Supplemental Data

Radiolabeling

For radiolabeling, 60 nmol of PP-F11N and 6 MBq ²²⁵Ac (12 pmol) were combined in 0.4 M ammonium acetate buffer (pH 5.5) supplemented with 21 µL of 0.5 M sodium ascorbate to a total volume of 510 µL and the reaction was carried out at 75 °C for 1 h. After labeling, 2 µL of 0.5 mM EDTA in metal-free water was added, and radiolabeled ²²⁵Ac-PP-F11N was separated from the unlabeled PP-F11N and free radionuclides using Merck Hitachi LaChrom 2D high-performance liquid chromatography (HPLC) system as previously described (*6*). The purified ²²⁵Ac-PP-F11N with the specific activity of 475 MBq/nmol was concentrated on SpeedVac and diluted in PBS prior *in vitro* and *in vivo* experiments.

Cell Culture and Proliferation Assay

A431/CCKBR cells were cultivated in Dulbecco's Modified Eagle Medium (DMEM) with 10% (v/v) fetal bovine serum, 2 mM glutamine, 0.1 mg/mL streptomycin, 100 IU/mL penicillin and 1.25 g/mL fungizone (BioConcept) in a humidified incubator with 5% CO₂ at 37°C. For proliferation assay, 4 x 10³ cells in 150 μ L medium were seeded on 96-well plates. Next day, cells were treated with 1-3 kBq/mL ²²⁵Ac-PP-F11N for 2 h, and the medium containing ²²⁵Ac-PP-F11N was replaced with 100 μ L fresh medium with or without 2, 5, or 10 μ M inhibitors, as indicated. After 24 or 48 h, cell proliferation was analyzed by using the CellTiter 96 AQueous Non-Radioactive Cell Proliferation Kit (Promega) according to the manufacturer's instruction and absorbance at 570nm with a reference of 650nm was measured using a MicroPlate Reader (PerkinElmer). The absorbance of the untreated control was set to 100% of cell viability. Each assay was performed in triplicates.

Preparation of Tryptic Peptides and Phosphopeptide Enrichment

A431/CCKBR cells were grown on 150 mm TC plates and 100% confluent cells were treated with 10 kBq/mL ²²⁵Ac-PP-F11N for 2 h. Control plates were incubated with medium without radiolabeled compound. After incubation time, control and treated cells were washed with PBS, and incubated with normal growth medium for another 2 h. The total protein lysates were prepared in 8 M urea lysis buffer in 0.1 M Ambic supplemented with cOmplete mini protease and PhosSTOP phosphatase inhibitors (Roche). For each sample, 500 µg of proteins were taken and used for on-filter digestion using an adaptation of the filter-aided sample preparation (FASP) protocol. Briefly, proteins were diluted in 200 µL of UT buffer (8 M Urea in 100 mM Tris/HCL, pH 8.2), loaded on Ultracel 30000 MWCO centrifugal unit (Amicon Ultra, Merck, Darmstadt, Germany) and centrifuged at 14000 g. SDS buffer was exchanged by one centrifugation round of 200 µL UT buffer. Alkylation of reduced proteins was carried by 5 min incubation with 100 µL iodoacetamide 0.05 M in UT buffer, followed by three 100 µL washing steps with UT and two 100 µL washing steps with Triethylammonium bicarbonate buffer (TEAB, pH 8). Finally, proteins were on-filter digested using 120 µL of 0.05 TEAB (pH 8) containing trypsin (Promega, Madison, WI, USA) in a ratio 1:50 (w/w). Digestion was performed overnight in a wet chamber at room temperature, and peptides were eluted by centrifugation at 14000 g for 20 minutes. After elution, 5 µL of peptide mixtures were taken and stored for later MS analysis of the proteomes. The remaining volume was dried almost to completeness for enrichment of the phosphopeptides by using a KingFisher Flex System (Thermo Fisher Scientific) and MagReSyn Ti-IMAC beads (ReSyn Biosciences, Gauteng, South Africa). Beads were conditioned following the manufacturer's instructions, consisting of 2 washes with 200 µL of 70% ethanol, 1 wash with 100 µL of 1 M NH₄OH and 3 washes with loading buffer (0.1 M glycolic acid in 80% ACN, 5% trifluoroacetic acid (TFA)). Samples were diluted with 200 µL of loading buffer. The beads, wash solutions and the samples were loaded into 96 deep well plates and transferred to the KingFisher. The protocol of the robot carried out the following steps: washing of the magnetic beads in loading buffer (5 min), binding

of the phosphopeptides to the beads (20 min), washing the beads in wash 1 (0.1 M glycolic acid in 80% ACN, 5% TFA, 2 min), wash 2 (80% ACN, 1% TFA, 2 min), wash 3 (10% ACN, 0.2% TFA, 2 min) and eluting the phosphopeptides from the magnetic beads (1 M NH₄OH, 10 min). The phosphopeptides were dried to the completeness and re-solubilized with 10 μ L of 3% acetonitrile, 0.1% formic acid for MS analysis. 1 μ L of iRT peptides (Biognosys) at 1:100 dilution were added to each samples.

Liquid Chromatography-Mass Spectrometry Analysis

The analysis of phosphoproteomics sample was performed on a Q Exactive HF mass spectrometer (Thermo Scientific) equipped with a Digital PicoView source (New Objective) and coupled to an M-Class UPLC (Waters). Solvent composition at the two channels was 0.1% formic acid for channel A and 0.1% formic acid, 99.9% acetonitrile for channel B. Column temperature was 50 °C. For each sample 4 µL of peptides were loaded on a commercial ACQUITY UPLC M-Class Symmetry C18 Trap Column (100Å, 5 µm, 180 µm x 20 mm, Waters) followed by ACQUITY UPLC M-Class HSS T3 Column (100Å, 1.8 µm, 75 µm X 250 mm, Waters). The peptides were eluted at a flow rate of 300 nL/min by a gradient from 5 to 40% B in 90 min. The column was cleaned after the run by increasing to 98% B and holding 95% B for 10 min prior to re-establishing the loading condition. Samples were acquired in a randomized order. The mass spectrometer was operated in data-dependent mode (DDA), acquiring a full-scan MS spectra (350-1'500 m/z) at a resolution of 120'000 at 200 m/z after accumulation to a target value of 3'000'000, and a maximum injection time of 50 ms followed by HCD (higher-energy collision dissociation) fragmentation on the ten most intense signals per cycle. HCD spectra were acquired at a resolution of 60'000 using a normalized collision energy of 25 and a maximum injection time of 120 ms. The automatic gain control (AGC) was set to 1'000'000 ions. Charge state screening was enabled. Singly, unassigned, and charge states higher than eight were rejected. Only precursors with intensity above 100'000 were selected for MS/MS. Precursor masses previously selected for

MS/MS measurement were excluded from further selection for 30 s, and the exclusion window was set at 10 ppm. The samples were acquired using internal lock mass calibration on m/z 371.1012 and 445.1200. MS analysis of the proteome samples was performed right after the acquisition of the phosphoproteomics data, on the same Q Exactive HF mass spectrometer, using the same UPLC conditions as of the phosphoproteomics experiment. Samples were dried and resolubilized with 15 μ L of 3% acetonitrile, 0.1% formic acid for MS analysis. 1 μ L of iRT peptides (Biognosys) at 1:100 dilution was added to each sample. Two microliters were injected. The MS method changed only for the following parameters: HCD fragmentation was performed on the twelve most intense signals per cycle. HCD spectra were acquired at a resolution of 30'000 using a normalized collision energy of 28 and a maximum injection time of 50 ms. The automatic gain control (AGC) was set to 100'000 ions. The MS proteomics data were handled using the local laboratory information management system (LIMS) and all relevant data have been deposited to the ProteomeXchange Consortium via the PRIDE (http://www.ebi.ac.uk/pride) partner repository (9).

Protein and Phosphopeptide Identification and Label-Free Quantification

The acquired raw MS data were processed by MaxQuant (version 1.6.2.3), followed by protein identification using the integrated Andromeda search engine. Spectra were searched against a canonical Uniprot reference proteome of Homo sapiens (UP000005640, version 2016-12-09), concatenated to common protein contaminants. Carbamidomethylation of cysteine was set as a fixed modification, while methionine oxidation and N-terminal protein acetylation were set as a variable. Additionally, serine, threonine, and tyrosine phosphorylation were set as variable modifications in the search for the phosphoproteome. Enzyme specificity was set to trypsin/P allowing a minimal peptide length of 7 amino acids and a maximum of two missed cleavages. MaxQuant Orbitrap default search settings were used. The maximum false discovery rate was set to 0.01 for peptides and 0.05 for proteins. Label-free quantification was enabled and a 2

minutes window for the match between runs was applied. In the MaxQuant experimental design template, each file is kept separate in the experimental design to obtain individual quantitative values. Statistics of the phosphopeptide analysis and the total proteome analysis were merged and the calculated p-values were adjusted for multiple testing (*q*-values). Values of q < 0.05 were considered statistically significant.

Bioinformatics

DAVID bioinformatics platform was used to annotate the function of the protein groups identified by phosphoproteomics and proteomics analysis (https://david.ncifcrf.gov/). The proteins, which contain peptides with significantly altered phosphorylation or total protein level after ²²⁵Ac-PP-F11N treatment were categorized based on their involvement in biological processes (GOTERM_BP) or signal transduction pathways (BIOCARTA) by using the Gene Ontology annotation tool. STRING 11.1 protein-protein interaction database (http://string-db.org/) was used to visualize the networks of proteins, which phosphorylation or protein level was changed in response to ²²⁵Ac-PP-F11N treatment. Present protein-protein associations were based on evidence with high confidence (interaction score > 0.7).

