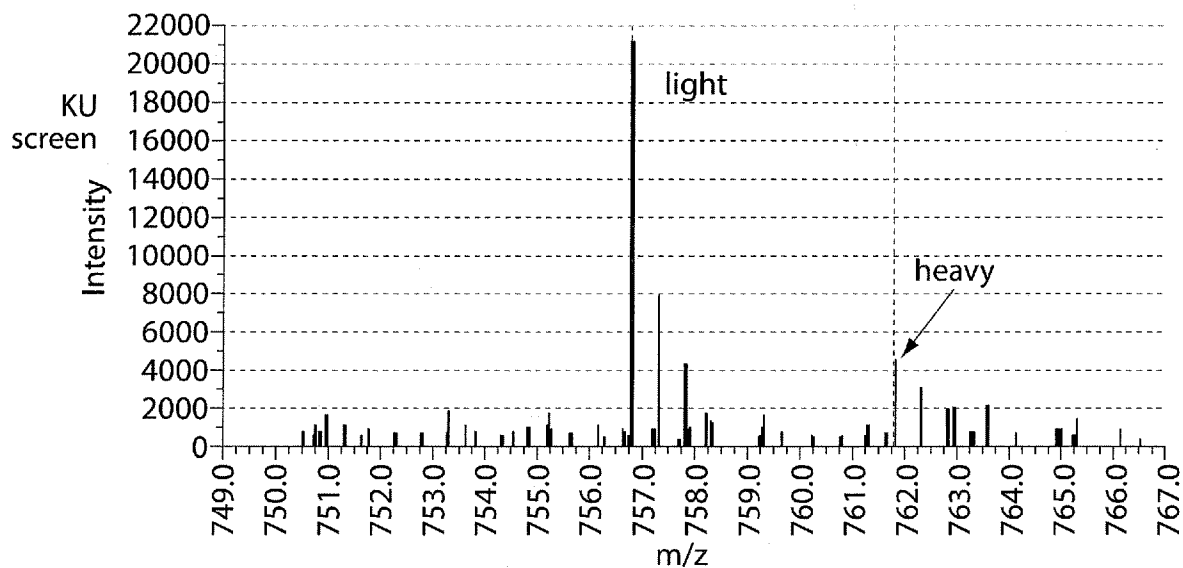
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NDRG1 S330/S333

Spectrum at 29.704 min (scan 2390)



Spectrum at 44.867 min (scan 5488)

