Electronic Supplementary Material (ESI) for

Chemical proteomics reveal CD147 as a functional target of pseudolaric acid B in human cancer cells

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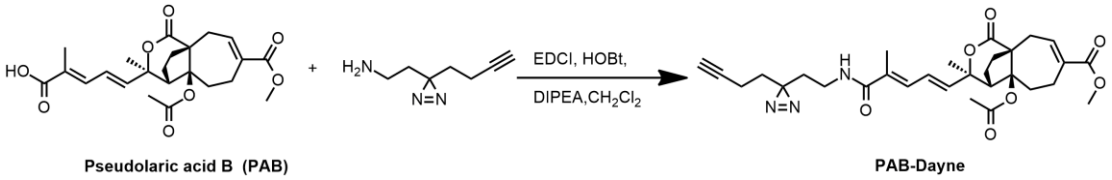
1. Chemistry

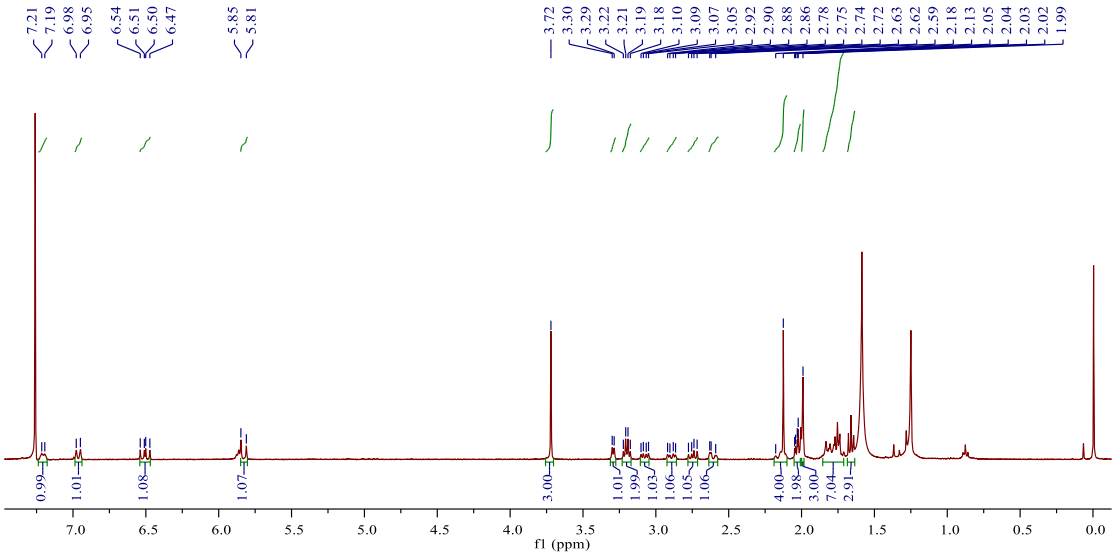
1.1 PAB-Dayne



Scheme S1 Synthesis of PAB-Dayne.

Pseudolaric acid B (7.0 mg, 0.016 mmol) was dissolved in anhydrous CH_2Cl_2 (3.0 mL), and then 1-(3-dimethyl-aminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (4.8 mg, 0.025 mmol), hydroxyl-benzotriazole (HOBt) (5.5 mg, 0.041 mmol), and *N,N*-diisopropyl-ethylamine (DIPEA) (6.7 µl, 0.038 mmol) were added into the solution. After 1 hour stirring, 2-(3-(but-3-yn-1-yl)-3H-diazirin-3-yl)ethan-1-amine (2.9 mg, 0.021 mmol)[1] was added to the reaction mixture followed by reaction at room temperature for another 3.5 h in the dark. The mixture was washed with saturated Na_2CO_3, 1N HCl and brine. The organic layer was dried by anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by HPLC to provide the desired product PAB-Dayne (7.2 mg, 80.6% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.20 (m, 1H), 6.96 (d, *J* = 11.4 Hz, 1H), 6.51 (dd, *J* = 15.0, 11.3 Hz, 1H), 5.83 (d, *J* = 15.0 Hz, 1H), 3.72 (s, 3H), 3.29 (d, *J* = 5.4 Hz, 1H), 3.20 (q, *J* = 6.4 Hz, 2H), 3.08 (dd, *J* = 14.3, 6.4 Hz, 1H), 2.89 (dd, *J* = 15.6, 6.3 Hz, 1H), 2.75 (dd, *J* = 15.1, 8.8 Hz, 1H), 2.64 - 2.58 (m, 1H), 2.19-2.10 (m, 4H), 2.04 (dd, *J* = 7.2, 2.6 Hz, 2H), 1.99 (s, 3H), 1.85-1.71 (m, 7H), 1.66 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 169.4, 168.6, 168.1, 142.5, 141.7, 134.5, 132.8, 130.6, 121.4, 90.1, 83.8, 82.7, 77.2, 69.4, 55.2, 52.1, 49.4, 34.8, 33.3, 32.4, 32.1, 30.7, 29.7, 28.6, 27.8, 24.3, 21.8, 20.2, 13.2; HRMS-ESI calcd. for $C_{30}H_{38}N_3O_7$ $[M+H]^+$: 552.2710; Found: 552.2704



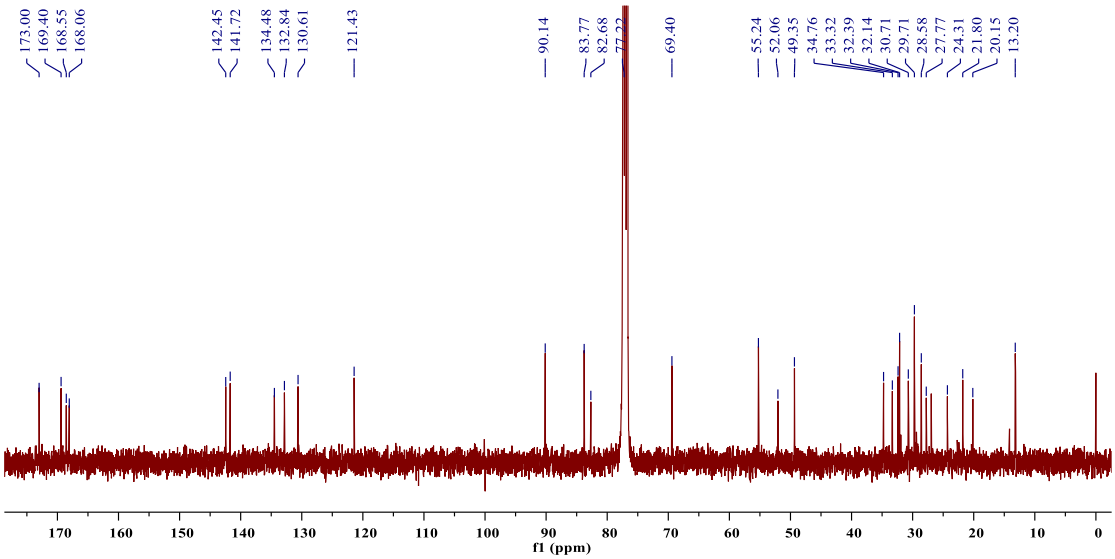
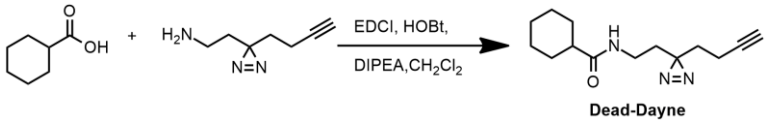


Fig. S1 ^{1}H-NMR and ^{13}C-NMR data of PAB-Dayne.

1.2 Dead-Dayne



Scheme S2 Synthesis of Dead-Dayne.

To a solution of cyclohexane carboxylic acid (13 mg, 1.2 eq) dissolved in DCM (3.0 mL) in ice bath was added 1-(3-dimethyl -aminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (20 mg, 1.2 eq), hydroxyl -benzotriazole (HOBt) (14 mg, 1.2 eq), and *N*,*N*-diisopropyl-ethylamine (DIPEA) (18 μL, 1.2 eq). After stirring for 5 min, 2-(2-azidoethyl)-2-(but-3-ynyl)-1,3-dioxolane (10 mg, 1 eq) was added to the reaction mixture. The resulting solution was warmed to room temperature slowly and stirred for overnight. The reaction mixture was diluted with EtOAc (30 mL), washed with 1 N HCl, saturated $NaHCO_3$, brine, and dried over anhydrous Na_2SO_4, filtered and concentrated. Purification by flash chromatography column afforded the product Dead-Dayne (16 mg, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.55 (s, 1H), 3.11 (q, *J* = 6.4, 5.8 Hz, 2H), 2.11-1.99 (m, 4H), 1.91-1.77 (m, 4H), 1.72-1.65 (m, 4H), 1.48-1.37 (m, 2H), 1.34-1.27 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.08, 82.69, 69.35, 45.52, 34.17, 32.52, 32.19, 29.70, 29.63, 26.91, 25.74, 13.22. HRMS-ESI calcd. for $C_{14}H_{22}N_3O$ $[M+H]^+$: 248.1685; Found: 248.1608.

