Supplementary

Table S1 Abbreviation list of 33 cancers from the TCGA

Abbreviation	Full term
ACC	Adrenocortical carcinoma
BLCA	Bladder urothelial carcinoma
BRCA	Breast invasive carcinoma
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma
CHOL	Cholangiocarcinoma
COAD	Colon adenocarcinoma
COADREAD	Colon adenocarcinoma/rectum adenocarcinoma esophageal carcinoma
DLBC	Lymphoid neoplasm diffuse large B-cell lymphoma
ESCA	Esophageal carcinoma
FPPP	FFPE pilot phase II
GBM	Glioblastoma multiforme
GBMLGG	Glioma
HNSC	Head and neck squamous cell carcinoma
KICH	Kidney chromophobe
KIPAN	Pan-kidney cohort (KICH + KIRC + KIRP)
KIRC	Kidney renal clear cell carcinoma
KIRP	Kidney renal papillary cell carcinoma
LAML	Acute myeloid leukemia
LGG	Brain lower grade glioma
LIHC	Liver hepatocellular carcinoma
LUAD	Lung adenocarcinoma
LUSC	Lung squamous cell carcinoma
MESO	Mesothelioma
OV	Ovarian serous cystadenocarcinoma
PAAD	Pancreatic adenocarcinoma
PCPG	Pheochromocytoma and Paraganglioma
PRAD	Prostate adenocarcinoma
READ	Rectum adenocarcinoma
SARC	Sarcoma
SKCM	Skin cutaneous melanoma
STAD	Stomach adenocarcinoma
STES	Stomach and esophageal carcinoma
TGCT	Testicular germ cell tumors
THCA	Thyroid carcinoma
THYM	Thymoma
UCEC	Uterine corpus endometrial carcinoma
UCS	Uterine carcinosarcoma
UVM	Uveal melanoma

Table S2 Basic information of GEO datasets included in this study

Cancer type	Datasets	Sample type	
		Normal (n)	Tumor (n)
BLCA	GSE13507	68	188
BRCA	GSE70947	148	148
CESC	GSE63514	100	28
CHOL	GSE26566	36	100
COAD	GSE166427	148	98
ESCA	GSE53625	179	179
GBM	GSE108474	28	295
HNSC	GSE13601	26	31
KIRP	GSE26574	10	34
LIHC	GSE89377	67	41
LUAD	GSE75037	83	83
LUSC	GSE18842	45	46

GEO, Gene Expression Omnibus.

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Table S3 RPN1 expression for response and non-response based on pre-treatment samples in each dataset