**Fig. 6B**

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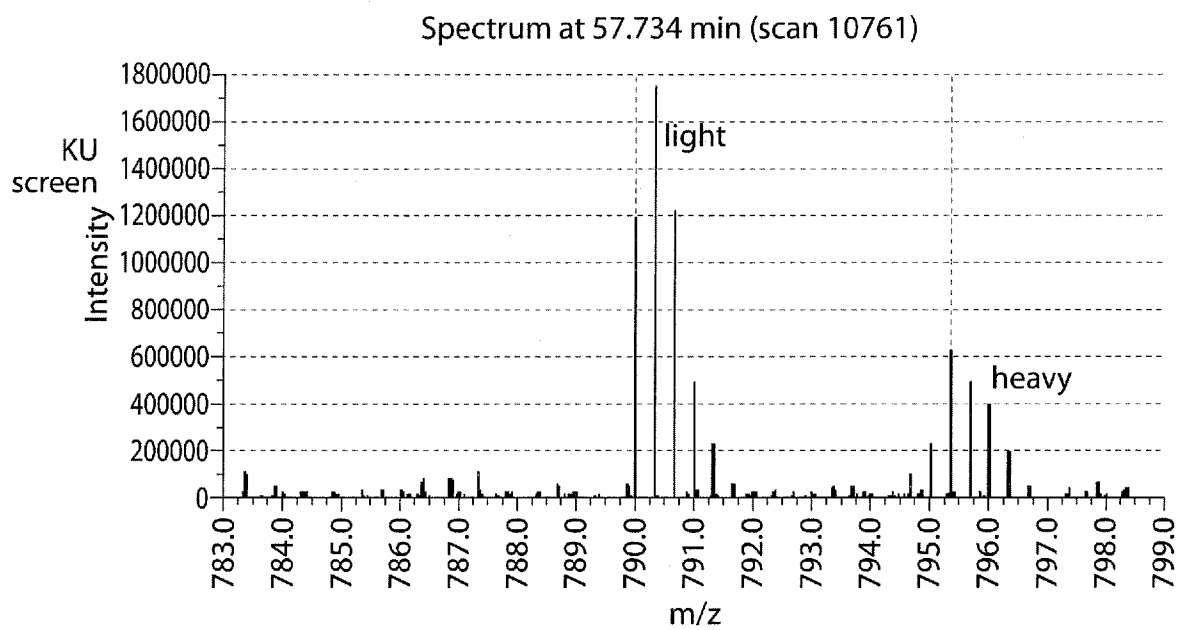
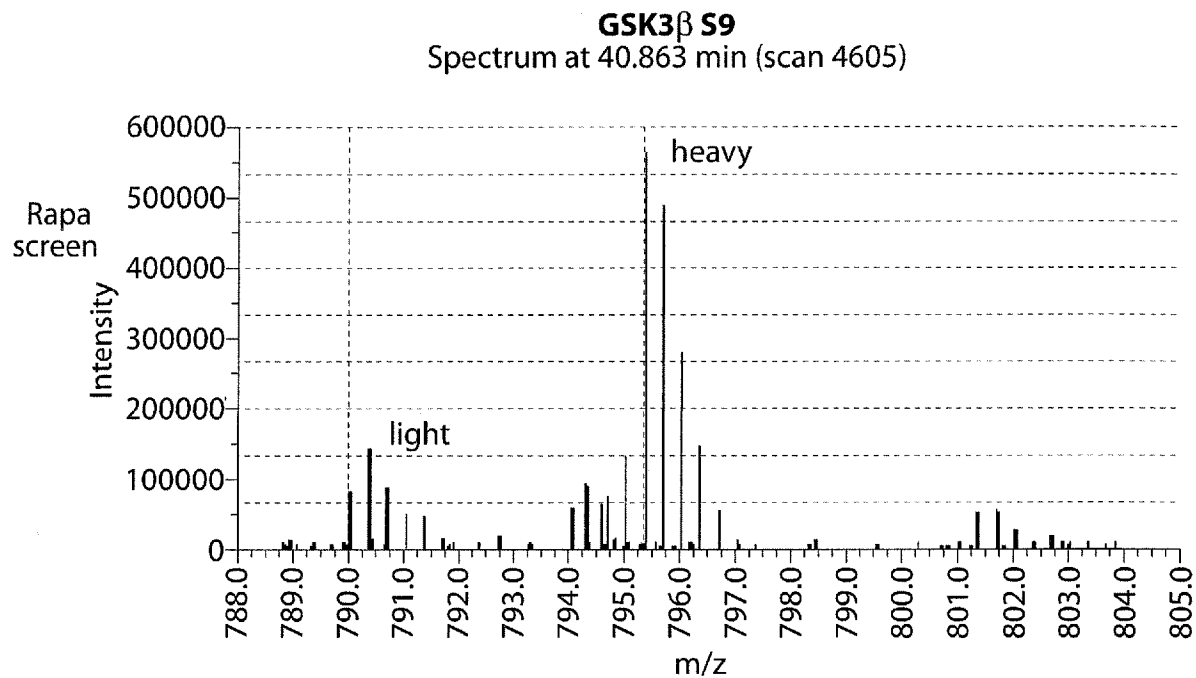