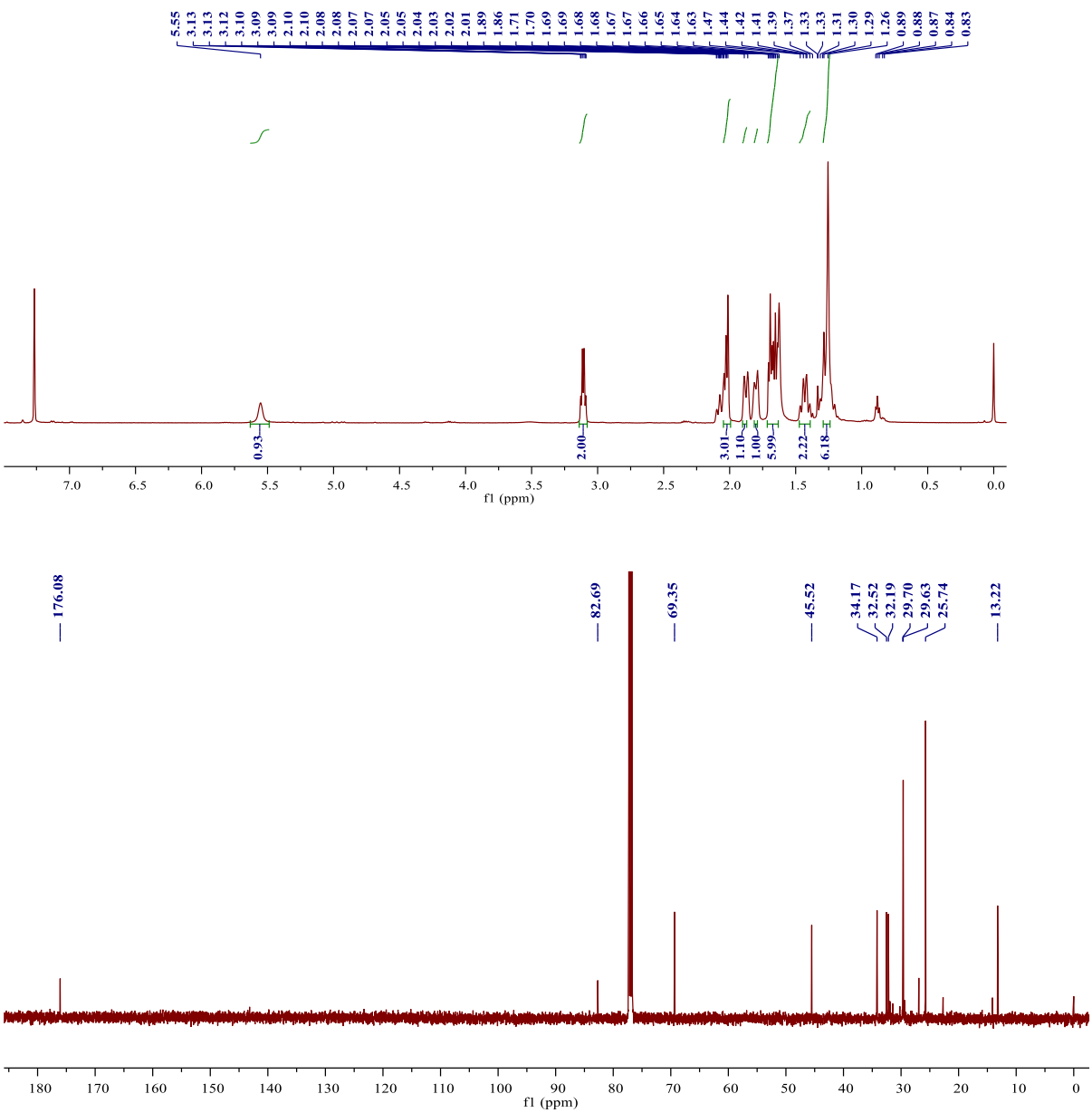


Fig. S2 ^{1}H-NMR and ^{13}C-NMR data of Dead-Dayne.

2. Biological experiments

2.1 Labeling of purified porcine brain tubulin

Purified porcine brain tubulin (Cytoskeleton, Inc.) was diluted to a final concentration of 0.1 mg/mL in PBS and incubated with probes as indicated for 30 minutes at room temperature. Samples were transferred to 96-well plate in a same line and irradiated with UV (365 nm, 8 Watt) on ice for 20 minutes. Each of 20 μL protein samples were transferred to 0.6 mL tube and added with 1% SDS and fresh prepared 0.25 μL each of TAMRA-N_3 (10 mM stock in DMSO, Lumiprobe), $CuSO_4$ (100 mM stock in H_2O, Sigma), THPTA (Tris(3-hydroxypropyltriazolylmethyl)amine, 10 mM stock in H_2O, Sigma) and sodium ascorbate (100 mM stock in H_2O). The samples were incubated at room temperature for 1 h and the reaction was quenched by boiling in 5 μL of SDS-PAGE loading buffer. 20 μL of each sample was applied to SDS-PAGE and detected by FUJIFILM FLA 9000 plus DAGE fluorescence scanner. Finally the gel was visualized by coomassie blue staining.

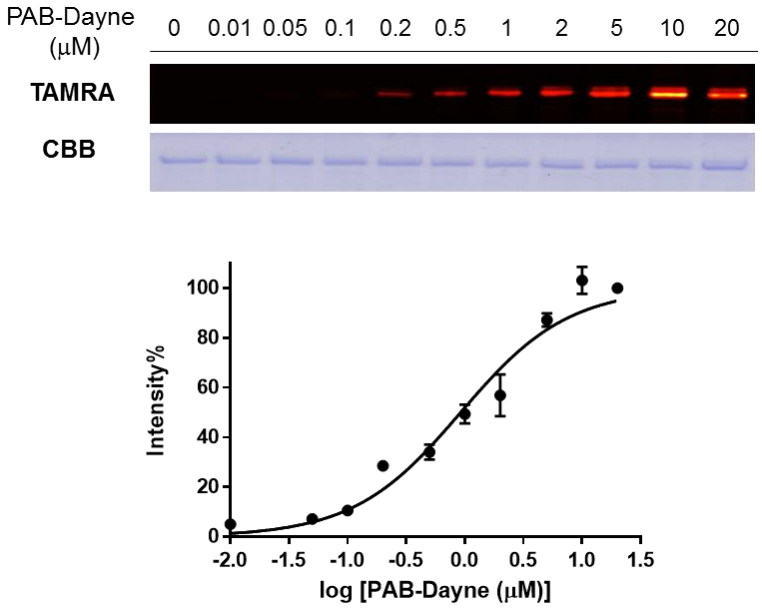


Fig. S3 Dose-dependent labeling of tubulin by PAB-Dayne.

2.2 Cell proliferation assay

Human cervical carcinoma HeLa cell line was grown in DMEM (Dulbecco's Modified Eagle Medium, Gibco) supplemented with 1% L-Glutamine, 1% Penicillin-Streptomycin and 10% Fetal Bovine Serum (FBS, Gibco). The culture incubator set is 37 ºC with 5% CO_2. HeLa cells cultured for three passages were diluted in respective culture medium to 8000 cells/mL. 100 μL of cell suspension were seeded to each well of 96-well plate and incubated at 37 ºC overnight. Various concentrations of compounds (PAB, PAB-Dayne, and Dead-Dayne) were dissolved in culture medium containing 0.5% DMSO. Cells in 96-well plate were treated with 100 μL of various concentrations of compounds and DMSO (negative control) for 48 hours in a 37 ºC incubator. Cell viability was assessed by CellTiter-Glo® Luminescent Kit (Promega).

Table S1. IC_{50} values of PAB and probes towards HeLa cells.

Compound	**IC_{50} (μM)**
PAB	0.35 ± 0.03
PAB-Dayne	1.17 ± 0.06
Dead-Dayne	> 100

2.3 Gel-based affinity-based protein profiling in HeLa cells

HeLa cells were grown in culture medium until 90% confluence. The medium was removed and cells were incubated respectively with Dead-Dayne (10 μM), PAB-Dayne (10 μM), and PAB-Dayne (10 μM) with excess PAB (50 μM) for 3 hours. The medium was aspirated, and cells were washed three times with ice-cold PBS to remove the excessive probe followed by UV irradiation (365 nm, 8 watt) for 20 min on ice. The cells were harvested by scraping the cells in ice-cold lysis buffer (50 mM HEPES pH 8.0, 150 mM NaCl, 0.1 mM EDTA, 0.1% Triton X-100 and complete protease inhibitors). The lysed cells were centrifuged at 14000 g for 5 minutes and the soluble fractions were diluted to 2 mg/mL with lysis buffer. 1% SDS (w/v) was added to each sample and click reaction was performed as below: for each reaction, 20 μL of protein samples were added to freshly prepared 0.25 μL each of TAMRA-N_3 (10 mM), $CuSO_4$ (100 mM), THPTA (10 mM) and NaVc (100 mM). The samples were incubated at room temperature for 1 hour, added with sample loading buffer, applied to SDS-PAGE and imaged by FUJIFILM FLA 9000 plus DAGE fluorescence scanner.