Study	Cancers	Anti-target	Response mean	Non-response mean	Log_2FC	P value	FDR
IMvigor210	Urothelial cancer	Anti-PD-L1	15,324.16	12,252.90	0.24	0.001	0.011
SRP217040	Non-small cell lung cancer	Anti-PD-L1	11,460.00	8,264.00	0.507	0.024	0.213
SRP230414	Melanoma	Anti-PD-1	17,035.00	20,126.00	−0.455	0.023	0.345
SRP070710	Melanoma	Anti-PD-1	16,011.00	17,133.00	−0.369	0.068	0.468
SRP011540	Melanoma	Anti-PD-1	5,509.50	5,521.00	0.085	0.329	0.63
SRP150548	Melanoma	Anti-PD-1	6,959.00	6,152.00	0.862	0.179	0.634
SRP155030	Glioblastoma	Anti-PD-1	4,549.50	4,487.50	0.291	0.18	0.724
ERP105482	Melanoma	Anti-PD-1	6,912.00	6,649.50	0.151	0.371	0.743
SRP183455	Non-small cell lung cancer	Anti-PD-1	6,056.00	6,587.00	0.317	0.478	0.774
ERP105482	Melanoma	Anti-PD-1 + anti-CTLA4	9,098.00	8,832.00	0.135	0.478	0.84
ERP107734	Gastric cancer	Anti-PD-1	10,346.00	8,400.00	0.052	0.703	0.875
GSE111636	Urothelial cancer	Anti-PD-1	3.97	3.67	0.306	0.207	0.91
SRP094781	Melanoma	Anti-PD-1	8,755.00	10,184.00	−0.059	0.683	0.936
PMID:33806963	Renal cell carcinoma	Anti-PD-1	12.6	12.27	0.332	0.214	0.939
GSE176307	Urothelial cancer	Anti-PD-1	12.72	12.65	0.069	0.608	0.954
SRP128156	RCC	Anti-PD-1/anti-PD-1 + anti-CTLA4	8,271.50	7,926.00	−0.168	0.494	0.959
PMID:32472114	Renal cell carcinoma	Anti-PD-1	34.73	34.78	−0.05	0.616	0.981
TCGA	Melanoma	Anti-CTLA4	12.56	12.92	−0.357	0.426	0.995
SRP011540	Melanoma	Anti-CTLA4	8,884.00	8,418.00	−0.027	0.905	0.996
GSE122220	Melanoma	Anti-PD-1	11.91	11.84	0.074	0.819	0.996
SRP250849	Melanoma	Anti-PD-1	3,342.67	3,798.50	−0.004	0.993	0.999
GSE99070	Malignant pleural mesothelioma	Anti-PD-1	9.97	9.69	0.283	0.33	1
GSE67501	Renal cell carcinoma	Anti-PD-1	11.24	11.35	−0.113	0.529	1
SRP128156	Renal cell carcinoma	Anti-PD-1 + anti-CTLA4	10,661.00	3,044.00	0.975	0.246	1
SRP128156	Renal cell carcinoma	Anti-PD-1	8,211.00	8,138.00	−0.185	0.592	1

FC, fold change; FDR, false discovery rate; TCGA, The Cancer Genome Atlas.

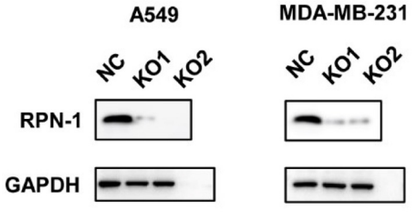

Figure S1 Analysis the expression of A549 and MDA-MB-231 with knockout RPN-1. Western blot analysis was conducted to assess the expression levels of RPN1 in the A549 and MDA-MB-231 cell lines following gene knockout. The NC group received no gene editing, while knockout groups KO1 and KO2 represent two distinct gene ablation variants. GAPDH was employed as a loading control to ensure equal protein quantification across samples. NC, negative control; KO, knockout.

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Table S4 KEGG functional enrichment analyses of *RPN1* in pan-cancer