Western Blot

A431/CCKBR cells were treated with 6 kBq/mL ²²⁵Ac-PP-F11N (2h internalization time) alone or in combination with 1 or 10 µM inhibitors for 2 h. Total protein lysates were prepared in lysis buffer containing 50 mM Tris-HCl pH 7.5, 150 mM NaCl, 1% Triton X, 0.1% SDS with 1 mM sodium orthovanadate, 1 mM NaF and protease inhibitor cocktail (Roche). Antibodies against phospho-P53 S15 (16G8), phospho-H2A.X S139 (2577), and GAPDH (14C10) were from Cell Signaling Technology (CST), whereas phospho-53BP1 S1778 (PA5-17462) was from EnoGene, and phospho-HDAC9/4/5 S246/S259/S220 (SAB4300269) was from Sigma-Aldrich. Secondary antirabbit and anti-mouse HRP-linked antibodies were from CST and the standard WB experiments were performed as described previously (11).

Immunocytochemistry

 3×10^4 cells per well were seeded on an 8-well chamber slide (iBidi). On the next day, cells were treated with 3 kBq/ml ²²⁵Ac-PP-F11N alone or in combination with 2 µM SAHA, as described above. After 24 h incubation, the PBS-washed cells were fixed in 4 % paraformaldehyde/ PBS and used for immunohistochemistry. Cells were first permeabilized with 1% NP40/PBS for 5 minutes and then blocked with a blocking buffer (1% BSA/ 0.3% Triton X-100/ PBS) for 1 hour. Cells were then incubated overnight at 4°C with 1:1000 diluted rabbit anti-phospho-histone H2A.X (Ser139) antibody (CST, #2577), washed three times with PBS, and then incubated with a Cy3-labeled donkey anti-rabbit antibody (Jackson ImmunoResearch). Nuclei were stained by incubating for 10 minutes in 1 µg/ml Hoechst 33258/ PBS. Images were collected on a Leica Stellaris confocal microscope with a 20x objective. Single sections with a resolution of 4096x4096 pixels were acquired. Images were analyzed with a CellProfiler pipeline as described by CellProfiler developers (https://cellprofiler.org/examples). Signals from 150–400 cell nuclei were counted for each condition. For statistical analysis one-way ANOVA followed by Tukey's multiple comparison tests were performed using GraphPad Prism 7.00 for Windows 10.

Supplemental Table 1. Significantly increased phosphopeptide abundance in A431/CCKBR cells treated with ²²⁵Ac-PP-F11N. MS-based quantification: $\log_2 \text{ ratio} > |1|$ and q < 0.05.

LOG ₂ (ratio) ²²⁵ Ac-PP- F11N / CON	q-VALUE	UniProt SYMBOL; NAME	SEQUENCE WINDOW POSITION (PROBABILITY>0.75)
4.00	0.00272	Q14980 NUMA1; Nuclear mitotic apparatus protein 1	LSQLEEHL <mark>S</mark> (1)QLQDNPPQEK
3.84	7.75E-05	Q8TAD8 SNIP1; Smad nuclear-interacting protein 1	NDVGGGGSE <mark>S</mark> (1)QELVPR
3.34	0.00013	P17096 HMGA1; High mobility group protein HMG-I/HMG-Y	KQPPVSPGTALVG <mark>S</mark> (1)QKEPSEVPTPK
3.28	0.00022	Q9BVJ6 UT14A; U3 small nucleolar RNA-associated protein 14 homolog A	DSG <mark>S</mark> (1)QEVLSELR
3.28	0.00017	Q14676 MDC1; Mediator of DNA damage checkpoint protein 1	QDG <mark>S</mark> (1)QEAPEAPLSSELEPFHPK
3.28	0.00058	Q969E4 TCAL3; Transcription elongation factor A protein-like 3	GTDDSPKD <mark>S</mark> (1)QEDLQER
3.25	0.00013	Q13428 TCOF; Treacle protein	GSLG <mark>S(</mark> 1)QGAKDEPEEELQK
3.21	0.00013	Q14566 MCM6; DNA replication licensing factor MCM6	MDLAAAAEPGAG <mark>S(</mark> 1)QHLEVR
3.20	0.00131	Q9H6F5 CCD86; Coiled-coil domain-containing protein 86	C <mark>S</mark> (1)QDQGVLASELAQNK
3.11	0.00013	O60934 NBN; Nibrin	ML <mark>S</mark> (1)QDAPTVK
3.10	0.00199	Q12888 TP53B; Tumor suppressor p53-binding protein 1	EEGGCSLASTPATTLHLLQL <mark>S</mark> (1)GQR
3.04	0.00013	Q15435 PP1R7; Protein phosphatase 1 regulatory subunit 7	GAGQQQ <mark>S</mark> (1)QEMMEVDR
3.03	0.00013	Q16539 MK14; Mitogen-activated protein kinase 14	S(1)QERPTFYR
3.00	0.00112	Q13451 FKBP5; Peptidyl-prolyl cis-trans isomerase FKBP5	GTD <mark>S</mark> (1)QAMEEEKPEGHV
2.99	0.00038	Q86U42 PABP2; Polyadenylate-binding protein 2	APPGAPGPGPGSGAPG <mark>S(</mark> 1)QEEEEEPGLVEGDPG DGAIEDPELEAIK
2.99	0.00156	O43768 ENSA; Alpha-endosulfine	<mark>S</mark> (1)QKQEEENPAEETGEEK
2.91	0.00089	O95232 LC7L3; Luc7-like protein 3	IDVLLQQIEELG <mark>S</mark> (1)EGKVEEAQGMMK
2.89	0.03692	P51522 ZNF83; Zinc finger protein 83	<mark>S(</mark> 1)NLASHQRIHTGEK
2.86	0.00058	Q86U44 MTA70; N6-adenosine-methyltransferase 70 kDa subunit	DHTP <mark>S</mark> (1)QELALTQSVGGDSSADR
2.84	0.00038	P25205 MCM3; DNA replication licensing factor MCM3	APGEQDGDAMPLGSAVDILATDDPNF <mark>S(</mark> 1)QEDQ QDTQIYEK
2.83	0.00222	O94782 UBP1; Ubiquitin carboxyl-terminal hydrolase 1	ALDFTDS(1)QENEEK
2.70	0.00289	Q12888 TP53B; Tumor suppressor p53-binding protein 1	LVSPETEAS(1)EES(1)LQFNLEKPATGER
2.70	0.00013	Q7Z5K2 WAPL; Wings apart-like protein homolog	SEDCILSLD <mark>S</mark> (1)DPLLEMK
2.69	0.00035	P68402 PA1B2; Platelet-activating factor acetylhydrolase IB subunit beta	<mark>S</mark> (1)QGDSNPAAIPHAAEDIQGDDR
2.69	0.00013	Q99733 NP1L4; Nucleosome assembly protein 1-like 4	ADHSF <mark>S</mark> (0.99)DGVP <mark>S</mark> (1)DSVEAAK
2.68	0.00085	Q92547 TOPB1; DNA topoisomerase 2-binding protein 1	NAVALSA <mark>S</mark> (0.99)PQLK
2.66	0.00058	Q13573 SNW1; SNW domain-containing protein 1	ALTSFLPAPTQL <mark>S</mark> (1)QDQLEAEEK
2.65	0.00089	Q14683 SMC1A; Structural maintenance of chromosomes protein 1A	GTMDDISQEEG <mark>SS</mark> (0.99)QGEDSVSGSQR
2.56	0.00123	Q96RL1 UIMC1; BRCA1-A complex subunit RAP80	EVN <mark>S(</mark> 1)QEEEEELLR
2.56	0.00277	Q12888 TP53B; Tumor suppressor p53-binding protein 1	LVSPETEAS(1)EES(1)LQFNLEKPATGER
2.56	0.00277	Q12888 TP53B; Tumor suppressor p53-binding protein 1	LVSPETEAS(1)EES(1)LQFNLEKPATGER
2.54	0.00841	Q9Y696 CLIC4; Chloride intracellular channel protein 4	LDEYLNSPLPDEIDEN <mark>S</mark> (1)MEDIK
2.52	0.00049	Q9BVJ6 UT14A; U3 small nucleolar RNA-associated protein 14 homolog A	SELSQDAEPAG <mark>S</mark> (1)QETK
2.48	0.01792	Q7RTP6 MICA3; Protein-methionine sulfoxide oxidase MICAL3	GPSQATSPIR <mark>S</mark> (0.91)PQESALLFIPVHSPSTEGPQL PPVPAATQEK