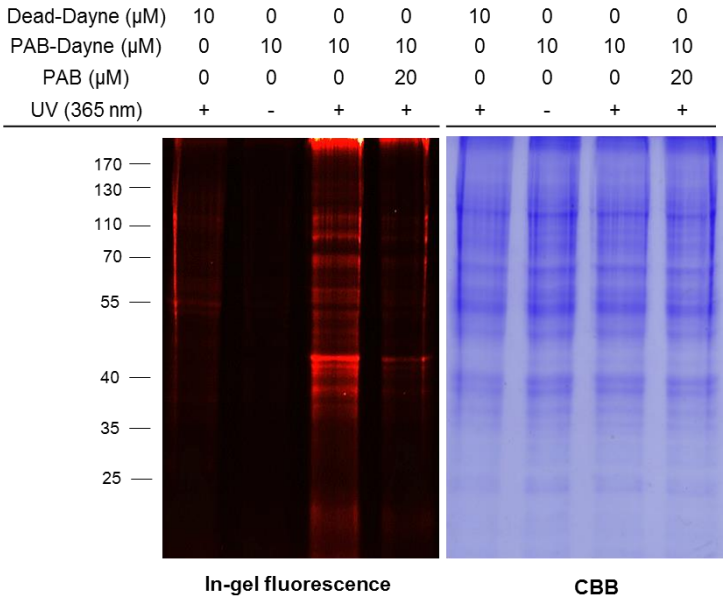


Fig. S5 Full imaging of gels in Fig. 2A.

2.4 Microscopy

HeLa cells were seeded on coverslips in a 6-well plate (Corning) and grown until 70% confluence. Cells were incubated with 10 μM of PAB-Dayne/Dead-Dayne in 2.0 mL of fresh DMEM growth medium for 3 hours. The medium was aspirated, and cells were washed with ice-cold PBS three times to remove the excessive probe, followed by UV irradiation (365 nm, 8 watt) for 20 min on ice. Next, the cells were fixed with 3.7% paraformaldehyde in PBS for 30 min at room temperature. After washing with PBS twice, the cells were permeabilized with 0.1% Triton X-100 in PBS for 10 min at room temperature. Cells were then washed twice with PBS again and blocked with 3% BSA in PBS (with 0.05% Tween-20) for 30 min at room temperature, and washed twice with PBS. The cells were then treated with a freshly prepared click chemistry reaction cocktail containing of TAMRA-N_3 (100 μM final concentration), THPTA (100 μM final concentration), NaVc (1.0 mM final concentration), and $CuSO_4$ (1.0 mM final concentration), in 1.0 mL PBS for 2 h at room temperature. The cells were then washed with PBS (0.05% Tween-20 and 0.5 mM of EDTA) for 3 times, and with PBS twice with gentle agitation. Cells were washed twice with PBS and treated with 10 μg/mL of 4',6-diamidino-2-phenylindole dihydrochloride (DAPI, Invitrogen) dissolved in PBS for 15 min at room temperature, followed by imaging with Leica TSC SP8 STED 3X fluorescence microscope.

2.5 Mass spectrometry-based ABPP in HeLa cells

The probe incubation and proteome preparation procedures were same as that of labeling studies mentioned above in section 2.3. The proteomics experiment was carried out in biological duplicates. Each of 500 μL of proteome sample was subjected to click reaction with Biotin-N_3 (500 μM, Biomatrick Inc.), $CuSO_4$ (1.0 mM), THTPA (100 μM) and NaVc (1.0 mM). The samples were precipitated with CH_3OH (600 μL) / $CHCl_3$ (150 μL) / H_2O (300 μL) sequentially and vortexed for a while. After centrifuge at 14,000 g for 3 minutes, the protein disk was washed twice with CH_3OH (500 μL), air-dried and re-dissolved in 200 μL of click buffer (50 mM HEPES pH 8.0, 1% SDS) by sonication. 50 μL of streptavidin-sepharose (GE Healthcare) beads were added to each sample and incubated at room temperature with continuous rotation for 1 hour. The beads were washed with PBS with 1% SDS (w/v) three times, PBS with 0.5 M NaCl three times, 4.0 M Urea in 100 mM triethylammonium bicarbonate (TEAB) twice, and 100 mM TEAB five times. Each wash was performed on a rotator for 15 minutes. The bounded proteins were subjected to on-beads reductive alkylation with 200 μL of 10 mM of tris(2-carboxyethyl)phosphine (TCEP) at 56 ℃ for 30 minutes and 200 μL of 55 mM iodoacetamide at 37 ℃ in dark for another 30 minutes, followed by wash with 100 mM TEAB three times. Bounded proteins on beads were digested with 0.25 μg of sequencing grade modified trypsin (Promega) reconstituted in 50 μL of 100 mM TEAB overnight at 37 ℃. The digests of both Dead-Dayne and PAB-Dayne treated-samples were labeled with TMT^2-126 and TMT^2-127 Isobaric Label Reagent (Thermo Scientific) respectively, according to the manufacturer's procedures. The labeled peptides were desalted by Pierce C18 spin columns and evaporated to dryness on a SpeedVac. Dried peptides were resuspended in 10 μL of ddH_2O containing 0.1% formic acid with sonication. A volume of 1.0 μL of each sample was desalted by loading on a Thermo C18 PepMap100 precolumn (300 μM × 5 mm) and eluted on a Thermo Acclaim PepMap RSLC analytical column (75 μM × 15 cm). Mobile phase A (0.1% formic acid in H_2O) and mobile phase B (0.1% formic acid in acetonitrile) were used to establish the 80 min gradient comprised of

55 min of 4−30% B, 7 min of 30−50% B, and 5 min of 50−90% B, followed by re-equilibrating at 4% B for 8 min. The flow rate was 0.3 μL/min. Peptides were then analyzed on Thermo Orbitrap Fusion Lumos proteomic mass spectrometer (Thermo Scientific) in a data-dependent manner, with automatic switching between MS and MS/MS scans using a cycle time 3 s. MS spectra were acquired at a resolution of 120,000 with AGC target value of 4×10^5 ions or a maximum integration time of 50 ms. The scan range was limited from 375 to 1500 m/z. Peptide fragmentation was performed via high energy collision dissociation (HCD) with the energy set at 38 NCE. The MS/MS spectra were acquired at a resolution of 50,000 with AGC target value of 1×10^5 ions or a maximum integration time of 10^5 ms. The fixed first m/z was 120, and the isolation window was 0.7 m/z.

Protein identification and quantification were performed using Proteome Discoverer 2.1 software (Thermo Scientific). Peptide sequences (and hence protein identity) were determined by matching Uniprot protein databases with the acquired fragmentation pattern by SEQUEST HT algorithm. The precursor mass tolerance was set to 10 ppm and fragment ion mass tolerance to 0.02 Da. One missed cleavage site of trypsin was allowed. Carbamidomethyl (C) and TMT-duplex (K and N-terminal) were used as a fixed modification. Oxidation (M) was used as variable modifications. All spectra were searched against protein database using a target false discovery rate (FDR) of 1%. The proteins identified in positive group (PAB-Dayne-treated samples) were additionally filtered by at least two spectral counts and one unique peptides in each experimental replicate. Protein ratios were calculated as the median of all peptide hits belonging to a protein. Statistical analysis was performed with Perseus 1.5.1.6. TMT ratios obtained from Proteome Discoverer 2.1 were transformed with $\log_{2}$-(x) and then normalized using *Z*-score and -$\log_{10}$-(*p*-value) were obtained by a two sided one sample t-test over three biological replicates. Only proteins identified have ratios higher than 4.0 and *p*-values less than 0.05 were considered statistical significant targets. The raw data and database search results were deposited to the ProteomeXchange Consortium *via* the PRIDE partner repository with the dataset identifier PXD006423.

2.6 Target validation by pull-down and western blot

Primary antibodies of human CD147 was ordered from Abcam. Primary antibodies of human CD98 was purchased from Sangon Biotech. Bound proteins on streptavidin beads from pull-down experiments as described in 2.5 were eluted by boiling in SDS-PAGE sample loading buffer for 15 minutes and separated by SDS-PAGE. Then the proteins were transferred onto nitrocellulose membrane (Millipore) and the membrane was blocked with 3% (w/v) BSA in tris-buffered saline (TBS) for 2 hours at room temperature. After blocking, membranes were incubated with respective primary antibodies (*anti*-CD147 or *anti*-CD98) at room temperature for one hour. After washing with TBST (TBS containing 0.1% Tween-20) three times, blots were further incubated with the HRP-conjugated anti-rabbit (Sangon Biotech) secondary antibody for 1 hour at room temperature. After incubation, the blot was washed again with TBST three times and developed by enhanced ECL chemiluminescent substrate kit (Pierce).

2.7 Labeling of recombinant CD147/CD98 proteins

Recombinant GST-tagged CD147 (ProteinTech) and His-tagged CD98 (Sinobiological, Inc.)

proteins, either along or mixed together, were diluted to a final concentration of 0.1 mg/mL in PBS and incubated with probes as indicated for 30 minutes at room temperature. Samples were transferred to 96-well plate in a same line and irradiated with UV (365 nm, 8 Watt) on ice for 20 minutes. The subsequent click reaction and in-gel fluorescence scan were performed same as above.

2.8 Disruption of CD147 oligomerization by PAB

Each of 100 ng of recombinant GST-tagged CD147 proteins (ProteinTech) reconstituted in PBS was incubated with DMSO or increasing concentrations of PAB (0.1 μM, 1 μM, 5 μM, and 10 μM) at room temperature for 1 hour. Then all samples were mixed with 4× Laemmli sample buffer lacking SDS and followed by resolution by 4-12% gradient SDS-PAGE without boiling. Western blot with anti-CD147 antibody was performed to examine the oligomerization of CD147 proteins.