Fig. 6C

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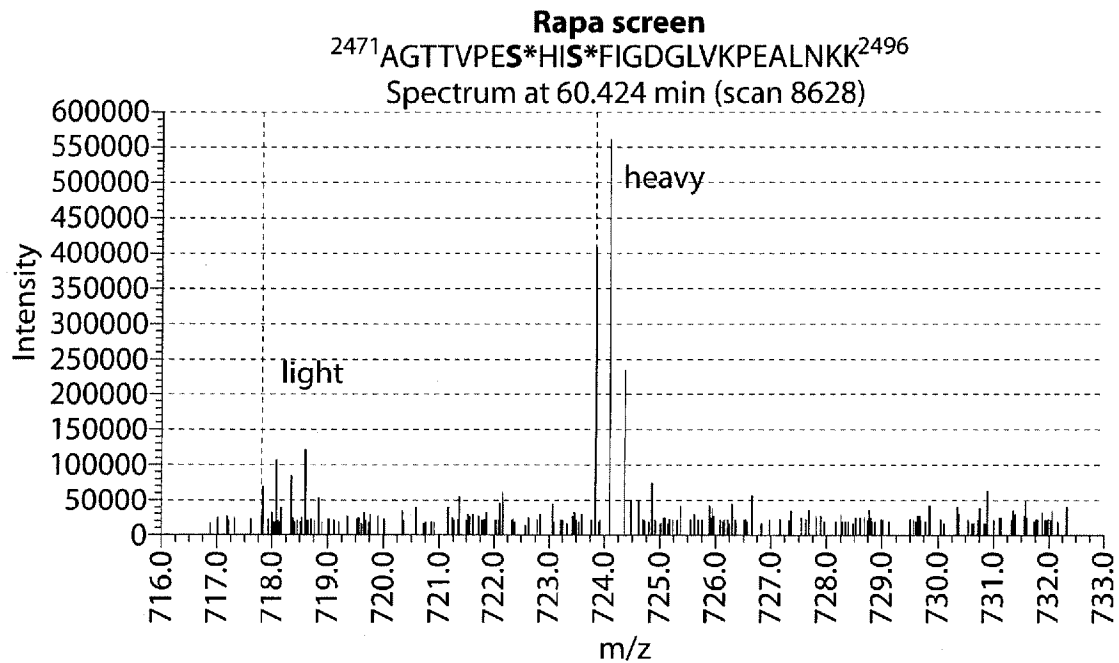


Fig. 7A

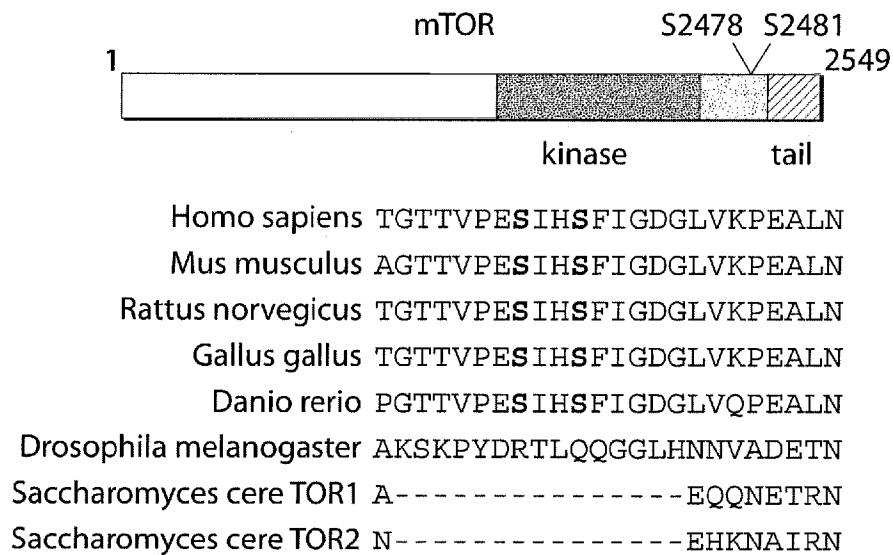


Fig. 7B

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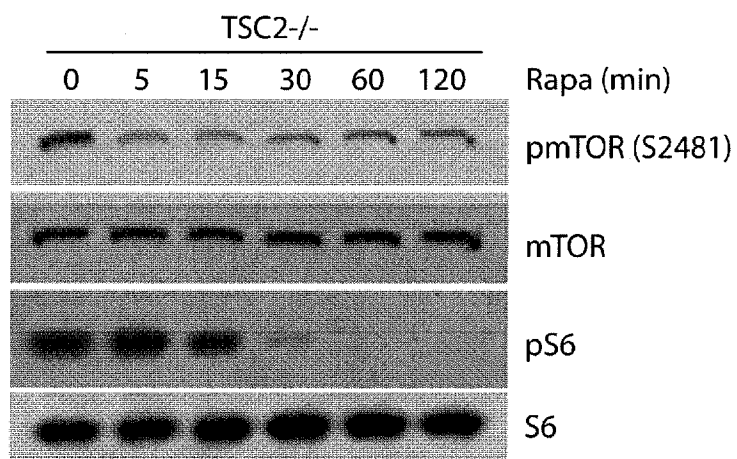