2.43	0.00022	Q14566 MCM6; DNA replication licensing factor MCM6	EIESEID <mark>S(</mark> 1)EEELINK
2.42	0.00038	Q92878 RAD50; DNA repair protein RAD50	LFDVCG <mark>S</mark> (1)QDFESDLDR
2.42	0.00132	Q9H1E3 NUCKS; Nuclear ubiquitous casein and cyclin- dependent kinase substrate 1	SGKN <mark>S(</mark> 1)QEDSEDSEDKDVK
2.40	0.00073	P20810 ICALM Calpastatin	SESELIDEL <mark>S</mark> (1)EDFDR
2.39	0.00111	Q96B01 R51A1; RAD51-associated protein 1	ELPTVTTNVQN <mark>S</mark> (1)QDK
2.38	0.00406	O00192 ARVC; Armadillo repeat protein deleted in velo-cardio- facial syndrome	GAL <mark>S</mark> (1)PGGFDDSTLPLVDK
2.37	0.00736	O60934 NBN; Nibrin	MDIETNDTFSDEAVPESSKIS(0.99)QENEIGK
2.33	0.00094	P16104H2AX; Histone H2AX	ATQA <mark>S</mark> (1)QEY
2.33	0.00132	Q9NZT2 OGFR; Opioid growth factor receptor	S(1)QGDEAGGHGEDRPEPLS(1)PK
2.33	0.00132	Q9NZT2OGFR; Opioid growth factor receptor	S(1)QGDEAGGHGEDRPEPLS(1)PK
2.32	0.00018	Q13185 CBX3; Chromobox protein homolog 3	LTWH <mark>S</mark> (0.99)CPEDEAQ
2.29	0.00035	Q14839 CHD4; Chromodomain-helicase-DNA-binding protein 4	QVNYNDG <mark>S</mark> (1)QEDR
2.27	0.0023	Q15554 TERF2; Telomeric repeat-binding factor 2	LVLEEDSQSTEPSAGLNS <mark>S</mark> (0.83)QEAASAPPSKPT VLNQPLPGEK
2.22	0.00277	Q13263 TIF1B; Transcription intermediary factor 1-beta	QGSG <mark>SS(</mark> 0.93)QPMEVQEGYGFGSGDDPYSSAEP HVSGVK
2.22	0.00022	Q9UQ35 SRRM2; Serine/arginine repetitive matrix protein 2	EQNSALPTS <mark>S</mark> (0.99)QDEELMEVVEK
2.20	0.00199	Q15326 ZMY11; Zinc finger MYND domain-containing protein 11	KEEPEPETEAVSS <mark>S</mark> (0.94)QEIPTMPQPIEK
2.06	0.04741	Q9NXH9 TRM1; tRNA (guanine(26)-N(2))-dimethyltransferase	SALLHADFRVS(1)L <mark>S</mark> (1)HACK
2.06	0.04741	Q9NXH9 TRM1; tRNA (guanine(26)-N(2))-dimethyltransferase	SALLHADFRVS(1)LS(1)HACK
2.06	0.00707	Q99575 POP1; Ribonucleases P/MRP protein subunit POP1	SAVCIADPLPTP <mark>S</mark> (1)QEK
2.03	0.00736	Q14839 CHD4; Chromodomain-helicase-DNA-binding protein 4	IEEN <mark>S</mark> (1)LKEEESIEGEK
2.00	0.00058	Q6PIW4 FIGL1; Fidgetin-like protein 1	FSVCGS <mark>S</mark> (0.95)QESDSLPNSAHDR
2.00	0.00071	Q8IZ73 RUSD2; RNA pseudouridylate synthase domain- containing protein 2	QSLDVLDLCEGDL <mark>S</mark> (1)PGLTDSTAPSSELGKDDLEE LAAAAQK
1.99	0.00131	Q96G28CFA36; Cilia- and flagella-associated protein 36	TEEPTVHSSEAAIMNN <mark>S</mark> (1)QGDGEHFAHPPSEVK
1.95	0.00214	Q96RL1 UIMC1; BRCA1-A complex subunit RAP80	SRPLATGP <mark>SS(</mark> 0.94)QSHQEK
1.95	0.02386	P20810 ICAL; Calpastatin	EQLPPMSEDFLLDAL <mark>S</mark> (0.99)EDFSGPQNASSLK
1.95	0.02325	Q9HB58 SP110; Sp110 nuclear body protein	MNAEED <mark>S</mark> (1)EEMPSLLTSTVQVASDNLIPQIR
1.91	0.00235	Q9H307 PININ; Pinin	QQD <mark>S</mark> (1)QPEEVMDVLEMVENVK
1.90	0.00113	P38398 BRCA1; Breast cancer type 1 susceptibility protein	VVDVEEQQLEE <mark>S</mark> (1)GPHDLTETSYLPR
1.87	0.00485	Q12888 TP53B; Tumor suppressor p53-binding protein 1	QSQQPMKPI <mark>S</mark> (1)PVKDPVSPASQK
1.87	0.00485	Q12888 TP53B; Tumor suppressor p53-binding protein 1	QSQQPMKPI <mark>S</mark> (1)PVKDPV <mark>S</mark> (1)PA <mark>S(</mark> 1)QK
1.87	0.00485	Q12888 TP53B; Tumor suppressor p53-binding protein 1	QSQQPMKPI <mark>S</mark> (1)PVKDPV <mark>S</mark> (1)PA <mark>S(</mark> 1)QK
1.86	0.00115	P10155 RO60; 60 kDa SS-A/Ro ribonucleoprotein	QIAN <mark>S</mark> (1)QDGYVWQVTDMNR
1.86	0.00087	P43243 MATR3; Matrin-3	<mark>S</mark> (1)QESGYYDR
1.83	0.01266	O75607 NPM3; Nucleoplasmin-3	AAGTAAALAFL <mark>S</mark> (0.97)QESR
1.82	0.00087	P18615 NELFE; Negative elongation factor E	SL <mark>S</mark> (1)EQPVMDTATATEQAK
1.81	0.04942	P49736 MCM2; DNA replication licensing factor MCM2	AIPELDAYEAEGLALDDEDVEELTA <mark>S</mark> (0.99)QR
1.77	0.00821	Q9UQ35 SRRM2; Serine/arginine repetitive matrix protein 2	HGGSPQPLATTPL <mark>S</mark> (0.99)QEPVNPPSEA <mark>S</mark> (0.82)P TR
1.76	0.00175	Q9BWU0 NADAP; Kanadaptin	ETQTHENMSQL <mark>S(</mark> 1)EEEQNK
1.75	0.01034	O43719 HTSF1; HIV Tat-specific factor 1	GFEGSC <mark>S</mark> (1)QKESEEGNPVR
1.74	0.00526	P78332 RBM6; RNA-binding protein 6	EGETQGVAFEHESPADFQN <mark>S(</mark> 1)Q <mark>S</mark> (1)PVQDQDK
1.74	0.00526	P78332 RBM6; RNA-binding protein 6	EGETQGVAFEHESPADFQN <mark>S(</mark> 1)Q <mark>S</mark> (1)PVQDQDK