2.9 Binding site identification

5 μg of recombinant GST-tagged CD147 protein (ProteinTech) in PBS (20 μL) were incubated with 10 μM of PAB-Dayne at room temperature for 1 hour, followed by UV irradiation (365 nm, 8 watt) for 20 min on ice. Buffer exchange (to 50 mM of NH_4HCO_3), chemical modification (reduction with 20 mM DTT and alkylation with 50 mM iodoacetamide) were performed according to filter-aided sample preparation (FASP) protocol in the upper chamber of 10-kDa ultrafiltration device. Then, 0.25 μg of trypsin (Thermo Scientific) was add to the sample and incubated at 37 °C overnight. The digests were desalted by Ziptip desalting column (Pierce) and evaporated to dryness on a SpeedVac. The dried peptides were resuspended in 8 μL ddH_2O containing 0.1% formic acid with sonication and analyzed by Thermo Orbitrap Fusion Lumos proteomic mass spectrometer as mentioned above. Data processing was performed using Proteome Discoverer 2.1 software (Thermo Scientific) and peptide sequences were determined by matching protein database with the acquired fragmentation pattern by SEQUEST HT algorithm. The precursor mass tolerance was set to 10 ppm and fragment ion mass tolerance to 0.02 Da. One missed cleavage site of trypsin was allowed. PAB-Dayne (any amino acids), Carbamidomethyl (C), Oxidation (M), were used as variable modifications. All spectra were searched against protein sequence of human CD147 isoform 2 (UniprotKB ID: P35613-2) using a target false discovery rate (FDR) of 1%. Manual verification was performed to ensure confident peptide identification. The raw data and database search results were deposited to the ProteomeXchange Consortium *via* the PRIDE partner repository with the dataset identifier PXD006423.

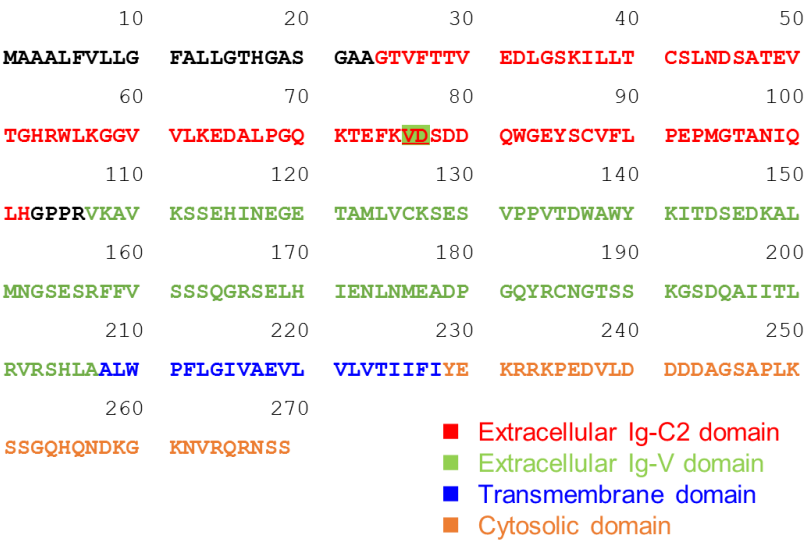


Fig. S5 Amino acid sequence of human CD147 isoform-2 (UniprotKB ID: P35613-2). V76 and D77 are possible probe-labeled residues.

2.10 Western blot analysis of expression level of MMPs upon PAB treatment

Primary antibodies of human MMP-2 was ordered from Abcam. Primary antibodies of human MMP-7, MMP-9 and GAPDH were purchased from Sangon Biotech. Hela cells were incubated with DMSO or PAB (1 μM and 5 μM) for 24 h. The cells were washed with PBS, harvested and lysed with SDT lysis buffer (100 mM Tris-HCl pH 7.6, 4% SDS, 0.1 M DTT) at 95 ºC for 3 min. The lysates were centrifuged at 14000 g for 5 minutes and the soluble fractions were diluted to 2 mg/mL with lysis buffer. Equal amount of protein samples were separated by SDS-PAGE, transferred onto nitrocellulose membrane (Millipore), and blotted with primary antibodies of *anti*-MMP-2, *anti*-MMP-7, *anti*-MMP-9 and *anti*-GAPDH as described in 2.6.

2.11 siRNA transfection

HeLa cells were transfected in OPTI-MEM with lipofectamin2000 (Invitrogen) with 100 nM of siRNA of CD147 (5'-GGU UCU UCG UGA GUU CCU CTT-3') or negative control RNA (5'-UUC UCC GAA CGU GUC ACG UTT-3') for 24 hours according to the manufacturer's protocols. The medium was removed and replaced for DMEM containing 10% FBS. Cells were then treated with various concentrations of compounds and DMSO for 24 hours in a 37 ºC incubator. Cell viability was assessed by CellTiter-Glo® Luminescent Kit (Promega).

2.12 Molecular modeling

Probable binding conformations were carried out using Molecular Operating Environment (MOE 2015.10) software. The CD147 structure was obtained from the Protein Data Bank (PDB ID: 3I85).[2] Molecular docking of pseudolaric acid B into the three dimensional X-ray structure of human CD147 protein were carried out using Molecular Operating Environment (MOE) version 2015.10 (Chemical Computing Group Inc., Montreal, QC, Canada). PAB was built using the

builder interface of the MOE program, docked into the Ig-C2 domain of CD147 and subjected to energy minimization using the included Force-field MMFF94x calculations. The macromolecule molecular surface (Figure 3B), ligand interactions and secondary structure (Supporting Information Figure S5) were displayed by MOE.

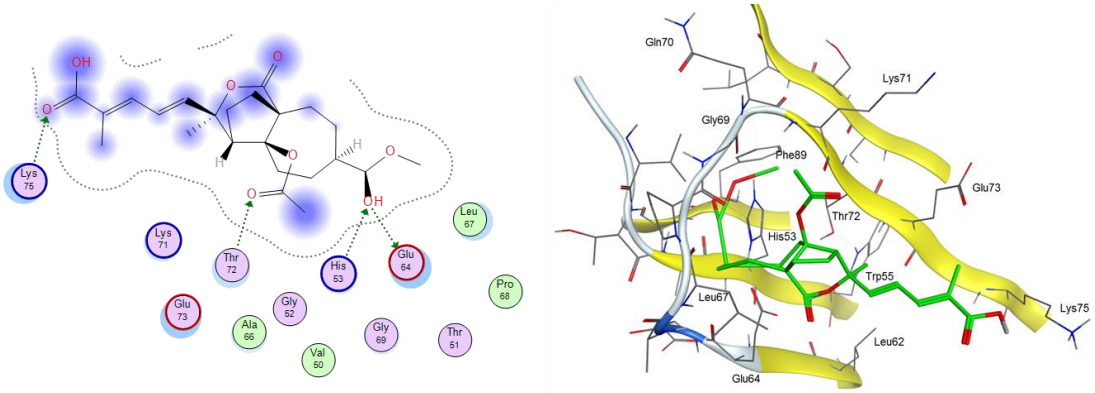


Fig. S6 Ligand interactions (left) and secondary structure (right) of PAB docked into N-terminal IgC2 domain of CD147 protein.

2.13 Global proteomic profiling of PAB-treated HeLa cells

Hela cells were incubated with DMSO or 1 μM of PAB for 24 h. The proteomics experiment was carried out in biological duplicates. Then the cells were washed with PBS, harvested and lysed with SDT lysis buffer (100 mM Tris-HCl pH 7.6, 4% SDS, 0.1 M DTT) at 95 ºC for 3 min. The cell lysates were centrifuged at 14,000 g for 15 min and the supernatants were collected. Each of 300 μg of protein was alkylated with 55 mM of iodoacetamide and subjected to in-solution tryptic digestion utilizing the FASP (filter aided sample preparation) protocol.[3] The digests were labeled with respective isobaric label reagents (ITRAQ^8-119 for DMSO and ITRAQ^8-121 for PAB). The labeled peptides were combined and fractionated by high-pH reversed-phase chromatography on a 1-mm Xbridge column (Waters), and 10 fractions were collected. Each fraction was evaporated to dryness on a SpeedVac and dried peptides were resuspended in 15 μL of ddH_2O containing 0.1% formic acid with sonication for subsequent MS analysis. A volume of 1 μL of each sample was desalted by loading on a Thermo C18 PepMap100 precolumn (300 μm × 5 mm) and eluted on a Thermo Acclaim PepMap RSLC analytical column (75 μm × 15 cm). Mobile phase A (0.1% formic acid in H_2O) and mobile phase B (0.1% formic acid in acetonitrile) were used to establish the 120 min gradient comprised of 85 min of 4−30% B, 15 min of 30−50% B, and 5 min of 90% B, followed by re-equilibrating at 4% B for 15 min. The flow rate was 0.3 μL/min. Peptides were then analyzed on Thermo Orbitrap Fusion Lumos proteomic mass spectrometer (Thermo Scientific) in a data-dependent manner, with automatic switching between MS and MS/MS scans using a cycle time 3 s. MS spectra were acquired at a resolution of 120,000 with AGC target value of 4×10^5 ions or a maximum integration time of 50 ms. The scan range was limited from 375 to 1500 m/z. Peptide fragmentation was performed via high energy collision dissociation (HCD) with the energy set at 38 NCE. The MS/MS spectra were acquired at a resolution of 50,000 with AGC target value of 1×10^5 ions or a maximum integration time of 105 ms. The fixed first m/z was 120, and the isolation window was 0.7 m/z.