Fig. 7C

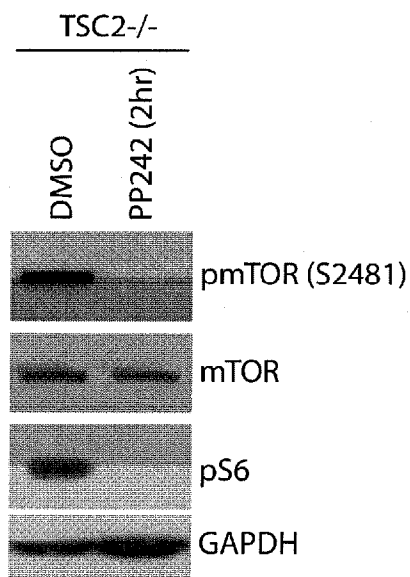


Fig. 7D

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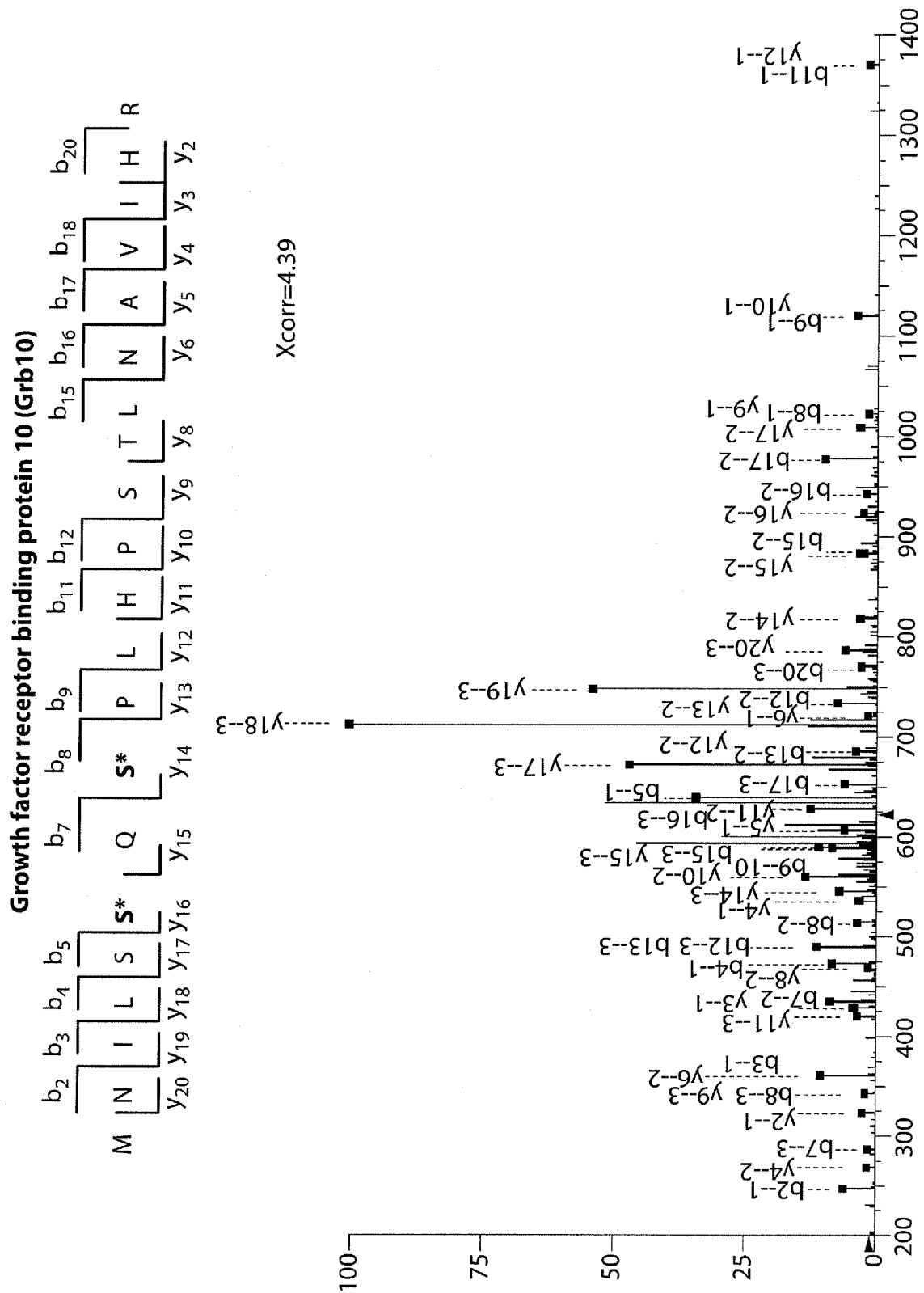