1.73	0.00113	P26651 TTP; mRNA decay activator protein ZFP36	LGPELSPSPT <mark>S</mark> (0.92)PTATSTTPSR	
1.73	0.01695	Q12888 TP53B; Tumor suppressor p53-binding protein 1	LPDGPTG <mark>S(0.98)S(0.99)EEEEEFLEIPPFNK</mark>	
1.73	0.00090	P19338 NUCL; Nucleolin	GFGFVDFN <mark>S</mark> (1)EEDAK	
1.70	0.00570	Q9Y580 RBM7; RNA-binding protein 7	SF <mark>S</mark> (1)SPENFQR	
1.69	0.00131	Q9C0C2 TB182; 182 kDa tankyrase-1-binding protein	GSGGLF <mark>S</mark> (1)PSTAHVPDGALGQR	
1.69	0.00131	Q9C0C2 TB182; 182 kDa tankyrase-1-binding protein	G <mark>S(</mark> 1)GGLF <mark>S</mark> (0.96)PSTAHVPDGALGQR	
1.66	0.00114	Q13263 TIF1B; Transcription intermediary factor 1-beta	<mark>S</mark> (1)GEGEVSGLMR	
1.62	0.00877	P49757 NUMB; Protein numb homolog	IVVGSSVAPGNTAPSPS <mark>S</mark> (0.99)PTS(0.99)PTSDAT TSLEMNNPHAIPR	
1.62	0.00877	P49757 NUMB; Protein numb homolog	IVVGSSVAPGNTAPSPS <mark>S</mark> (0.99)PTS(0.99)PTSDAT TSLEMNNPHAIPR	
1.61	0.04667	P04637P53; Cellular tumor antigen p53	MEEPQ <mark>S(</mark> 1)DPSVEPPL <mark>S</mark> (0.99)QETFSDLWK	
1.61	0.00128	Q96RL1 UIMC1; BRCA1-A complex subunit RAP80	LLLEEEPTTSHGQ <mark>SS</mark> (0.88)QGIVEETSEEGNSVPAS QSVAALTSK	
1.61	0.03573	Q9H2P0ADNP; Activity-dependent neuroprotector homeobox protein	KLDDDSD <mark>S</mark> (0.99)PSFFEEKPEEPVVLALDPK	
1.61	0.04715	Q8N201 INT1; Integrator complex subunit 1	EGEEVY <mark>S</mark> (1)WSESQDQVFLR	
1.60	0.00128	Q9NYF8 BCLF1; Bcl-2-associated transcription factor 1	S(1)QEEPKDTFEHDPSESIDEFNK	
1.54	0.00495	P04637P53; Cellular tumor antigen p53	MEEPQ <mark>S(1)DPSVEPPLS</mark> (0.99)QETFSDLWK	
1.54	0.01212	Q99708 COM1; DNA endonuclease RBBP8	C <mark>S</mark> (1)PDNKPSLQIK	
1.54	0.01631	Q9NRF2 SH2B1; SH2B adapter protein 1	ASGSLSPPILAPL <mark>S</mark> (1)PGAEISPHDLSLESCR	
1.54	0.01631	Q9NRF2 SH2B1; SH2B adapter protein 1	ASGSL <mark>S</mark> (0.94)PPILAPL <mark>S</mark> (1)PGAEISPHDLSLESCR	
1.54	0.00144	Q9UK76 HN1; haematological and neurological expressed 1 protein	GEGDIHENVDTDLPG <mark>S</mark> (1)LGQSEEKPVPAAPVPSP VAPAPVPSR	
1.54	0.03680	O00139 KIF2A; Kinesin-like protein KIF2A	EIDLESIFSLNPDLVPDEEIEP <mark>S</mark> (1)PET(0.99)PPPPAS SAK	
1.54	0.03680	O00139 KIF2A; Kinesin-like protein KIF2A	EIDLESIFSLNPDLVPDEEIEPS(1)PET(0.99)PPPPAS SAK	
1.53	0.00246	Q01105 SET; Protein SET	LNEQA <mark>S</mark> (1)EEILK	
1.52	0.00736	Q969E4 TCAL3; Transcription elongation factor A protein-like 3	REDEGEPGDEGQLEDEG <mark>S(</mark> 1)QEK	
1.50	0.00263	O60784 TOM1; Target of Myb protein 1	GLEFPMTDLDML <mark>S(</mark> 1)PIHT(1)PQR	
1.50	0.04679	P85037 FOXK1; Forkhead box protein K1	EEAPA <mark>S(</mark> 1)PLRPLYPQI <mark>S</mark> (1)PLK	
1.49	0.00348	Q9BQG0 MBB1A; Myb-binding protein 1A	SP <mark>S</mark> (1)LLQSGAK	
1.48	0.02957	O15355 PPM1G; Protein phosphatase 1G	KLEEVL <mark>S</mark> (0.91)TEGAEENGNSDK	
1.48	0.00662	P47974 TISD; Zinc finger protein 36, C3H1 type-like 2	RH <mark>S(</mark> 0.99)ASNLHALAHPAPSPGSCSPK	
1.46	0.00131	Q12888 TP53B; Tumor suppressor p53-binding protein 1	HEEQ <mark>S</mark> (1)NEDIPIAEQSSK	
1.46	0.00131	Q12888 TP53B; Tumor suppressor p53-binding protein 1	QDKPMDTSVL <mark>S</mark> (1)EEGGEPFQK	
1.44	0.00765	P49366 DHYS; Deoxyhypusine synthase	KLEPL <mark>S</mark> (1)QDEDQHADLTQSR	
1.44	0.00662	Q9C0C2 TB182; 182 kDa tankyrase-1-binding protein	GSGGLF <mark>S</mark> (1)PSTAHVPDGALGQR	
1.44	0.04306	Q13501 SQSTM; Sequestosome-1	SS <mark>S</mark> (0.92)QPSSCCSDPSKPGGNVEGATQSLAEQM R	
1.44	0.033	Q07157Z01; Tight junction protein ZO-1	PVYAQVGQPDVDLPV <mark>S</mark> (1)PSDGVLPNSTHEDGILR	
1.43	0.01988	Q99611 SPS2; Selenide, water dikinase 2	GLVGGQEEA <mark>S</mark> (1)QEAGLPAGAGPSPTFPALGIGM DSCVIPLR	
1.42	0.00715	Q8ND82Z280C; Zinc finger protein 280C	GTNTS <mark>S(</mark> 0.85)PYDAGADYLR	
1.42	0.00398	O75822 EIF3J; Eukaryotic translation initiation factor 3 subunit J	VLT(1)PEEQLADK	
1.41	0.03582	Q8IVT2 MISP; Mitotic interactor and substrate of PLK1	NALFPEVF <mark>S</mark> (0.97)PTPDENSDQNSR	
1.40	0.00655	Q12888 TP53B; Tumor suppressor p53-binding protein 1	L <mark>S</mark> (1)DVDANTAIK	
1.40	0.00246	Q9UQ35 SRRM2; Serine/arginine repetitive matrix protein 2	EN <mark>S(</mark> 1)FG <mark>S</mark> (1)PLEFR	

1.37	0.01278	Q12888 TP53B; Tumor suppressor p53-binding protein 1	TS <mark>S</mark> (1)GTSLSAMHSSGSSGK
1.35	0.03983	Q00839 HNRPU; Heterogeneous nuclear ribonucleoprotein U	PAMEPGNG <mark>S</mark> (1)LDLGGDSAGR
1.34	0.01269	Q9Y6W5WASF2; Wiskott-Aldrich syndrome protein family member 2	SSVVS(0.97)PSHPPPAPPLGSPPGPK
1.34	0.00263	Q12888 TP53B; Tumor suppressor p53-binding protein 1	GNLLHFPSS(1)QGEEEKEK
1.33	0.00983	Q9HAW4 CLSPN; Claspin	SL <mark>S</mark> (0.99)SDSTLLLFK
1.32	0.02456	Q9BYG3 MK67I; MKI67 FHA domain-interacting nucleolar phosphoprotein	S(1)QVAELNDDDKDDEIVFK
1.31	0.00306	P15407 FOSL1; Fos-related antigen 1	SSSSSGDPSSDPLG <mark>S</mark> (1)PTLLAL
1.31	0.00765	Q9UBQ5 EIF3K; Eukaryotic translation initiation factor 3 subunit	IDFDSVSSIMA <mark>SS</mark> (0.99)Q
1.30	0.02611	A1L390 PKHG3; Pleckstrin homology domain-containing family G member 3	KPVLSLFDYEQLMAQEHS(1)PPKPSSAGEMSPQR
1.30	0.02611	A1L390 PKHG3; Pleckstrin homology domain-containing family G member 3	KPVLSLFDYEQLMAQEH <mark>S</mark> (0.99)PPKPSSAGEM <mark>S(</mark> 0 .81)PQR
1.30	0.00597	Q9Y4H2 IRS2; Insulin receptor substrate 2	HN <mark>S</mark> (1)ASVENVSLR
1.29	0.01374	P28066 PSA5; Proteasome subunit alpha type-5	IT <mark>S</mark> (1)PLMEPSSIEK
1.28	0.00311	P27816 MAP4; Microtubule-associated protein 4	<mark>S</mark> (0.99)PSTLLPK
1.27	0.01093	O14579 COPE; Coatomer subunit epsilon	APPAPGPASGG <mark>S</mark> (0.99)GEVDELFDVK
1.27	0.02613	Q3KQU3 MA7D1; MAP7 domain-containing protein 1	PASPCPSPGPGHT(0.92)LPPKPPSPR
1.26	0.00869	Q12888 TP53B; Tumor suppressor p53-binding protein 1	SGTAETEPVEQDS <mark>S</mark> (0.99)QPSLPLVR
1.25	0.04715	P60866 RS20; 40S ribosomal protein S20	DTGKT(0.99)PVEPEVAIHR
1.24	0.04411	P18615 NELFE; Negative elongation factor E	SDS(0.99)FPER
1.23	0.00878	Q9Y6W5 WASF2; Wiskott-Aldrich syndrome protein family member 2	RS <mark>S</mark> (0.76)VVS(0.95)PSHPPPAPPLGSPPGPK
1.23	0.00452	Q9C0C2 TB182; 182 kDa tankyrase-1-binding protein	NMAPGAVC <mark>S</mark> (1)PGESK
1.21	0.01208	P34932 HSP74; Heat shock 70 kDa protein 4	MQVDQEEPHVEEQQQQTPAENKAE <mark>S</mark> (0.99)EEM ETSQAGSK
1.20	0.00570	Q8NFH5 NUP53; Nucleoporin NUP53	CALS <mark>S</mark> (1)PSLAFTPPIK
1.19	0.01691	P16402 H13; Histone H1.3	<mark>S(</mark> 0.85)ETAPLAPTIPAPAEK
1.18	0.00410	Q5VZK9CARL1; F-actin-uncapping protein LRRC16A	S(1)PPVDCPR
1.18	0.01675	Q15642CIP4; Cdc42-interacting protein 4	NKPRPPPL <mark>S</mark> (1)PLGGPVPSALPNGPP <mark>S</mark> (1)PR
1.18	0.01675	Q15642 CIP4; Cdc42-interacting protein 4	NKPRPPPL <mark>S</mark> (1)PLGGPVPSALPNGPP <mark>S</mark> (1)PR
1.17	0.04306	P35611 ADDA; Alpha-adducin	AAVVT <mark>S</mark> (1)PPPTTAPHK
1.16	0.00877	P17096 HMGA1; High mobility group protein HMG-I/HMG-Y	EPSEVPT(1)PK
1.16	0.00877	P17096 HMGA1; High mobility group protein HMG-I/HMG-Y	KQPPVSPGTALVG <mark>S</mark> (1)QKEPSEVPTPK
1.16	0.02860	Q9UKV3 ACINU; Apoptotic chromatin condensation inducer in the nucleus	LSEGS(1)QPAEEEEDQETPSR
1.14	0.03153	Q8IY33 MILK2; MICAL-like protein 2	PGRPL <mark>S(</mark> 1)PANVPALPGETVT <mark>S(</mark> 0.79)PVR
1.14	0.03153	Q8IY33 MILK2; MICAL-like protein 2	PGRPL <mark>S(</mark> 1)PANVPALPGETVT <mark>S(</mark> 0.79)PVR
1.14	0.01888	Q9UQ35 SRRM2; Serine/arginine repetitive matrix protein 2	SEEPAGQILSHL <mark>S</mark> (0.93)SELK
1.14	0.00693	P43358 MAGA4; Melanoma-associated antigen 4	QPNEGS <mark>S(</mark> 0.98) <mark>S</mark> (1)QEEEGPSTSPDAESLFR
1.14	0.02578	Q8N1G2 CMTR1; Cap-specific mRNA (nucleoside-2-O-)- methyltransferase 1	QHSSD <mark>S(</mark> 0.94)FDDAFK
1.14	0.02075	P16949 STMN1; Stathmin	RAS(1)GQAFELIL <mark>S</mark> (1)PR
1.13	0.02855	Q9H7M9 VISTA; V-type immunoglobulin domain-containing suppressor of T-cell activation	HLLSEPSTPLS(0.82)PPGPGDVFFPSLDPVPDS(0.9 4)PNFEVI
1.12	0.01815	Q9BXP5 SRRT; Serrate RNA effector molecule homolog	NITDYLIEEVSAEEEELLGS <mark>S</mark> (0.8)GGAPPEEPPK
1.12	0.01109	Q9NX74 DUS2L; tRNA-dihydrouridine(20) synthase [NAD(P)+]- like	KPFVALGSGEE <mark>S</mark> (1)PLEGW