Protein identification and quantification were performed using Proteome Discoverer 2.1 software

(Thermo Scientific). Peptide sequences (and hence protein identity) were determined by matching Uniprot protein databases with the acquired fragmentation pattern by SEQUEST HT algorithm. The precursor mass tolerance was set to 10 ppm and fragment ion mass tolerance to 0.02 Da. One missed cleavage site of trypsin was allowed. Carbamidomethyl (C) and ITRAQ-8plex (K, Y and N-terminal) were used as a fixed modification. Oxidation (M) was used as variable modifications. All spectra were searched against protein database using a target false discovery rate (FDR) of 1%. The proteins identified in both channels were additionally filtered by at least two spectral counts and one unique peptides in each experimental replicate. Protein ratios were calculated as the median of peptide with S/N ratio higher than 10 of a protein. Statistical analysis was performed with Perseus 1.5.1.6. Isobaric ratios obtained from Proteome Discoverer 2.1 were transformed with $\log_2$-(x) and then normalized using *Z*-score and -$\log_{10}$-(*p*-value) were obtained by a two sided one sample t-test over biological duplicates. Only proteins identified have normalized ratios higher than 3.0 and *p*-values less than 0.05 were considered statistical significant hits.

Fig. S7 Gene Ontology (GO) biological processes analysis of over- and under-expressed proteins of HeLa cells upon PAB treatment

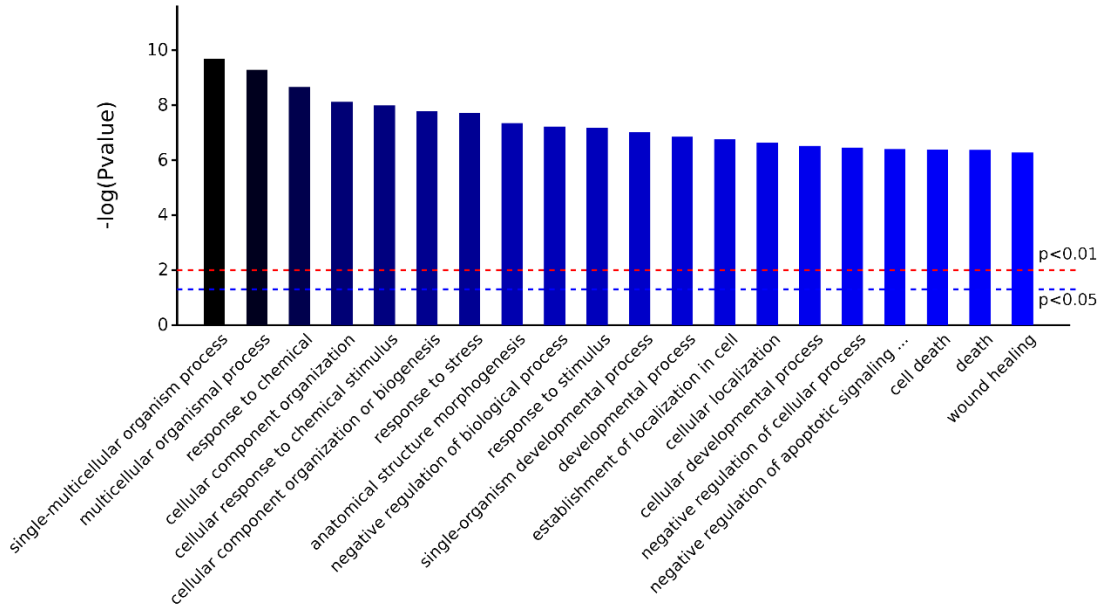


Table S2 Significantly up- (red) and down-regulated (blue) proteins by PAB treatment.

ID	*Protein*	*Ratio*	*p-value*	*Go Molecular Function*	*GO Biological Process*
O00622	**CYR61**	**11.86**	0.046	receptor-binding, growth factor	cell adhesion, cell death, cell-cell signaling, regulation of biological process, response to stimulus, signal transduction
P05121	**SERPINE1**	**6.11**	0.008	serine-type endopeptidase inhibitor activity, serine-type peptidase activity	regulation of biological process
P08195	**OSMR**	**6.11**	0.001	cytokine activity, defense/immunity protein	B cell mediated immunity, hemopoiesis, nervous system development
P31431	**SDC4**	**4.89**	0.025	cell adhesion molecule, cytoskeletal protein, defense/immunity protein, extracellular matrix glycoprotein, membrane-bound signaling molecule	cellular component movement, localization, locomotion
Q9BZH6	**WDR11**	**3.93**	0.034	N/A	N/A
Q9Y696	**CLIC4**	**3.76**	0.003	anion channel activity, transferase activity, cytoskeletal protein, epimerase/racemase, reductase, signaling molecule, transferase, translation elongation factor	anion transport, cellular amino acid metabolic process, cellular process, nitrogen compound metabolic process, sulfur compound metabolic process
P04179	**SOD2**	**3.83**	0.036	oxidoreductase	N/A
P53814	**SMTN**	**3.24**	0.022	actin binding, structural constituent of muscle	muscle organ development, smooth muscle contraction
P09884	**POLA1**	**2.86**	0.029	3'-5' exonuclease activity, 4 Fe-4 S cluster binding, chromatin binding, DNA binding, DNA-directed DNA polymerase activity, metal ion binding, nucleoside binding, nucleotide binding, protein kinase binding	cell proliferation, DNA replication, G1/S transition of mitotic cell cycle, lagging strand elongation, leading strand elongation, regulation of transcription involved in G1/S transition of mitotic cell cycle, telomere maintenance via recombination, viral process
Q9BY77	**POLDIP3**	**2.81**	0.031	RNA binding	mRNA 3'-end processing, mRNA export from nucleus, positive regulation of translation, RNA export from nucleus, termination of RNA polymerase II transcription

ID	*Protein*	*Ratio*	*p-value*	*Go Molecular Function*	*GO Biological Process*
P17676	**CEBPB**	**-2.21**	0.047	chromatin binding, DNA binding, protein binding, protein hetero-dimerization activity, transcriptional activator activity	cellular response to chemicals, immune response, inflammatory response, regulation of transcription, response to endoplasmic reticulum stress
Q9BRA2	**TXNDC17**	**-2.36**	0.020	peroxidase activity, protein-disulfide reductase activity	tumor necrosis factor-mediated signaling pathway
P68366	**TUBA4A**	**-2.92**	0.013	enzyme binding, GTPase activity, GTP binding, structural constituent of cytoskeleton	ciliary basal body docking, G2/M transition of mitotic cell cycle, microtubule-based process, platelet degranulation
Q9NQC3	**RTN4**	**-3.12**	0.014	membrane traffic protein	cell differentiation, cell recognition, cellular component morphogenesis, nervous system development
P47914	**RPL29**	**-3.08**	0.004	structural constituent of ribosome	biosynthetic process, cellular process, translation
P07437	**TUBB**	**-3.28**	0.023	GTPase activating protein binding, GTPase activity, GTP binding, MHC class I protein binding, protein complex binding, protein domain specific binding, structural constituent of cytoskeleton, structural molecule activity, ubiquitin protein ligase binding	cell division, cellular process, G2/M transition of mitotic cell cycle, microtubule-based process, movement of cell or subcellular component, natural killer cell mediated cytotoxicity, neutrophil degranulation, spindle assembly
Q9BQE3	**TUBA1C**	**-3.01**	0.038	GTP binding，structural constituent of cytoskeleton, structural molecule activity	cell division, cytoskeleton-dependent intracellular transport, microtubule-based process
O95197	**RTN3**	**-3.15**	0.017	membrane traffic protein	endoplasmic reticulum tubular network formation, apoptotic process, vesicle-mediated transport
P55039	**DRG2**	**-3.36**	0.011	GTP binding	signal transduction
Q9BV73	**CEP250**	**-4.71**	0.035	kinase modulator, protein binding	G2/M transition of mitotic cell cycle, protein localization

3. Quantitative data of proteomic studies

Table S3 Proteins identified from the pull-down/LC-MS experiments.