Fig. 8A

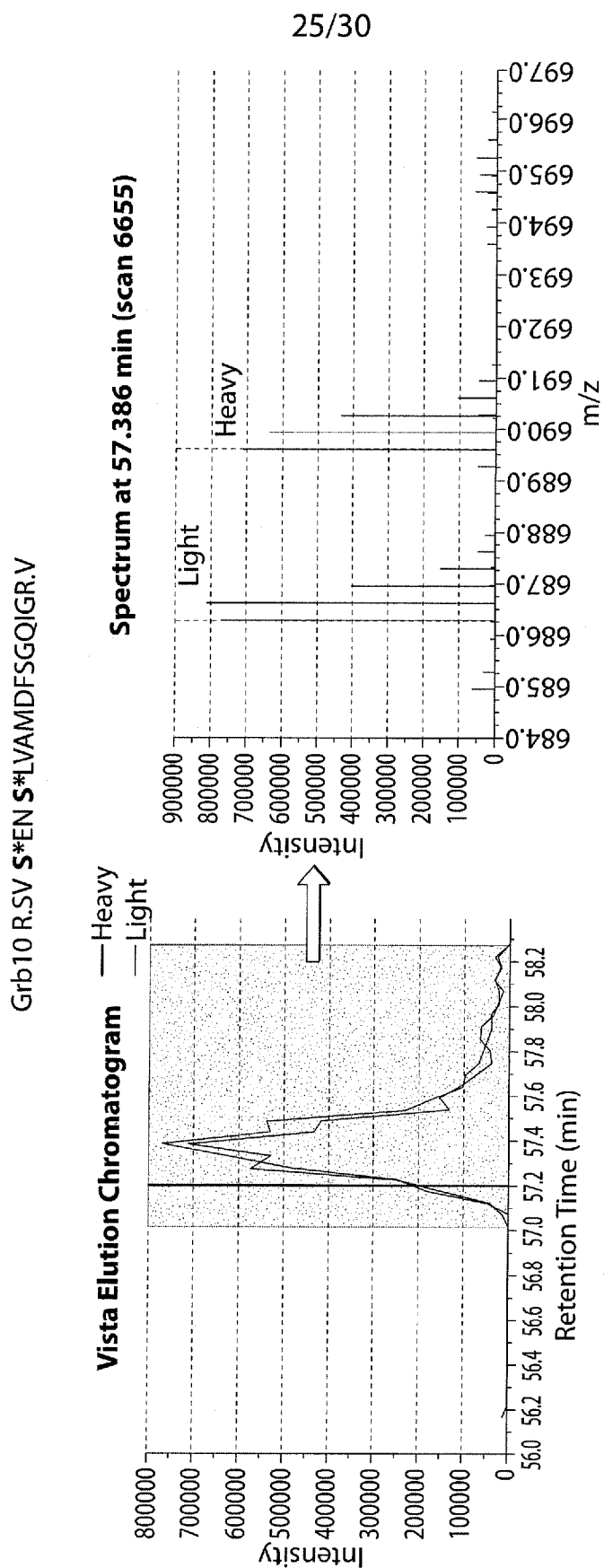


Fig. 8B

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