Cancer types	Description	Set size	Enrichment score	NES	P value	P.adjust	q-value	rank	Leading_edge
BLCA	KEGG_TASTE_TRANSDUCTION	51	−0.775669872	−2.12754	0.022727	0.24031	0.224398	1280	tags =45%, list =7%, signal =42%
	KEGG_PORPHYRIN_AND_CHLOROPHYLL_METABOLISM	39	−0.772544046	−2.07528	0.022727	0.24031	0.224398	1552	tags =36%, list =8%, signal =33%
	KEGG_ASCORBATE_AND_ALDARATE_METABOLISM	23	−0.81823678	−1.9752	0.022727	0.24031	0.224398	1552	tags =52%, list =8%, signal =48%
	KEGG_PENTOSE_AND_GLUCURONATE_INTERCONVERSIONS	26	−0.778617435	−1.96123	0.022727	0.24031	0.224398	1552	tags =46%, list =8%, signal =42%
	KEGG_DRUG_METABOLISM_CYTOCHROME_P450	68	−0.63209882	−1.86861	0.021277	0.24031	0.224398	2594	tags =46%, list =14%, signal =40%
	KEGG_RETINOL_METABOLISM	62	−0.634345171	−1.82002	0.022727	0.24031	0.224398	1831	tags =39%, list =10%, signal =35%
	KEGG_DRUG_METABOLISM_OTHER_ENZYMES	49	−0.656754345	−1.81241	0.023256	0.24031	0.224398	1552	tags =35%, list =8%, signal =32%
	KEGG_STEROID_HORMONE_BIOSYNTHESIS	53	−0.651739415	−1.80872	0.023256	0.24031	0.224398	2205	tags =42%, list =11%, signal =37%
	KEGG_METABOLISM_OF_XENOBIOTICS_BY_CYTOCHROME_P450	66	−0.613447641	−1.79924	0.022727	0.24031	0.224398	2594	tags =47%, list =14%, signal =41%
	KEGG_SYSTEMIC_LUPUS_ERYTHEMATOSUS	133	0.564458628	1.735455	0.016667	0.24031	0.224398	3493	tags =42%, list =18%, signal =35%
	KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	80	0.551794825	1.598971	0.016129	0.24031	0.224398	3461	tags =39%, list =18%, signal =32%
	KEGG_STARCH_AND_SUCROSE_METABOLISM	48	−0.574254754	−1.57919	0.022727	0.24031	0.224398	1816	tags =33%, list =9%, signal =30%
	KEGG_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	263	0.475283809	1.56346	0.015385	0.24031	0.224398	3245	tags =39%, list =17%, signal =33%
	KEGG_CELL_CYCLE	124	0.511742639	1.561072	0.016949	0.24031	0.224398	5011	tags =46%, list =26%, signal =34%
	KEGG_NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY	131	0.500650886	1.540065	0.016393	0.24031	0.224398	4092	tags =40%, list =21%, signal =31%
	KEGG_JAK_STAT_SIGNALING_PATHWAY	155	0.479263926	1.499954	0.016393	0.24031	0.224398	3245	tags =32%, list =17%, signal =27%
	KEGG_OLFACTORY_TRANSDUCTION	382	0.427092884	1.452915	0.015385	0.24031	0.224398	882	tags =26%, list =5%, signal =25%
	KEGG_CALCIUM_SIGNALING_PATHWAY	177	−0.409269882	−1.33934	0.021277	0.24031	0.224398	3584	tags =32%, list =19%, signal =26%
	KEGG_GRAFT_VERSUS_HOST_DISEASE	37	0.68669566	1.723974	0.032787	0.320966	0.299714	4714	tags =70%, list =25%, signal =53%
	KEGG_LEISHMANIA_INFECTION	69	0.541447196	1.47671	0.035088	0.326316	0.304709	5299	tags =48%, list =28%, signal =35%
	KEGG_ARACHIDONIC_ACID_METABOLISM	58	−0.521935183	−1.45406	0.046512	0.391579	0.365651	3672	tags =48%, list =19%, signal =39%
BRCA	KEGG_OLFACTORY_TRANSDUCTION	382	−0.826392141	−2.69726	0.01087	0.599034	0.58649	1500	tags =66%, list =8%, signal =62%
	KEGG_DNA_REPLICATION	36	0.691735965	1.919958	0.038462	0.599034	0.58649	4441	tags =75%, list =23%, signal =58%
	KEGG_FOLATE_BIOSYNTHESIS	11	0.863989757	1.882977	0.025641	0.599034	0.58649	141	tags =27%, list =1%, signal =27%