1.10	0.02934	Q09666 AHNK; Neuroblast differentiation-associated protein AHNAK	MYFPDVEFDIK <mark>S</mark> (1)PK
1.10	0.01208	P47974 TISD; Zinc finger protein 36, C3H1 type-like 2	RH <mark>S</mark> (0.99)ASNLHALAHPAPSPGSCSPK
1.10	0.01372	Q9UJM3 ERRFI; ERBB receptor feedback inhibitor 1	EPL <mark>S</mark> (1)PSNSR
1.09	0.00641	Q9UKV0 HDAC9; Histone deacetylase 9	TQ <mark>S</mark> (0.99)APLPQSTLAQLVIQQQHQQFLEK
1.09	0.00663	Q8NC51PAIRB; Plasminogen activator inhibitor 1 RNA-binding protein	DELTE <mark>S</mark> (1)PK
1.09	0.03903	Q9NYZ3 GTSE1; G2 and S phase-expressed protein 1	PSPVVGQLIDLSSPLIQL <mark>S</mark> (1)PEADKENVDSPLLK
1.09	0.01998	Q9C0C2 TB182; 182 kDa tankyrase-1-binding protein	EEAGKEEPPPL <mark>T</mark> (1)PPAR
1.08	0.03001	Q9H201 EPN3; Epsin-3	TPVLPAGPPTTDPWALN <mark>S</mark> (1)PHHK
1.08	0.02288	Q13263 TIF1B; Transcription intermediary factor 1-beta	QGS(0.99)GSSQPMEVQEGYGFGSGDDPYSSAEP HVSGVK
1.07	0.02535	O15014 ZN609; Zinc finger protein 609	AP <mark>S</mark> (0.99)LTDLVK
1.06	0.01760	Q7Z3T8 ZFY16; Zinc finger FYVE domain-containing protein 16	NEIIQ <mark>S</mark> (0.99)PISQVPSVEK
1.06	0.02855	Q08357 S20A2; Sodium-dependent phosphate transporter 2	VQEAE <mark>S</mark> (1)PVFK
1.05	0.01813	Q32MZ4 LRRF1; Leucine-rich repeat flightless-interacting protein 1	ALD <mark>S</mark> (1)NSLENDDLSAPGR
1.05	0.03443	Q86WB0 NIPA; Nuclear-interacting partner of ALK	<mark>S</mark> (1)WDSSSPVDRPEPEAASPTTR
1.05	0.00825	Q9UHY1 NRBP; Nuclear receptor-binding protein	PQQPQQEEVT <mark>S(</mark> 0.99)PVVPPSVK
1.05	0.00736	P17535 JUND; Transcription factor jun-D	LA <mark>S</mark> (1)PELER
1.05	0.04258	Q5VUA4ZN318; Zinc finger protein 318	YISQEEGPL <mark>S</mark> (1)PFLGQLDEDYR
1.05	0.04258	Q5VUA4ZN318; Zinc finger protein 318	YI <mark>S</mark> (1)QEEGPL <mark>S</mark> (1)PFLGQLDEDYR
1.05	0.01811	Q13887 KLF5; Krueppel-like factor 5	QAEMLQNLT(1)PPPSYAATIASK
1.05	0.00932	Q86W92 LIPB1; Liprin-beta-1	ALEYSNGIFDCQ <mark>S</mark> (1)PT <mark>S</mark> (0.99)PFMGSLR
1.05	0.00932	Q86W92 LIPB1; Liprin-beta-1	ALEYSNGIFDCQ <mark>S</mark> (1)PT <mark>S</mark> (0.99)PFMGSLR
1.05	0.03692	Q8NFC6 BD1L1; Biorientation of chromosomes in cell division protein 1-like 1	RL <mark>S</mark> (0.98)ESLHVVDENKNESK
1.05	0.00736	Q96JY6 PDL12; PDZ and LIM domain protein 2	AG <mark>S</mark> (1)PF <mark>S</mark> (1)PPPSSSSLTGEAAISR
1.04	0.02322	Q9HCN4 GPN1; GPN-loop GTPase 1	DSL <mark>S</mark> (1)PVLHPSDLILTR
1.04	0.01810	P67809 YBOX1; Nuclease-sensitive element-binding protein 1	<mark>S(</mark> 1)VGDGETVEFDVVEGEK
1.04	0.01813	P55036 PSMD4; 26S proteasome non-ATPase regulatory subunit 4	AAAASAAEAGIATTGTED <mark>S</mark> (1)DDALLK
1.04	0.01631	Q9BST9 RTKN; Rhotekin	VRA <mark>S</mark> (0.99)LDSAGGSGSSPILLPTPVVGGPR
1.02	0.01212	O00515 LAD1; Ladinin-1	LPS(1)VEEAEVPKPLPPASKDEDEDIQSILR
1.01	0.00736	Q9Y6G9 DC1L1; Cytoplasmic dynein 1 light intermediate chain 1	KPVTVSPTTP <mark>TS(</mark> 1)PTEGEAS
1.00	0.02934	O60271 JIP4; C-Jun-amino-terminal kinase-interacting protein 4	ERPI <mark>S</mark> (1)LGIFPLPAGDGLL <mark>T</mark> (1)PDAQK

Supplemental Table 2. Significantly decreased phosphopeptide abundance in A431/CCKBR cells treated with ²²⁵Ac-PP-F11N. MS-based quantification: $\log_2 ratio > |1|$ and q < 0.05.