Accession	Description	Log_2(PAB-Dayne/Dead-Dayne)				$-Log_{10}$(p-value)	Significance
		1#	2#	3#	Avg.		
P35613	Basigin OS=Homo sapiens GN=BSG PE=1 SV=2	2.28	3.35	2.67	2.77	1.90	+
P21796	Voltage-dependent anion-selective channel protein 1 OS=Homo sapiens GN=VDAC1 PE=1 SV=2	2.88	2.77	2.55	2.73	2.92	+
P08195	4F2 cell-surface antigen heavy chain OS=Homo sapiens GN=SLC3A2 PE=1 SV=3	3.19	1.92	2.73	2.61	1.70	+
P45880	Voltage-dependent anion-selective channel protein 2 OS=Homo sapiens GN=VDAC2 PE=1 SV=2	2.48	2.49	2.76	2.58	2.91	+
P07437	Tubulin beta chain OS=Homo sapiens GN=TUBB PE=1 SV=2	1.83	1.45	1.86	1.71	2.23	+
P55060	Exportin-2 OS=Homo sapiens GN=CSE1L PE=1 SV=3	1.54	1.48	1.83	1.62	2.35	+
Q92973	Transportin-1 OS=Homo sapiens GN=TNPO1 PE=1 SV=2	1.56	1.65	1.48	1.57	3.00	+
P08238	Heat shock protein HSP 90-beta OS=Homo sapiens GN=HSP90AB1 PE=1 SV=4	1.24	1.29	1.85	1.46	1.77	+
P68371	Tubulin beta-4B chain OS=Homo sapiens GN=TUBB4B PE=1 SV=1	1.29	1.34	1.72	1.45	2.07	+
O95373	Importin-7 OS=Homo sapiens GN=IPO7 PE=1 SV=1	1.02	1.54	1.64	1.40	1.74	+
O14980	Exportin-1 OS=Homo sapiens GN=XPO1 PE=1 SV=1	1.30	1.36	1.48	1.38	2.85	+
P78527	DNA-dependent protein kinase catalytic subunit OS=Homo sapiens GN=PRKDC PE=1 SV=3	1.13	1.49	1.51	1.38	2.11	+
O60313	Dynamin-like 120 kDa protein, mitochondrial OS=Homo sapiens GN=OPA1 PE=1 SV=3	1.56	1.53	0.97	1.35	1.72	+
Q7L1Q6	Basic leucine zipper and W2 domain-containing protein 1 OS=Homo sapiens GN=BZW1 PE=1 SV=1	0.76	2.58	0.66	1.34	0.78	
Q71U36	Tubulin alpha-1A chain OS=Homo sapiens GN=TUBA1A PE=1 SV=1	-0.27	1.98	2.29	1.33	0.62	
P05141	ADP/ATP translocase 2 OS=Homo sapiens GN=SLC25A5 PE=1 SV=7	1.37	1.61	0.91	1.30	1.62	+
Q9Y6E2	Basic leucine zipper and W2 domain-containing protein 2 OS=Homo sapiens GN=BZW2 PE=1 SV=1	1.06	1.54	1.16	1.25	1.86	+
Q8NFJ5	Retinoic acid-induced protein 3 OS=Homo sapiens GN=GPRC5A PE=1 SV=2	0.96	0.21	2.58	1.25	0.67	
P68104	Elongation factor 1-alpha 1 OS=Homo sapiens GN=EEF1A1 PE=1 SV=1	1.19	1.21	1.24	1.21	3.80	+
P42704	Leucine-rich PPR motif-containing protein, mitochondrial OS=Homo sapiens GN=LRPPRC PE=1 SV=3	1.02	1.40	1.20	1.20	2.09	+
P27635	60S ribosomal protein L10 OS=Homo sapiens GN=RPL10 PE=1 SV=4	0.69	1.70	1.15	1.18	1.25	
P05023	Sodium/potassium-transporting ATPase subunit alpha-1 OS=Homo sapiens GN=ATP1A1 PE=1 SV=1	1.11	1.29	1.02	1.14	2.30	+
P27348	14-3-3 protein theta OS=Homo sapiens GN=YWHAQ PE=1 SV=1	1.35	1.36	0.56	1.09	1.27	

P68366	Tubulin alpha-4A chain OS=Homo sapiens GN=TUBA4A PE=1 SV=1	1.08	2.01	0.17	1.09	0.75	
P53618	Coatomer subunit beta OS=Homo sapiens GN=COPB1 PE=1 SV=3	0.90	1.21	1.05	1.06	2.16	+
O00410	Importin-5 OS=Homo sapiens GN=IPO5 PE=1 SV=4	1.12	1.02	0.91	1.02	2.47	+
P31943	Heterogeneous nuclear ribonucleoprotein H OS=Homo sapiens GN=HNRNPH1 PE=1 SV=4	1.49	0.96	0.51	0.99	1.13	
P60709	Actin, cytoplasmic 1 OS=Homo sapiens GN=ACTB PE=1 SV=1	0.71	1.30	0.94	0.98	1.54	+
O75533	Splicing factor 3B subunit 1 OS=Homo sapiens GN=SF3B1 PE=1 SV=3	0.86	0.81	0.93	0.86	2.78	+
Q9HAV4	Exportin-5 OS=Homo sapiens GN=XPO5 PE=1 SV=1	0.86	1.01	0.53	0.80	1.52	+
P41252	Isoleucine--tRNA ligase, cytoplasmic OS=Homo sapiens GN=IARS PE=1 SV=2	0.96	0.62	0.78	0.79	1.82	+
Q9BQE3	Tubulin alpha-1C chain OS=Homo sapiens GN=TUBA1C PE=1 SV=1	2.37	0.43	-0.48	0.77	0.34	
P12956	X-ray repair cross-complementing protein 6 OS=Homo sapiens GN=XRCC6 PE=1 SV=2	0.95	0.24	1.07	0.75	0.99	
P53621	Coatomer subunit alpha OS=Homo sapiens GN=COPA PE=1 SV=2	1.03	0.33	0.87	0.74	1.13	
P62979	Ubiquitin-40S ribosomal protein S27a OS=Homo sapiens GN=RPS27A PE=1 SV=2	0.80	0.56	0.76	0.71	1.96	+
P16615	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2 OS=Homo sapiens GN=ATP2A2 PE=1 SV=1	0.63	0.89	0.60	0.71	1.79	+
P07814	Bifunctional glutamate/proline--tRNA ligase OS=Homo sapiens GN=EPRS PE=1 SV=5	0.56	1.08	0.47	0.70	1.18	
Q9Y3U8	60S ribosomal protein L36 OS=Homo sapiens GN=RPL36 PE=1 SV=3	1.30	-0.31	1.09	0.69	0.52	
P00966	Argininosuccinate synthase OS=Homo sapiens GN=ASS1 PE=1 SV=2	0.86	0.72	0.48	0.69	1.60	+
P25705	ATP synthase subunit alpha, mitochondrial OS=Homo sapiens GN=ATP5A1 PE=1 SV=1	0.14	1.02	0.88	0.68	0.89	
P17987	T-complex protein 1 subunit alpha OS=Homo sapiens GN=TCP1 PE=1 SV=1	0.46	0.70	0.85	0.67	1.55	+
Q14204	Cytoplasmic dynein 1 heavy chain 1 OS=Homo sapiens GN=DYNC1H1 PE=1 SV=5	0.77	0.58	0.54	0.63	1.91	+
P10809	60 kDa heat shock protein, mitochondrial OS=Homo sapiens GN=HSPD1 PE=1 SV=2	0.56	0.64	0.66	0.62	2.64	+
Q01650	Large neutral amino acids transporter small subunit 1 OS=Homo sapiens GN=SLC7A5 PE=1 SV=2	0.96	0.58	0.32	0.62	1.09	
Q93008	Probable ubiquitin carboxyl-terminal hydrolase FAF-X OS=Homo sapiens GN=USP9X PE=1 SV=3	0.70	0.25	0.86	0.60	1.09	
Q14974	Importin subunit beta-1 OS=Homo sapiens GN=KPNB1 PE=1 SV=2	0.46	0.64	0.68	0.59	1.91	+
Q8N1F7	Nuclear pore complex protein Nup93 OS=Homo sapiens GN=NUP93 PE=1 SV=2	0.53	1.01	0.22	0.59	0.90	
P57678	Gem-associated protein 4 OS=Homo sapiens GN=GEMIN4 PE=1 SV=2	0.48	0.95	0.32	0.58	1.04	
Q86VP6	Cullin-associated NEDD8-dissociated protein 1 OS=Homo sapiens GN=CAND1 PE=1 SV=2	0.32	1.04	0.38	0.58	0.89	
Q92616	eIF-2-alpha kinase activator GCN1 OS=Homo sapiens GN=GCN1 PE=1 SV=6	0.68	0.60	0.39	0.56	1.63	+
P52292	Importin subunit alpha-1 OS=Homo sapiens GN=KPNA2 PE=1 SV=1	0.67	1.08	-0.08	0.56	0.62	