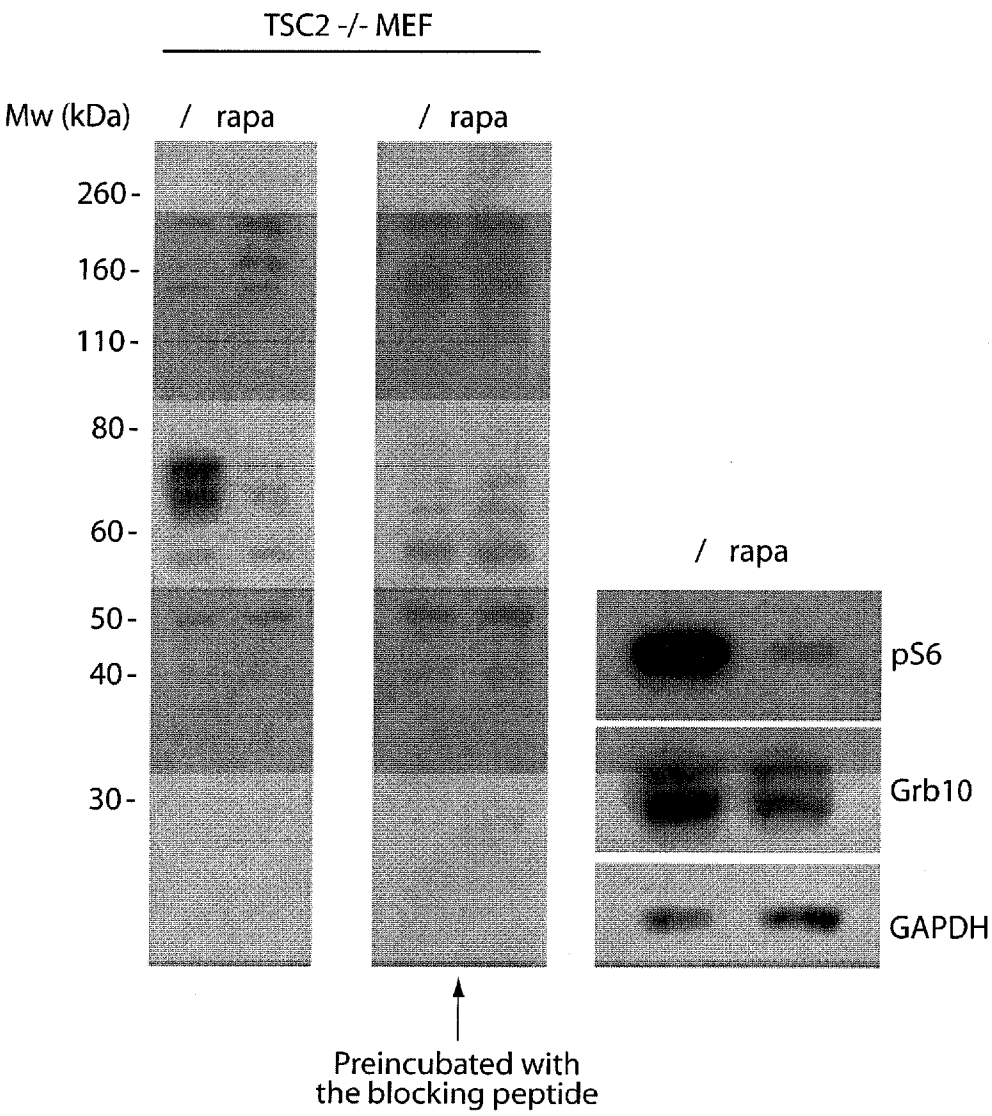
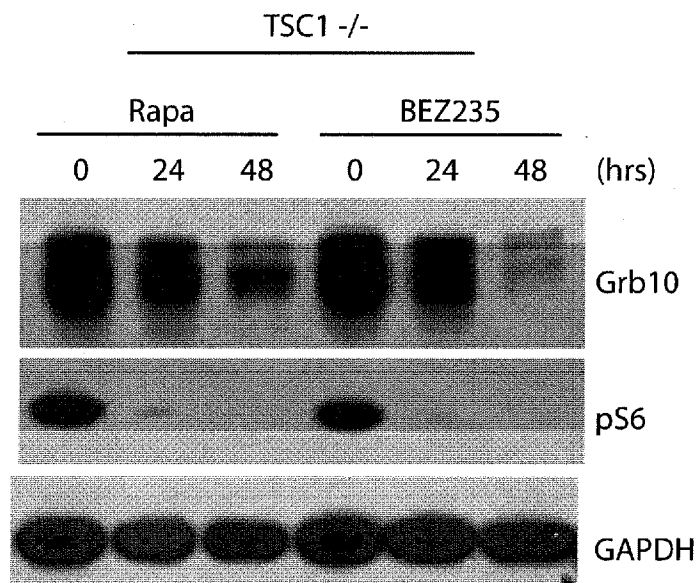
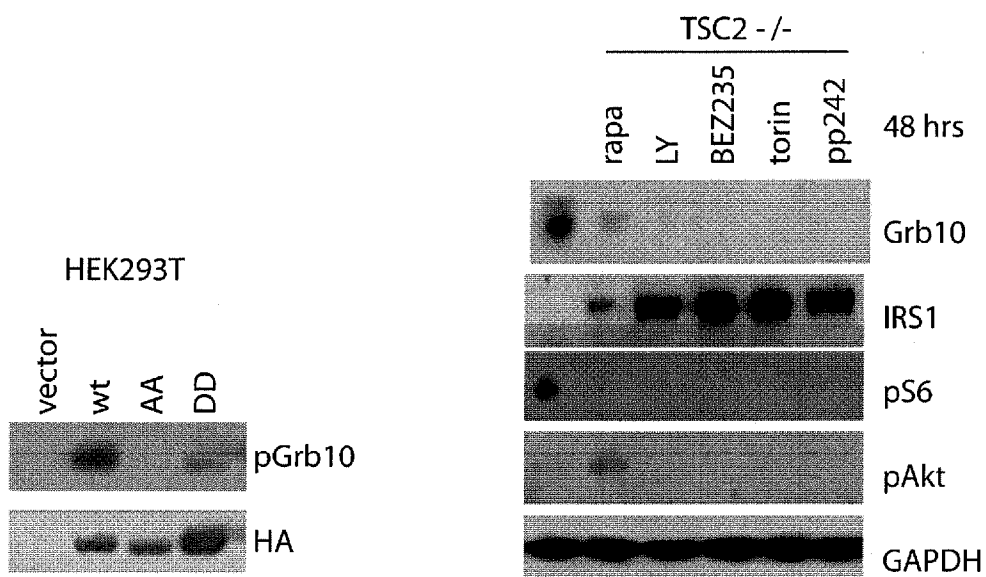