LOG ₂ (ratio) ²²⁵ Ac-PP- F11N /CON	q-VALUE	UniProt SYMBOL; NAME	SEQUENCE WINDOW POSITION (PROBABILITY>0.75)
-1.00	0.00858	Q8NCD3 HJURP; Holliday junction recognition protein	GGPA <mark>S</mark> (1)PGGLQGLETR
-1.01	0.0441	Q9BVC5 ASHWN; Ashwin	SPSGPVK <mark>S</mark> (1)PPLSPVGTT(0.85)PVK
-1.01	0.00821	Q13428 TCOF; Treacle protein	S(1)PQVKPASTMGMGPLGK
-1.01	0.04306	P56211 ARP19; cAMP-regulated phosphoprotein 19	VT <mark>S</mark> (1)PEKAEEAK
-1.02	0.01109	P18887 XRCC1; DNA repair protein XRCC1	TSPVTASDPAGPSYAAATLQASSAASSA <mark>S</mark> (0. 98)PVSR
-1.02	0.01424	Q14186 TFDP1; Transcription factor Dp-1	VFIDQNLS(1)PGK
-1.02	0.00701	Q9BQG0 MBB1A; Myb-binding protein 1A	EIPSATQ <mark>S</mark> (0.99)PISK
-1.03	0.01988	Q86WB0 NIPA; Nuclear-interacting partner of ALK	SQDATF <mark>S</mark> (1)PGSEQAEK
-1.03	0.01988	Q86WB0 NIPA;Nuclear-interacting partner of ALK	<mark>S</mark> (1)PGPIVSR
-1.03	0.02298	P28749 RBL1; Retinoblastoma-like protein 1	VIAIDSDAE <mark>S</mark> (0.99)PAK
-1.03	0.02058	Q8WVB6CTF18; Chromosome transmission fidelity protein 18 homolog	GDAA <mark>SS(</mark> 0.98)PAPAASVGSSQGGAR
-1.03	0.01424	Q9BVC5 ASHWN; Ashwin	K <mark>S</mark> (0.99)PSGPVK <mark>S</mark> (1)PPLSPVGTTPVK
-1.03	0.01424	Q9BVC5 ASHWN; Ashwin	SPSGPVK <mark>S</mark> (1)PPL <mark>S</mark> (1)PVGTTPVK
-1.03	0.01921	P06400 RB; Retinoblastoma-associated protein	TLQTDSIDSFETQRT(1)PR
-1.04	0.04121	Q9BZQ8 NIBAN; Protein Niban	HNLFEDNMALPSESVS <mark>S</mark> (0.95)LTDLKPPTG S(0.74)NQAS(0.99)PAR
-1.04	0.02901	Q9C0C2 TB182; 182 kDa tankyrase-1-binding protein	VNLFPG <mark>LS</mark> (0.83)PSALK
-1.04	0.04152	Q14684 RRP1B; Ribosomal RNA processing protein 1 homolog B	VAFDPEQKPLHGVLK <mark>T</mark> (0.99)PTS <mark>S(</mark> 0.99)PA SSPLVAK
-1.04	0.04152	Q14684 RRP1B; Ribosomal RNA processing protein 1 homolog B	VAFDPEQKPLHGVLK <mark>T</mark> (0.99)PTSSPAS <mark>S(</mark> 0. 87)PLVAK
-1.05	0.02855	Q9Y6D5 BIG2; Brefeldin A-inhibited guanine nucleotide- exchange protein 2	HLDVDLDRQ <mark>S</mark> (0.99)L <mark>S</mark> (0.90)SIDKNPSER
-1.06	0.03177	O60684 IMA7; Importin subunit alpha-7	METMA <mark>S</mark> (1)PGKDNYR
-1.06	0.03463	P10412 H14; Histone H1.4	SETAPAAPAAPAPAEK <mark>T</mark> (1)PVKK
-1.07	0.02453	Q9ULH1 ASAP1; Arf-GAP with SH3 domain, ANK repeat and PH domain-containing protein 1	QEEIDE <mark>S</mark> (1)DDDLDDKP <mark>S</mark> (1)PIKK
-1.07	0.02453	Q9ULH1 ASAP1; Arf-GAP with SH3 domain, ANK repeat and PH domain-containing protein 1	QEEIDE <mark>S</mark> (1)DDDLDDKP <mark>S</mark> (1)PIKK
-1.07	0.03781	O60890 OPHN1; Oligophrenin-1	<mark>S</mark> (0.96)PSRPILDGK
-1.07	0.00877	Q15149 PLEC; Plectin	AQLEPVA <mark>S</mark> (1)PAK
-1.08	0.00841	Q9UQ35 SRRM2; Serine/arginine repetitive matrix protein 2	HGG <mark>S(</mark> 1)PQPLATT(0.96)PLSQEPVNPPSEA S(0.77)PTR
-1.08	0.00877	Q9BTU6P4K2A; Phosphatidylinositol 4-kinase type 2-alpha	VAAAAGSGP <mark>S(</mark> 1)PPGSPGHDR
-1.09	0.00736	Q96JM3 CHAP1; Chromosome alignment-maintaining phosphoprotein 1	<mark>S</mark> (1)PAG <mark>S</mark> (1)PELR
-1.09	0.00736	Q96JM3 CHAP1; Chromosome alignment-maintaining phosphoprotein 1	<mark>S</mark> (1)PAG <mark>S</mark> (1)PELR
-1.09	0.00736	Q96JM3 CHAP1; Chromosome alignment-maintaining phosphoprotein 1	KPGPPL <mark>S(</mark> 1)PEIR <mark>S(</mark> 1)PAG <mark>S(</mark> 1)PELR
-1.09	0.01753	O96028 NSD2; Histone-lysine N-methyltransferase NSD2	IQDPTEDAEAEDT(0.99)PR
-1.09	0.01820	Q16513 PKN2; Serine/threonine-protein kinase N2	ATSVALPGW <mark>S</mark> (0.92)PSETR
-1.10	0.01235	P08559 ODPA; Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial	YGMGT <mark>S</mark> (0.96)VER

-1.10	0.03934	Q6PL18 ATAD2; ATPase family AAA domain-containing protein 2 LSSAGPRS(1)PYCK		
-1.11	0.00877	O60502 OGA; Protein O-GlcNAcase	S(1)PEMSMQEDCISDIAPMQTDEQTNK	
-1.11	0.01066	Q9ULM3 YETS2; YEATS domain-containing protein 2	ISTASQVSQGTG <mark>S</mark> (0.99)PVPK	
-1.12	0.03677	Q15717 ELAV1; ELAV-like protein 1	NVALLSQLYH <mark>S</mark> (1)PAR	
-1.12	0.03449	Q14847 LASP1; LIM and SH3 domain protein 1	GFSVVADT(1)PELQR	
-1.13	0.00849	Q9UIG0 BAZ1B; Tyrosine-protein kinase BAZ1B	SLSG <mark>S</mark> (1)PLK	
-1.13	0.03449	Q6XZF7 DNMBP; Dynamin-binding protein	HET <mark>S</mark> (0.81)DHEAEEPDCIISEAPTSPLGHLTS EYDTDR	
-1.13	0.00837	P41229 KDM5C; Lysine-specific demethylase 5C	VQGLLENGDSVT <mark>S(</mark> 0.88)PEK	
-1.13	0.04817	Q8WYP5 ELYS; Protein ELYS	TTSFFLN <mark>S</mark> (1)PEKEHQEMDEGSQSLEK	
-1.14	0.01810	Q96JM3 CHAP1; Chromosome alignment-maintaining phosphoprotein 1	KPSPSE <mark>S</mark> (0.76)PEPWKPFPAV <mark>S</mark> (1)PEPR	
-1.14	0.00772	P53985 MOT1; Monocarboxylate transporter 1	EEET <mark>S(</mark> 0.99)IDVAGKPNEVTK	
-1.15	0.00636	A1L390 PKHG3; Pleckstrin homology domain-containing family G member 3	<mark>S</mark> (1)PL <mark>S</mark> (1)PTETFSWPDVR	
-1.15	0.01995	Q9Y5K6 CD2AP; CD2-associated protein	FNGGH <mark>S</mark> (0.99)PTH <mark>S</mark> (1)PEK	
-1.15	0.01995	Q9Y5K6 CD2AP; CD2-associated protein	FNGGH <mark>S</mark> (0.99)PTH <mark>S</mark> (1)PEK	
-1.18	0.03673	Q69YH5 CDCA2; Cell division cycle-associated protein 2	TICTFDSSGFESM <mark>S</mark> (1)PIKETVSSR	
-1.18	0.01988	Q9ULW0 TPX2; Targeting protein for Xklp2	<mark>S</mark> (1)PAFALK	
-1.20	0.01135	P13994 CC130; Coiled-coil domain-containing protein 130	QDKPL <mark>S(</mark> 1)PAGSSQEAADTPDTR	
-1.20	0.00841	Q5T200ZC3HD; Zinc finger CCCH domain-containing protein 13	SKL <mark>S</mark> (1)PSPSLR	
-1.21	0.033	Q14573 ITPR3; Inositol 1,4,5-trisphosphate receptor type 3	LGFVDVQNCI <mark>S(</mark> 1)R	
-1.21	0.01066	Q8N5I9 CL045; Uncharacterized protein C12orf45	IEVLD <mark>S(</mark> 0.99)PASK	
-1.21	0.02322	Q9ULW0 TPX2; Targeting protein for Xklp2	DPQ <mark>T</mark> (1)PVLQTK	
-1.21	0.03287	Q9Y6G9 DC1L1; Cytoplasmic dynein 1 light intermediate chain 1	SVSSNVASV <mark>S</mark> (0.99)PIPAGSK	
-1.22	0.04433	P33981 TTK; Dual specificity protein kinase TTK	YVLGQLVGLN <mark>S</mark> (0.92)PNSILK	
-1.22	0.04448	Q5QJE6 TDIF2; Deoxynucleotidyltransferase terminal-interacting protein 2	QILIAC <mark>S</mark> (1)PVSSVR	
-1.22	0.03983	Q14191 WRN; Werner syndrome ATP-dependent helicase	STEHLSPNDNENDTSYVIE <mark>S</mark> (1)DEDLEMEM LK	
-1.22	0.00825	Q9NRZ9 HELLS; Lymphoid-specific helicase	ETIEL <mark>S</mark> (0.99)PTGRPK	
-1.22	0.03390	Q5SQI0 ATAT; Alpha-tubulin N-acetyltransferase 1	LLLAADPGG <mark>S</mark> (1)PAQR	
-1.24	0.00517	Q7Z2Z1 TICRR; Treslin	SLLFGAMSEM <mark>IS</mark> (0.97)PSEK	
-1.24	0.00701	Q12802 AKP13; A-kinase anchor protein 13	ALQLSN <mark>S</mark> (1)PGASSAFLK	
-1.26	0.02606	P10244 MYBB; Myb-related protein B	TLPF <mark>S</mark> (0.99)PSQFLNFWNK	
-1.26	0.00554	Q14980 NUMA1; Nuclear mitotic apparatus protein 1	VSLEPHQGPG <mark>T</mark> (1)PESK	
-1.27	0.02145	Q14160 SCRIB; Protein scribble homolog	MAESPCSPSGQQPPS(1)PPS(1)PDELPANV K	
-1.27	0.00749	Q969E4 TCAL3; Transcription elongation factor A protein-like 3	GTDD <mark>S</mark> (1)PKDSQEDLQER	
-1.28	0.03132	Q8IXM2 BAP18; Chromatin complexes subunit BAP18	VASGVL <mark>S</mark> (1)PPPAAPPPSSSSVPEAGGPPIK	
-1.28	0.00825	P51991 ROA3; Heterogeneous nuclear ribonucleoprotein A3	MEVKPPPGRPQPD <mark>S</mark> (1)GR	
-1.28	0.01988	Q9BVJ6 UT14A; U3 small nucleolar RNA-associated protein 14 homolog A	EQMIDLQNLLTT(0.75)QSPSVK	
-1.29	0.02501	Q6PGN9 PSRC1; Proline/serine-rich coiled-coil protein 1	L <mark>S</mark> (1)LGPL <mark>S</mark> (1)PEKLEEILDEANR	
-1.29	0.02501	Q6PGN9 PSRC1; Proline/serine-rich coiled-coil protein 1	L <mark>S</mark> (1)LGPL <mark>S</mark> (1)PEKLEEILDEANR	
-1.29	0.01820	Q7L2J0 MEPCE; 7SK snRNA methylphosphate capping enzyme	DITDPLSLNTCTDEGHVVLA <mark>S</mark> (1)PLK	
-1.29	0.00655	Q92797 SYMPK; Symplekin	EER <mark>S</mark> (1)PQTLAPVGEDAMK	
-1.31	0.00311	Q6ZSR9 YJ005; Uncharacterized protein FLJ45252	LGGAVPFAPPEV <mark>S</mark> (1)PEQAK	