Q5T4S7	E3 ubiquitin-protein ligase UBR4 OS=Homo sapiens GN=UBR4 PE=1 SV=1	0.43	0.77	0.39	0.53	1.32	+
P54136	Arginine--tRNA ligase, cytoplasmic OS=Homo sapiens GN=RARS PE=1 SV=2	0.56	0.61	0.33	0.50	1.54	+
P13639	Elongation factor 2 OS=Homo sapiens GN=EEF2 PE=1 SV=4	0.36	0.31	0.81	0.50	1.05	
P00338	L-lactate dehydrogenase A chain OS=Homo sapiens GN=LDHA PE=1 SV=2	0.18	0.71	0.56	0.48	1.03	
P62829	60S ribosomal protein L23 OS=Homo sapiens GN=RPL23 PE=1 SV=1	1.20	0.00	0.14	0.45	0.44	
P04406	Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3	0.39	0.54	0.32	0.41	1.61	+
Q04637	Eukaryotic translation initiation factor 4 gamma 1 OS=Homo sapiens GN=EIF4G1 PE=1 SV=4	0.98	0.25	0.01	0.41	0.53	
P62258	14-3-3 protein epsilon OS=Homo sapiens GN=YWHAE PE=1 SV=1	0.49	0.00	0.70	0.40	0.71	
Q01813	ATP-dependent 6-phosphofructokinase, platelet type OS=Homo sapiens GN=PFKP PE=1 SV=2	0.56	0.28	0.31	0.38	1.29	
Q06830	Peroxiredoxin-1 OS=Homo sapiens GN=PRDX1 PE=1 SV=1	0.42	0.31	0.41	0.38	2.10	+
P48643	T-complex protein 1 subunit epsilon OS=Homo sapiens GN=CCT5 PE=1 SV=1	0.13	0.73	0.20	0.35	0.69	
P17655	Calpain-2 catalytic subunit OS=Homo sapiens GN=CAPN2 PE=1 SV=6	-0.16	0.27	0.88	0.33	0.41	
Q96P70	Importin-9 OS=Homo sapiens GN=IPO9 PE=1 SV=3	0.01	0.30	0.57	0.29	0.67	
P14625	Endoplasmin OS=Homo sapiens GN=HSP90B1 PE=1 SV=1	0.41	-0.02	0.49	0.29	0.69	
Q07065	Cytoskeleton-associated protein 4 OS=Homo sapiens GN=CKAP4 PE=1 SV=2	0.39	-0.01	0.49	0.29	0.71	
Q99832	T-complex protein 1 subunit eta OS=Homo sapiens GN=CCT7 PE=1 SV=2	0.53	0.33	-0.04	0.27	0.61	
P52701	DNA mismatch repair protein Msh6 OS=Homo sapiens GN=MSH6 PE=1 SV=2	0.45	0.15	0.15	0.25	0.88	
P11142	Heat shock cognate 71 kDa protein OS=Homo sapiens GN=HSPA8 PE=1 SV=1	0.06	0.30	0.29	0.22	0.97	
Q16576	Histone-binding protein RBBP7 OS=Homo sapiens GN=RBBP7 PE=1 SV=1	0.22	-0.07	0.45	0.20	0.50	
P62937	Peptidyl-prolyl cis-trans isomerase A OS=Homo sapiens GN=PPIA PE=1 SV=2	0.13	0.29	0.05	0.15	0.79	
P50991	T-complex protein 1 subunit delta OS=Homo sapiens GN=CCT4 PE=1 SV=4	-0.16	0.67	-0.08	0.14	0.19	
Q9Y6G9	Cytoplasmic dynein 1 light intermediate chain 1 OS=Homo sapiens GN=DYNC1LI1 PE=1 SV=3	-0.05	0.13	0.26	0.11	0.47	
O43175	D-3-phosphoglycerate dehydrogenase OS=Homo sapiens GN=PHGDH PE=1 SV=4	0.26	0.23	-0.25	0.08	0.18	
P50416	Carnitine O-palmitoyltransferase 1, liver isoform OS=Homo sapiens GN=CPT1A PE=1 SV=2	-0.30	0.24	0.28	0.08	0.14	
Q9Y678	Coatomer subunit gamma-1 OS=Homo sapiens GN=COPG1 PE=1 SV=1	0.14	0.42	-0.35	0.07	0.11	
Q5VYK3	Proteasome-associated protein ECM29 homolog OS=Homo sapiens GN=ECM29 PE=1 SV=2	0.27	0.01	-0.08	0.07	0.23	
P06576	ATP synthase subunit beta, mitochondrial OS=Homo sapiens GN=ATP5B PE=1 SV=3	0.23	0.13	-0.17	0.06	0.19	
P26639	Threonine--tRNA ligase, cytoplasmic OS=Homo sapiens GN=TARS PE=1 SV=3	-0.35	0.74	-0.24	0.05	0.04	

P17858	ATP-dependent 6-phosphofructokinase, liver type OS=Homo sapiens GN=PFKL PE=1 SV=6	0.05	-0.25	0.33	0.04	0.09	
P08237	ATP-dependent 6-phosphofructokinase, muscle type OS=Homo sapiens GN=PFKM PE=1 SV=2	0.21	0.10	-0.22	0.03	0.08	
P50990	T-complex protein 1 subunit theta OS=Homo sapiens GN=CCT8 PE=1 SV=4	0.29	-0.02	-0.18	0.03	0.07	
Q00610	Clathrin heavy chain 1 OS=Homo sapiens GN=CLTC PE=1 SV=5	-0.11	0.00	0.19	0.03	0.11	
Q92538	Golgi-specific brefeldin A-resistance guanine nucleotide exchange factor 1 OS=Homo sapiens GN=GBF1 PE=1 SV=2	-0.03	0.19	-0.12	0.01	0.05	
Q9BUF5	Tubulin beta-6 chain OS=Homo sapiens GN=TUBB6 PE=1 SV=1	-0.32	-0.18	0.52	0.01	0.01	
P07900	Heat shock protein HSP 90-alpha OS=Homo sapiens GN=HSP90AA1 PE=1 SV=5	0.21	-0.24	0.05	0.01	0.02	
P36578	60S ribosomal protein L4 OS=Homo sapiens GN=RPL4 PE=1 SV=5	-0.19	0.08	0.10	0.00	0.01	
Q8TEX9	Importin-4 OS=Homo sapiens GN=IPO4 PE=1 SV=2	0.08	0.06	-0.22	-0.02	0.08	
P07737	Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	0.14	0.34	-0.56	-0.03	0.03	
P08758	Annexin A5 OS=Homo sapiens GN=ANXA5 PE=1 SV=2	-0.43	-0.08	0.42	-0.03	0.04	
P04792	Heat shock protein beta-1 OS=Homo sapiens GN=HSPB1 PE=1 SV=2	0.17	-0.35	0.06	-0.04	0.09	
P0CW18	Serine protease 56 OS=Homo sapiens GN=PRSS56 PE=1 SV=1	-0.23	0.29	-0.21	-0.05	0.10	
P18124	60S ribosomal protein L7 OS=Homo sapiens GN=RPL7 PE=1 SV=1	-0.13	0.28	-0.38	-0.07	0.14	
P62826	GTP-binding nuclear protein Ran OS=Homo sapiens GN=RAN PE=1 SV=3	0.15	-0.31	-0.10	-0.09	0.24	
Q9UBB4	Ataxin-10 OS=Homo sapiens GN=ATXN10 PE=1 SV=1	-0.01	-0.37	0.08	-0.10	0.26	
P56192	Methionine--tRNA ligase, cytoplasmic OS=Homo sapiens GN=MARS PE=1 SV=2	0.20	-0.23	-0.29	-0.11	0.25	
P39023	60S ribosomal protein L3 OS=Homo sapiens GN=RPL3 PE=1 SV=2	-0.01	-0.18	-0.15	-0.11	0.78	
P62753	40S ribosomal protein S6 OS=Homo sapiens GN=RPS6 PE=1 SV=1	-0.24	-0.26	0.10	-0.13	0.42	
P38606	V-type proton ATPase catalytic subunit A OS=Homo sapiens GN=ATP6V1A PE=1 SV=2	-0.56	0.10	0.02	-0.15	0.26	
P40429	60S ribosomal protein L13a OS=Homo sapiens GN=RPL13A PE=1 SV=2	-0.52	0.05	0.00	-0.16	0.32	
P49368	T-complex protein 1 subunit gamma OS=Homo sapiens GN=CCT3 PE=1 SV=4	-0.29	-0.19	-0.01	-0.16	0.74	
P46940	Ras GTPase-activating-like protein IQGAP1 OS=Homo sapiens GN=IQGAP1 PE=1 SV=1	-0.18	-0.07	-0.30	-0.19	0.97	
O60610	Protein diaphanous homolog 1 OS=Homo sapiens GN=DIAPH1 PE=1 SV=2	-0.23	-0.21	-0.13	-0.19	1.65	+
Q02543	60S ribosomal protein L18a OS=Homo sapiens GN=RPL18A PE=1 SV=2	-0.30	-0.36	0.06	-0.20	0.58	
P26641	Elongation factor 1-gamma OS=Homo sapiens GN=EEF1G PE=1 SV=3	-0.40	-0.23	0.00	-0.21	0.68	
P38646	Stress-70 protein, mitochondrial OS=Homo sapiens GN=HSPA9 PE=1 SV=2	-0.15	-0.22	-0.29	-0.22	1.47	+