	KEGG_TASTE_TRANSDUCTION	51	−0.699560364	−1.84802	0.013333	0.599034	0.58649	2220	tags =45%, list =12%, signal =40%
	KEGG_GRAFT_VERSUS_HOST_DISEASE	37	0.638696146	1.787945	0.038462	0.599034	0.58649	2628	tags =38%, list =14%, signal =33%
	KEGG_RIBOSOME	87	0.501222135	1.674301	0.04	0.599034	0.58649	9368	tags =99%, list =49%, signal =51%
	KEGG_AUTOIMMUNE_THYROID_DISEASE	50	−0.626514685	−1.6697	0.013158	0.599034	0.58649	1033	tags =26%, list =5%, signal =25%
	KEGG_PROTEASOME	44	0.559477516	1.549183	0.041667	0.599034	0.58649	4854	tags =84%, list =25%, signal =63%
	KEGG_PRION_DISEASES	35	−0.581057426	−1.46398	0.040541	0.599034	0.58649	3291	tags =26%, list =17%, signal =21%
	KEGG_VIRAL_MYOCARDITIS	68	−0.521890268	−1.4424	0.025974	0.599034	0.58649	2270	tags =16%, list =12%, signal =14%
	KEGG_COMPLEMENT_AND_COAGULATION_CASCADES	69	−0.521169303	−1.44182	0.026316	0.599034	0.58649	5025	tags =51%, list =26%, signal =38%
	KEGG_RIG_I_LIKE_RECEPTOR_SIGNALING_PATHWAY	71	−0.510927023	−1.41491	0.026316	0.599034	0.58649	901	tags =14%, list =5%, signal =13%
	KEGG_NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION	270	−0.40665914	−1.28715	0.045977	0.599034	0.58649	2575	tags =34%, list =13%, signal =30%
CESC	KEGG_CYTOSOLIC_DNA_SENSING_PATHWAY	55	0.835769783	2.002696	0.017544	0.405229	0.405229	808	tags =16%, list =4%, signal =16%
	KEGG_RIG_I_LIKE_RECEPTOR_SIGNALING_PATHWAY	71	0.783403458	1.921115	0.016949	0.405229	0.405229	808	tags =13%, list =4%, signal =12%
	KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	80	0.766108716	1.890643	0.016667	0.405229	0.405229	1188	tags =15%, list =6%, signal =14%
	KEGG_REGULATION_OF_AUTOPHAGY	35	0.871449753	1.843614	0.018868	0.405229	0.405229	808	tags =29%, list =4%, signal =27%
	KEGG_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	102	0.70585673	1.793689	0.017241	0.405229	0.405229	808	tags =9%, list =4%, signal =8%
	KEGG_AUTOIMMUNE_THYROID_DISEASE	50	0.740487679	1.714448	0.019608	0.405229	0.405229	808	tags =18%, list =4%, signal =17%
	KEGG_NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY	131	0.635740396	1.710937	0.017857	0.405229	0.405229	1188	tags =9%, list =6%, signal =9%
	KEGG_OLFACTORY_TRANSDUCTION	382	0.50091399	1.513406	0.019231	0.405229	0.405229	833	tags =27%, list =4%, signal =27%
	KEGG_JAK_STAT_SIGNALING_PATHWAY	155	0.53932737	1.463154	0.018519	0.405229	0.405229	1758	tags =11%, list =9%, signal =10%
CHOL	KEGG_FOLATE_BIOSYNTHESIS	11	0.918388993	1.656381	0.022727	1	1	596	tags =27%, list =3%, signal =26%
	KEGG_MATURITY_ONSET_DIABETES_OF_THE_YOUNG	25	0.789171776	1.587703	0.041667	1	1	1706	tags =40%, list =9%, signal =36%
	KEGG_ARRHYTHMOGENIC_RIGHT_VENTRICULAR_CARDIOMYOPATHY_ARVC	74	−0.626732046	−1.5341	0.039216	1	1	3178	tags =35%, list =17%, signal =29%
	KEGG_CARDIAC_MUSCLE_CONTRACTION	77	−0.615117963	−1.51462	0.039216	1	1	1967	tags =19%, list =10%, signal =18%
	KEGG_OLFACTORY_TRANSDUCTION	382	−0.506242236	−1.45919	0.022222	1	1	839	tags =20%, list =4%, signal =20%
COAD	KEGG_OLFACTORY_TRANSDUCTION	382	−0.757080341	−1.64506	0.009901	0.67029	0.67029	1775	tags =55%, list =9%, signal =51%
	KEGG_TASTE_TRANSDUCTION	51	−0.781820751	−1.58799	0.01087	0.67029	0.67029	1721	tags =43%, list =9%, signal =39%