Fig. 9A

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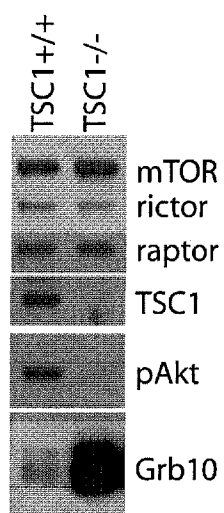


Fig. 9E

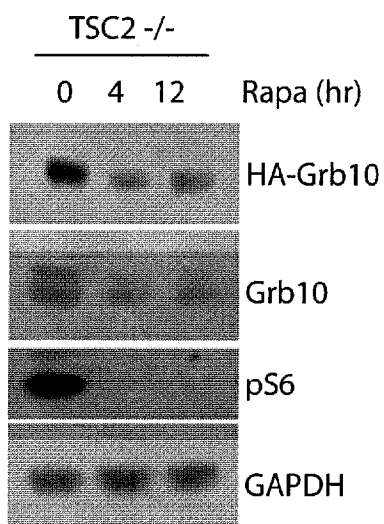


Fig. 9F

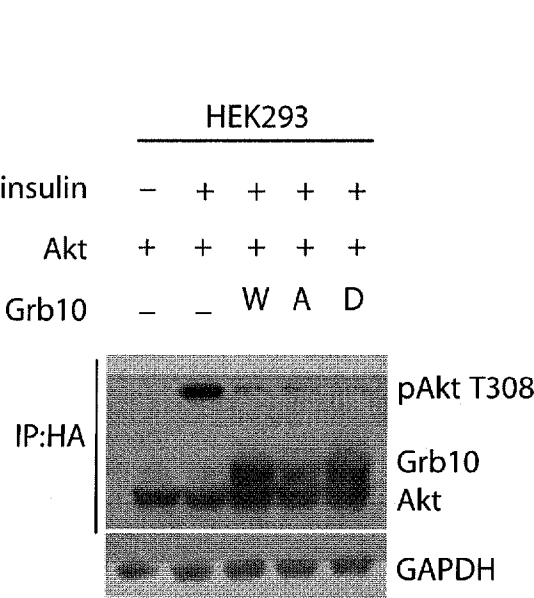


Fig. 10A

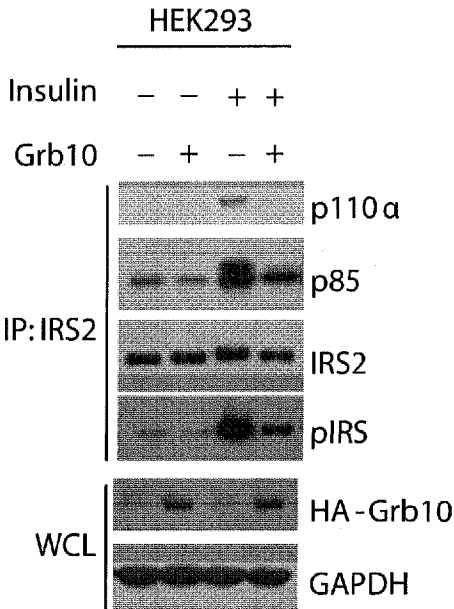