-1.31	0.00821	P00533 EGFR; Epidermal growth factor receptor	GSHQIS(1)LDNPDYQQDFFPK	
-1.31	0.01129	P41002 CCNF; Cyclin-F	SCLQCRPP <mark>S</mark> (1)PPESSVPQQQVK	
-1.32	0.03177	Q08945 SSRP1; FACT complex subunit SSRP1	QLSE <mark>S(</mark> 1)FK	
-1.33	0.02288	Q9NYF8 BCLF1; Bcl-2-associated transcription factor 1	EEEWDPEY <mark>T</mark> (1)PK	
-1.33	0.02288	Q9Y2W1 TR150; Thyroid hormone receptor-associated protein 3	NREEEWDPEYT(1)PK	
-1.33	0.00636	Q14181 DPOA2; DNA polymerase alpha subunit B	AIST(0.99)PETPLTK	
-1.33	0.02611	P35568 IRS1; Insulin receptor substrate 1	VNL <mark>S</mark> (1)PNR	
-1.33	0.03680	P16402 H13; Histone H1.3	SETAPLAPTIPAPAEKT(1)PVK	
-1.34	0.01206	Q96JM3 CHAP1; Chromosome alignment-maintaining phosphoprotein 1	KPSG <mark>S</mark> (0.99)PDLWKL <mark>S</mark> (1)PDQR	
-1.34	0.01206	Q96JM3 CHAP1; Chromosome alignment-maintaining phosphoprotein 1	KPSG <mark>S</mark> (0.99)PDLWKL <mark>S</mark> (1)PDQR	
-1.34	0.01066	Q66K74 MAP1S; Microtubule-associated protein 1S	S(1)AS(1)PHDVDLCLVSPCEFEHR	
-1.35	0.02613	075152 ZC11A; Zinc finger CCCH domain-containing protein 11A	KVEAPETNIDKT(1)PK	
-1.39	0.00144	Q8IWS0 PHF6; PHD finger protein 6	TAHNSEADLEE <mark>S(</mark> 1)FNEHELEPS <mark>S(</mark> 0.91)PK	
-1.41	0.04391	O43399 TPD54; Tumor protein D54	NSATFK <mark>S(</mark> 1)FEDR	
-1.42	0.00588	O95297 MPZL1; Myelin protein zero-like protein 1	DYTGCSTSESL <mark>S</mark> (0.99)PVK	
-1.42	0.00548	P78347 GTF2I; General transcription factor II-I	TNT(1)PVKEDWNVR	
-1.43	0.00517	P49792 RBP2; E3 SUMO-protein ligase RanBP2	SAL <mark>S</mark> (0.99)PSK <mark>S</mark> (1)PAK	
-1.43	0.00517	P49792 RBP2; E3 SUMO-protein ligase RanBP2	SAL <mark>S</mark> (0.99)PSK <mark>S</mark> (1)PAK	
-1.43	0.00643	P21359 NF1; Neurofibromin	GSEGYLAATYPTVGQT(0.85)SPR	
-1.43	0.02610	P55327 TPD52; Tumor protein D52	NSPTFK <mark>S</mark> (1)FEEK	
-1.43	0.03719	P00533 EGFR; Epidermal growth factor receptor	DPHYQDPHSTAVGNPE <mark>Y</mark> (1)LNTVQPTCVN STFDSPAHWAQK	
-1.44	0.03328	Q69YH5 CDCA2; Cell division cycle-associated protein 2	GENLENIEPLQVSFAVLS <mark>S</mark> (0.98)PNK	
-1.49	0.00640	Q9NVP2 ASF1B; Histone chaperone ASF1B	LEAIETQDPSLGCGLPLNCT(1)PIK	
-1.50	0.00695	O76021 RL1D1; Ribosomal L1 domain-containing protein 1	FFT <mark>T</mark> (0.88)PSK	
-1.52	0.00342	Q53F19 NCBP3; Nuclear cap-binding protein subunit 3	MISTP <mark>S</mark> (0.99)PK	
-1.52	0.00128	Q8IWS0 PHF6; PHD finger protein 6	TAHNSEADLEESFNEHELEP <mark>SS(</mark> 0.99)PK	
-1.54	0.01631	O60341 KDM1A; Lysine-specific histone demethylase 1A	ASPPGGLAEPPGSAGPQAGPTVVPGSATP METGIAET(0.99)PEGR	
-1.54	0.00164	Q15648 MED1; Mediator of RNA polymerase II transcription subunit 1	LA <mark>S</mark> (1)PMKPVPGT(0.94)PPSSK	
-1.54	0.00164	Q15648 MED1; Mediator of RNA polymerase II transcription subunit 1	LA <mark>S</mark> (1)PMKPVPGT(0.98)PPSSK	
-1.55	0.01852	Q14684 RRP1B; Ribosomal RNA processing protein 1 homolog B	VAFDPEQKPLHGVLKT(0.99)PTSS(0.99)PA SSPLVAK	
-1.55	0.00296	Q9H2D6 TARA; TRIO and F-actin-binding protein	QALDYVELSPLTQA <mark>S</mark> (1)PQR	
-1.55	0.00277	Q01082 SPTB2; Spectrin beta chain, non-erythrocytic 1	AQTLPTSVVTITSE <mark>S(</mark> 0.82)SPGKR	
-1.56	0.01135	P18887 XRCC1; DNA repair protein XRCC1	K <mark>T</mark> (0.98)PSKPPAQL <mark>S</mark> (0.99)PSVPK	
-1.56	0.00216	P17096 HMGA1; High mobility group protein HMG-I/HMG-Y	EPSEVPT(1)PK	
-1.57	0.00112	Q6MZP7 LIN54; Protein lin-54 homolog	IA <mark>IS(</mark> 1)PLK <mark>S</mark> (1)PNK	
-1.57	0.00112	Q6MZP7 LIN54; Protein lin-54 homolog	IA <mark>IS(</mark> 1)PLK <mark>S</mark> (1)PNK	
-1.58	0.00213	Q12888 TP53B; Tumor suppressor p53-binding protein 1	EQLSAQELMESGLQIQK <mark>S</mark> (1)PEPEVLSTQE DLFDQSNK	
-1.59	0.00087	P43487 RANG; Ran-specific GTPase-activating protein	DTHEDHDTS(0.99)TENTDESNHDPQFEPIV SLPEQEIK	
-1.59	0.01109	P08729 K2C7; Keratin, type II cytoskeletal 7	SIHF <mark>SS(</mark> 0.99)PVFTSR	
-1.60	0.00610	Q14684 RRP1B; Ribosomal RNA processing protein 1 homolog B	VAFDPEQKPLHGVLK <mark>T</mark> (0.99)PTSSPAS <mark>S</mark> (0. 87)PLVAK	