P49411	Elongation factor Tu, mitochondrial OS=Homo sapiens GN=TUFM PE=1 SV=2	-0.80	-0.46	0.54	-0.24	0.22	
O43592	Exportin-T OS=Homo sapiens GN=XPOT PE=1 SV=2	-0.36	-0.37	-0.13	-0.29	1.17	
P46779	60S ribosomal protein L28 OS=Homo sapiens GN=RPL28 PE=1 SV=3	-0.12	-0.30	-0.45	-0.29	1.03	
P62917	60S ribosomal protein L8 OS=Homo sapiens GN=RPL8 PE=1 SV=2	-0.22	-0.39	-0.28	-0.29	1.58	+
P49327	Fatty acid synthase OS=Homo sapiens GN=FASN PE=1 SV=3	-0.55	-0.03	-0.31	-0.30	0.73	
Q9UHG3	Prenylcysteine oxidase 1 OS=Homo sapiens GN=PCYOX1 PE=1 SV=3	0.81	-0.76	-0.97	-0.31	0.19	
P63244	Receptor of activated protein C kinase 1 OS=Homo sapiens GN=RACK1 PE=1 SV=3	-0.34	-0.28	-0.38	-0.33	2.15	+
Q16637	Survival motor neuron protein OS=Homo sapiens GN=SMN1 PE=1 SV=1	-0.36	-0.37	-0.27	-0.33	2.08	+
O00159	Unconventional myosin-Ic OS=Homo sapiens GN=MYO1C PE=1 SV=4	-0.26	-0.22	-0.53	-0.34	1.12	
P08621	U1 small nuclear ribonucleoprotein 70 kDa OS=Homo sapiens GN=SNRNP70 PE=1 SV=2	-0.32	-0.31	-0.43	-0.35	1.95	+
P19338	Nucleolin OS=Homo sapiens GN=NCL PE=1 SV=3	-0.44	-0.35	-0.30	-0.36	1.89	+
P30153	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform OS=Homo sapiens GN=PPP2R1A PE=1 SV=4	-0.71	0.00	-0.39	-0.36	0.66	
P46781	40S ribosomal protein S9 OS=Homo sapiens GN=RPS9 PE=1 SV=3	-0.40	-0.45	-0.25	-0.37	1.59	+
P40227	T-complex protein 1 subunit zeta OS=Homo sapiens GN=CCT6A PE=1 SV=3	-0.58	-0.21	-0.34	-0.38	1.13	
P02786	Transferrin receptor protein 1 OS=Homo sapiens GN=TFRC PE=1 SV=2	0.70	-0.74	-1.15	-0.40	0.26	
P15924	Desmoplakin OS=Homo sapiens GN=DSP PE=1 SV=3	-0.43	-0.51	-0.28	-0.41	1.57	+
P31327	Carbamoyl-phosphate synthase [ammonia], mitochondrial OS=Homo sapiens GN=CPS1 PE=1 SV=2	-0.92	-0.24	-0.13	-0.43	0.65	
P29401	Transketolase OS=Homo sapiens GN=TKT PE=1 SV=3	-0.69	-0.44	-0.26	-0.46	1.18	
P43246	DNA mismatch repair protein Msh2 OS=Homo sapiens GN=MSH2 PE=1 SV=1	-0.64	-0.55	-0.22	-0.47	1.18	
Q63HN8	E3 ubiquitin-protein ligase RNF213 OS=Homo sapiens GN=RNF213 PE=1 SV=3	-0.66	-0.30	-0.46	-0.47	1.34	+
P34932	Heat shock 70 kDa protein 4 OS=Homo sapiens GN=HSPA4 PE=1 SV=4	-0.59	-0.49	-0.35	-0.48	1.69	+
P27708	CAD protein OS=Homo sapiens GN=CAD PE=1 SV=3	-0.74	-0.37	-0.44	-0.52	1.36	+
P0DMV9	Heat shock 70 kDa protein 1B OS=Homo sapiens GN=HSPA1B PE=1 SV=1	-0.95	-0.13	-0.47	-0.52	0.79	
Q12931	Heat shock protein 75 kDa, mitochondrial OS=Homo sapiens GN=TRAP1 PE=1 SV=3	-0.40	-0.25	-0.91	-0.52	0.92	
Q15021	Condensin complex subunit 1 OS=Homo sapiens GN=NCAPD2 PE=1 SV=3	-0.81	-0.09	-0.74	-0.55	0.85	
P60174	Triosephosphate isomerase OS=Homo sapiens GN=TPI1 PE=1 SV=3	0.33	-1.25	-0.77	-0.56	0.45	
P14618	Pyruvate kinase PKM OS=Homo sapiens GN=PKM PE=1 SV=4	-0.65	-0.20	-0.90	-0.58	0.98	

Q96RQ3	Methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial OS=Homo sapiens GN=MCCC1 PE=1 SV=3	-0.48	-0.72	-0.55	-0.58	1.82	+
P62263	40S ribosomal protein S14 OS=Homo sapiens GN=RPS14 PE=1 SV=3	-0.52	-0.79	-0.50	-0.60	1.63	+
P55786	Puromycin-sensitive aminopeptidase OS=Homo sapiens GN=NPEPPS PE=1 SV=2	-0.28	-0.59	-0.93	-0.60	1.07	
O95347	Structural maintenance of chromosomes protein 2 OS=Homo sapiens GN=SMC2 PE=1 SV=2	-0.58	-0.48	-0.75	-0.60	1.78	+
Q9P2J5	Leucine--tRNA ligase, cytoplasmic OS=Homo sapiens GN=LARS PE=1 SV=2	-1.28	-0.73	0.12	-0.63	0.58	
P55072	Transitional endoplasmic reticulum ATPase OS=Homo sapiens GN=VCP PE=1 SV=4	-0.40	-1.04	-0.48	-0.64	1.07	
P07195	L-lactate dehydrogenase B chain OS=Homo sapiens GN=LDHB PE=1 SV=2	-0.42	-1.79	0.21	-0.67	0.42	
P53396	ATP-citrate synthase OS=Homo sapiens GN=ACLY PE=1 SV=3	-1.05	-0.55	-0.54	-0.71	1.28	
P22314	Ubiquitin-like modifier-activating enzyme 1 OS=Homo sapiens GN=UBA1 PE=1 SV=3	-0.33	-0.87	-0.95	-0.71	1.18	
Q9NTJ3	Structural maintenance of chromosomes protein 4 OS=Homo sapiens GN=SMC4 PE=1 SV=2	-1.22	0.03	-1.00	-0.73	0.70	
P06733	Alpha-enolase OS=Homo sapiens GN=ENO1 PE=1 SV=2	-0.47	-0.83	-0.94	-0.75	1.46	+
P55209	Nucleosome assembly protein 1-like 1 OS=Homo sapiens GN=NAP1L1 PE=1 SV=1	-1.20	-0.33	-0.76	-0.76	1.03	
P21333	Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4	-0.92	-0.71	-0.77	-0.80	2.20	+
P15880	40S ribosomal protein S2 OS=Homo sapiens GN=RPS2 PE=1 SV=2	-0.95	-0.93	-0.61	-0.83	1.76	+
P11021	78 kDa glucose-regulated protein OS=Homo sapiens GN=HSPA5 PE=1 SV=2	-0.74	-1.15	-0.66	-0.85	1.51	+
P35579	Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4	-1.19	-0.81	-0.71	-0.90	1.62	+
Q15365	Poly(rC)-binding protein 1 OS=Homo sapiens GN=PCBP1 PE=1 SV=2	-0.85	-1.05	-0.83	-0.91	2.24	+
P61313	60S ribosomal protein L15 OS=Homo sapiens GN=RPL15 PE=1 SV=2	-0.82	-0.96	-1.15	-0.98	2.03	+
P62899	60S ribosomal protein L31 OS=Homo sapiens GN=RPL31 PE=1 SV=1	-0.61	-1.11	-1.35	-1.02	1.37	+
Q8WUM4	Programmed cell death 6-interacting protein OS=Homo sapiens GN=PDCD6IP PE=1 SV=1	-0.94	-1.23	-0.97	-1.05	2.11	+
P22102	Trifunctional purine biosynthetic protein adenosine-3 OS=Homo sapiens GN=GART PE=1 SV=1	-1.31	-0.98	-0.97	-1.09	1.98	+
P07355	Annexin A2 OS=Homo sapiens GN=ANXA2 PE=1 SV=2	-1.16	-1.16	-0.95	-1.09	2.39	+
P62241	40S ribosomal protein S8 OS=Homo sapiens GN=RPS8 PE=1 SV=2	-1.82	-0.72	-0.92	-1.15	1.12	
P05165	Propionyl-CoA carboxylase alpha chain, mitochondrial OS=Homo sapiens GN=PCCA PE=1 SV=4	-0.97	-1.10	-1.40	-1.15	1.92	+
P63104	14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1	-0.71	-1.31	-1.55	-1.19	1.39	+
Q07020	60S ribosomal protein L18 OS=Homo sapiens GN=RPL18 PE=1 SV=2	-1.40	-1.10	-1.18	-1.23	2.28	+
Q9Y490	Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3	-1.43	-1.04	-1.43	-1.30	2.00	+
P26373	60S ribosomal protein L13 OS=Homo sapiens GN=RPL13 PE=1 SV=4	-1.23	-1.48	-1.28	-1.33	2.51	+

Q02878	60S ribosomal protein L6 OS=Homo sapiens GN=RPL6 PE=1 SV=3	-1.61	-1.35	-1.32	-1.43	2.38	+
P49207	60S ribosomal protein L34 OS=Homo sapiens GN=RPL34 PE=1 SV=3	-1.70	-1.31	-1.45	-1.49	2.24	+
P11498	Pyruvate carboxylase, mitochondrial OS=Homo sapiens GN=PC PE=1 SV=2	-1.73	-1.49	-1.56	-1.60	2.69	+
Q9UQ35	Serine/arginine repetitive matrix protein 2 OS=Homo sapiens GN=SRRM2 PE=1 SV=2	-1.75	-1.54	-1.67	-1.65	2.86	+
P78371	T-complex protein 1 subunit beta OS=Homo sapiens GN=CCT2 PE=1 SV=4	-2.04	-2.03	-1.23	-1.77	1.66	+
P04843	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1 OS=Homo sapiens GN=RPN1 PE=1 SV=1	-0.31	-1.94	-3.09	-1.78	0.80	
Q13085	Acetyl-CoA carboxylase 1 OS=Homo sapiens GN=ACACA PE=1 SV=2	-1.94	-1.67	-1.80	-1.81	2.73	+
Q9H4B7	Tubulin beta-1 chain OS=Homo sapiens GN=TUBB1 PE=1 SV=1	-2.14	-1.52	-2.15	-1.94	1.95	+
Q13011	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial OS=Homo sapiens GN=ECH1 PE=1 SV=2	-4.38	-3.81	-4.06	-4.08	2.78	+

Table S4 Global proteomic profiling of PAB-treated HeLa cells.

(Please see accompanying EXCEL file)

4. References

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