Fig. 10B

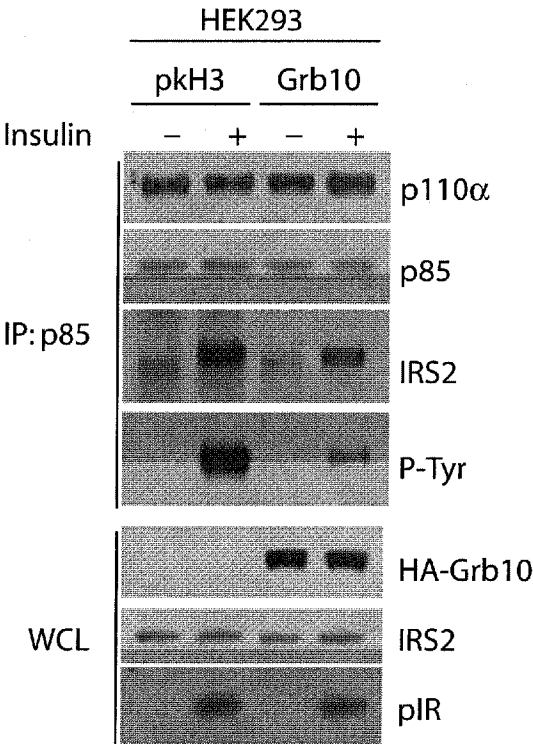


Fig. 10C

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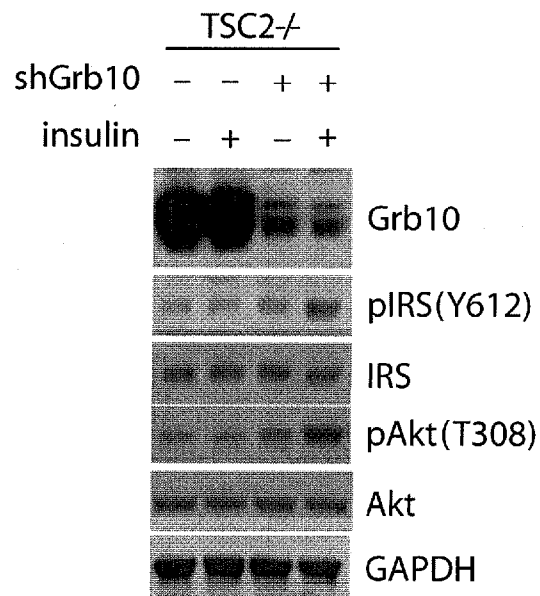


Fig. 10D

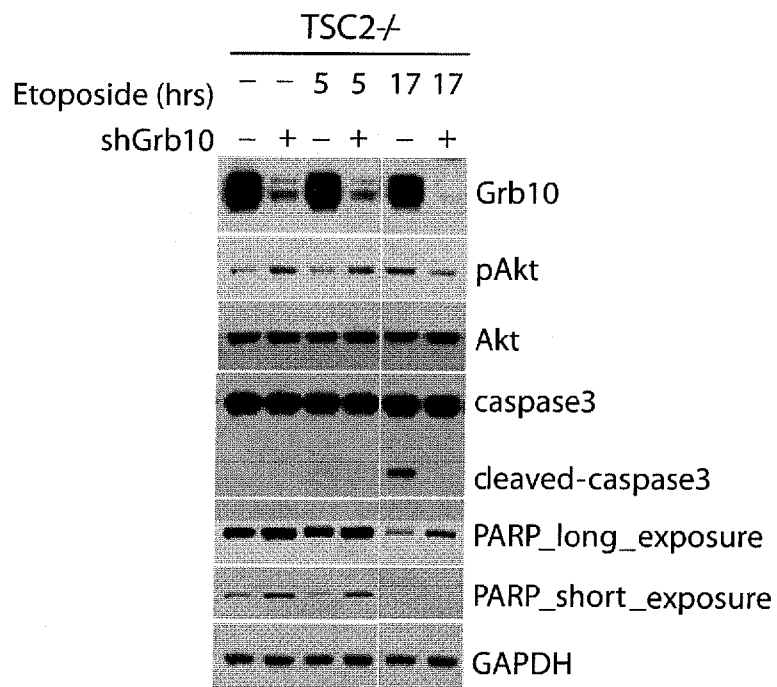


Fig. 10E