-1.60	0.00610	Q14684 RRP1B; Ribosomal RNA processing protein 1 homolog B		
-1.60	0.00131	Q9UJX2 CDC23; Cell division cycle protein 23 homolog	RVS(1)PLNLSSVT(1)P	
-1.60	0.00131	Q9UJX2 CDC23; Cell division cycle protein 23 homolog	RV <mark>S</mark> (1)PLNLSSVT(1)P	
-1.60	0.00144	P22234 PUR6; Multifunctional protein ADE2	EVYELLD <mark>S(</mark> 1)PGK	
-1.61	0.00610	Q96Q89 KI20B; Kinesin-like protein KIF20B	FGDFLQH <mark>S</mark> (0.99)PSILQSK	
-1.64	0.01695	Q5VUA4 ZN318; Zinc finger protein 318	ISAPELLLH <mark>S</mark> (1)PAR	
-1.65	0.01806	075475 PSIP1; PC4 and SFRS1-interacting protein	AVDITT(0.78)PK	
-1.65	0.01372	P07948 LYN; Tyrosine-protein kinase Lyn	AEERPTFDYLQSVLDDFYTATEGQY(1)QQQ P	
-1.65	0.01248	P35251 RFC1; Replication factor C subunit 1	IGEVS <mark>S(</mark> 0.75)PK	
-1.66	0.00476	Q99638 RAD9A; Cell cycle checkpoint control protein RAD9A	DSLLDGHFVLATLSDTDSH <mark>S(</mark> 1)QDLG <mark>S(</mark> 1)P ER	
-1.66	0.01129	Q9UKM9 RALY; RNA-binding protein Raly	TRDDGDEEGLLTHSEEELEHSQDT(0.77)DA DDGALQ	
-1.67	0.00572	Q13330 MTA1; Metastasis-associated protein MTA1	VAPVINNG <mark>S</mark> (0.99)PTILGK	
-1.67	0.00115	Q9BYG3 MK67I; MKI67 FHA domain-interacting nucleolar phosphoprotein	TVDSQGPT(1)PVCT(1)PTFLER	
-1.67	0.00115	Q9BYG3 MK67I; MKI67 FHA domain-interacting nucleolar phosphoprotein	TVDSQGPT(1)PVCT(0.99)PTFLER	
-1.68	0.00131	Q9NR30 DDX21; Nucleolar RNA helicase 2	KAEPSEVDMN <mark>S(</mark> 1)PK	
-1.70	0.01206	Q86YP4 P66A; Transcriptional repressor p66-alpha	GTTATSAQANSTPTSVASVVTSAES(0.92)P ASR	
-1.71	0.03915	Q9NWH9 SLTM; SAFB-like transcription modulator	QAIEEEGGDPDNIELTVSTDT(0.81)PNKKP TK	
-1.71	0.01109	Q99504 EYA3; Eyes absent homolog 3	LSSGDPSTSPSLSQTT(0.88)PSKDTDDQSR	
-1.73	0.00115	Q96JM3 CHAP1; Chromosome alignment-maintaining	PAPSVS(1)PGPWKPIPSVS(1)PGPWKPTPS VSSASWK	
-1.73	0.00115	Q96JM3 CHAP1; Chromosome alignment-maintaining phosphoprotein 1	PAPSVS(1)PGPWKPIPSVS(1)PGPWKPTPS VSSASWK	
-1.74	0.00164	Q9H211 CDT1; DNA replication factor Cdt1	LACRT(1)PS(1)PARPALR	
-1.74	0.00164	Q9H211 CDT1; DNA replication factor Cdt1	LACRT(1)PS(1)PARPALR	
-1.78	0.01698	Q86YP4P66A; Transcriptional repressor p66-alpha	GVLHTF <mark>S(</mark> 0.99)PSPK	
-1.79	0.00131	P11388 TOP2A; DNA topoisomerase 2-alpha	TQMAEVLP <mark>S</mark> (1)PR	
-1.80	0.01135	Q92614 MY18A; Unconventional myosin-XVIIIa	VASGSDLHLTDID <mark>S</mark> (0.92)DSNR	
-1.84	0.00080	Q12834 CDC20; Cell division cycle protein 20 homolog	EAAGPAP <mark>S</mark> (1)PMR	
-1.87	0.00175	Q9UKM9 RALY; RNA-binding protein Raly	TRDDGDEEGLLTH <mark>S</mark> (1)EEELEHSQDTDADD GALQ	
-1.94	0.03692	P27816 MAP4; Microtubule-associated protein 4	DGVLTLANNVT(1)PAKDVPPLSETEATPVPI K	
-1.94	0.00841	P49792 RBP2; E3 SUMO-protein ligase RanBP2	NLFASFPTEESSINYTFKT(1)PEK	
-1.96	0.01235	Q9NQ88 TIGAR; Fructose-2,6-bisphosphatase TIGAR	EQF <mark>S</mark> (0.92)QGSPSNCLETSLAEIFPLGK	
-2.02	0.00932	Q14978NOLC1; Nucleolar and coiled-body phosphoprotein 1	VAGGAAPSKP <mark>AS(</mark> 0.95)AK	
-2.10	0.01154	P06748 NPM; Nucleophosmin	MQA <mark>S(</mark> 1)IEK	
-2.16	0.01631	P19338 NUCL; Nucleolin	VAVAT(1)PAK	
-2.17	0.00399	Q9NQS7 INCE; Inner centromere protein	H <mark>S</mark> (1)PIAPS <mark>S</mark> (0.92)PSPQVLAQK	
-2.23	0.00199	Q9H1E3NUCKS; Nuclear ubiquitous casein and cyclin- dependent kinase substrate 1	ATVT(0.99)PS(1)PVKGK	
-2.23	0.00199	Q9H1E3NUCKS; Nuclear ubiquitous casein and cyclin- dependent kinase substrate 1	ATV <mark>T(</mark> 0.99)P <mark>S(</mark> 1)PVKGK	
-2.23	0.00131	Q14978 NOLC1; Nucleolar and coiled-body phosphoprotein 1	S(1)PAVKPAAAPK	
-2.49	0.00399	O60318 GANP; Germinal-center associated nuclear protein	KPGDGEVSPSTEDAPFQH <mark>S(</mark> 1)PLGK	

-2.50	0.00021	P78332 RBM6; RNA-binding protein 6	EGETQGVAFEHESPADFQN <mark>S(</mark> 1)Q <mark>S(</mark> 1)PVQ DQDK
-2.84	0.00277	Q14978 NOLC1; Nucleolar and coiled-body phosphoprotein 1	VADN <mark>S</mark> (1)FDAK
-3.51	0.00013	Q14978NOLC1; Nucleolar and coiled-body phosphoprotein 1	LQT(1)PNT(1)FPK
-3.51	0.00013	Q14978NOLC1; Nucleolar and coiled-body phosphoprotein 1	LQT(1)PNT(1)FPK
-3.53	0.00017	P18887 XRCC1; DNA repair protein XRCC1	KT(0.98)PSKPPAQL <mark>S</mark> (0.99)PSVPK
-3.53	0.00017	P18887 XRCC1; DNA repair protein XRCC1	KT(0.98)PSKPPAQL <mark>S</mark> (0.99)PSVPK

Supplemental Table 3. Significant changes in relative total protein abundance levels after ²²⁵Ac-PP-F11N treatment in A431/CCKBR cells. MS-based quantification shown as log_2 ratio, q < 0.05.

LOG ₂ RATIO: ²²⁵ Ac-PP- F11N/CON	<i>q</i> -value	UniProt	PROTEIN
1.54	0.0186	Q9H8M7 F188A_HUMAN	Ubiquitin carboxyl-terminal hydrolase MINDY-3
1.10	0.0496	P47974 TISD_HUMAN	mRNA decay activator protein ZFP36L2
-1.65	0.0192	Q96S97 MYADM_HUMAN	Myeloid-associated differentiation marker

Supplemental Table 4. Significantly enriched (*P*<0.01) biological processes and signal transduction pathways in response to ²²⁵Ac-PP-F11N treatment.

225 Ac-PP-F11N	Fold En.	P-value		
RNA transcription and processing				
Regulation of transcription from RNA polymerase II promoter (BRCA1, FOSL1, HTATSF1, JUND, LRRFIP1, RBBP8, RB1, RBL1, SLTM, SNW1, CHD4, FOXK1, GTF2I, KDM1A, MAPK14, NUCKS1, TCEAL3,TFDP1) GOTERM_BP	3.0	1.0E-4		
Transcription, DNA-template (ATAD2, BCLAF1, BRCA1, EYA3, GATAD2A, HTATSF1, LRRFIP1, MYBBP1A, PSIP1, PHF6, RALY, RB1, RBL1, SLTM, SP110, WHSC1, ADNP, ASF1B, BAZ1B, CBX3, CHD4, DNTTIP2,FOXK1, HELLS, HDAC9, LIN54, KDM1A, KDM5C, MTA1, MAPK14, PNN, PKN2, RFC1, TCEAL3, TFDP1, TP53BP1, TP53, UIMC1, ZMYND11, ZNF280C, ZNF318, ZNF83) GOTERM_BP	1.6	2.6E-3		
mRNA splicing, via spliceosome (ELAVL1, HTATSF1, RALY, SNW1, YBX1, HNRNPA3, HNRNPU, METTL3, PNN, PABPN1, SRRM2, SRRT) GOTERM_BP	4.0	2.2E-4		
Regulation of mRNA stability (ELAVL1, SERBP1, SET, ZFP36L2, ZFP36, PSMD4, PSMA5) GOTERM_BP	5.0	2.7E-3		
mRNA transport (AHCTF1, ZFP36, HNRNPA3, MCM3AP, NCBP3) GOTERM_BP	7.9	3.6E-3		
Cell morphology, adhesion, and phenotype				
Cell-cell adhesion (AHNAK, ASAP1, LASP1, LRRFIP1, NUMB, PPFIBP1, RANBP1, SERBP1, WASF2, ADD1, CAST, LAD1, PAICS, PLEC, PKN2, RSL1D1, SPTBN1, TNKS1BP1, TJP1) GOTERM_BP	5.2	2.9E-8		
Transport and protein modifications				
Protein sumoylation (BRCA1, RANBP2, WRN, INCENP, MDC1, MTA1, NUP35, SMC1A, TOP2A, TRIM28, TP53BP1, TP53) GOTERM_BP	7.6	5.1E-7		
Positive regulation of glucose import (ARPP19, IRS1, IRS2, MAPK14) GOTERM_BP	9.9	7.5E-3		



Supplemental Figure 1. Viability analysis in ATM, HDAC, and p38 inhibitor-treated cells. Viability of A431/CCKBR cells 24 h after incubation with 1, 2, 5, and 10 μ M of AZD1390, TMP269, SB202190, and SAHA. Results are shown as % viability compared with control cells.



Supplemental Figure 2. Treatment with HDAC inhibitor SAHA sensitizes A431/CCKBR cells to 225 Ac-PP-F11N. Cell viability 24 h after treatment with 3 kBq/ml 225Ac-PP-F11N or 2 μ M SAHA alone or in combination 225 Ac-PP-F11N. Bars represent mean ± SD. **p* < 0.05.



Supplemental Figure 3. Body weight of A431/CCKBR-tumor bearing nude mice during PRRT with radiolabeled minigastrin and HDAC inhibitor SAHA. (A) Schematic representation of the treatment. (B) Body weight of control and treated mice with 30 kBq ²²⁵Ac-PP-F11N alone or in combination with 10 doses of 50 mg/kg SAHA administrated daily. Values represent mean ± SD.