	KEGG_RIG_I_LIKE_RECEPTOR_SIGNALING_PATHWAY	71	−0.665782331	−1.4216	0.010309	0.67029	0.67029	1140	tags =15%, list =6%, signal =15%
	KEGG_NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION	270	−0.592191954	−1.27758	0.019802	0.915842	0.915842	3974	tags =47%, list =21%, signal =38%
	KEGG_CYTOSOLIC_DNA_SENSING_PATHWAY	55	−0.671224693	−1.38524	0.031915	1	1	1140	tags =16%, list =6%, signal =15%
KIRP	KEGG_GRAFT_VERSUS_HOST_DISEASE	37	0.721837787	1.735208	0.025641	0.676364	0.669856	3966	tags =78%, list =21%, signal =62%
	KEGG_CHEMOKINE_SIGNALING_PATHWAY	187	0.555980774	1.663481	0.034483	0.676364	0.669856	3621	tags =43%, list =19%, signal =35%
	KEGG_CELL_ADHESION_MOLECULES_CAMS	131	0.550284405	1.609644	0.030303	0.676364	0.669856	3625	tags =45%, list =19%, signal =37%
	KEGG_OLFACTORY_TRANSDUCTION	382	−0.571963663	−1.58599	0.012195	0.676364	0.669856	1393	tags =44%, list =7%, signal =41%
	KEGG_COMPLEMENT_AND_COAGULATION_CASCADES	69	0.599400626	1.546885	0.04	0.676364	0.669856	3022	tags =54%, list =16%, signal =45%
	KEGG_LEISHMANIA_INFECTION	69	0.597794875	1.542741	0.04	0.676364	0.669856	3611	tags =52%, list =19%, signal =43%
	KEGG_PROXIMAL_TUBULE_BICARBONATE_RECLAMATION	23	−0.775788034	−1.53592	0.016129	0.676364	0.669856	2496	tags =35%, list =13%, signal =30%
	KEGG_INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION	46	0.635841441	1.52564	0.032258	0.676364	0.669856	2972	tags =59%, list =15%, signal =50%
	KEGG_HEMATOPOIETIC_CELL_LINEAGE	85	0.542853368	1.49999	0.032258	0.676364	0.669856	3040	tags =55%, list =16%, signal =47%
	KEGG_LYSOSOME	121	0.512473347	1.491893	0.026316	0.676364	0.669856	6400	tags =58%, list =33%, signal =39%
	KEGG_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	263	0.458157968	1.407721	0.034483	0.676364	0.669856	3087	tags =46%, list =16%, signal =39%
LUAD	KEGG_OLFACTORY_TRANSDUCTION	382	−0.807733285	−2.33266	0.010101	0.341912	0.340557	991	tags =55%, list =5%, signal =53%
	KEGG_RIG_I_LIKE_RECEPTOR_SIGNALING_PATHWAY	71	−0.717814912	−1.77533	0.0125	0.341912	0.340557	1365	tags =20%, list =7%, signal =18%
	KEGG_TASTE_TRANSDUCTION	51	−0.757505853	−1.74236	0.013889	0.341912	0.340557	1393	tags =41%, list =7%, signal =38%
	KEGG_CYTOSOLIC_DNA_SENSING_PATHWAY	55	−0.732839374	−1.68825	0.014706	0.341912	0.340557	623	tags =16%, list =3%, signal =16%
	KEGG_AUTOIMMUNE_THYROID_DISEASE	50	−0.695642664	−1.60615	0.013889	0.341912	0.340557	623	tags =28%, list =3%, signal =27%
	KEGG_REGULATION_OF_AUTOPHAGY	35	−0.724265417	−1.54246	0.014085	0.341912	0.340557	623	tags =26%, list =3%, signal =25%
	KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	80	−0.606641741	−1.51632	0.0125	0.341912	0.340557	623	tags =11%, list =3%, signal =11%
	KEGG_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	102	−0.558293712	−1.46164	0.011905	0.341912	0.340557	3403	tags =22%, list =18%, signal =18%
	KEGG_PROTEASOME	44	0.686548583	1.802937	0.03125	0.611842	0.609418	5543	tags =91%, list =29%, signal =65%
	KEGG_NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION	270	−0.466064432	−1.31121	0.041667	0.611842	0.609418	2689	tags =34%, list =14%, signal =30%
LUSC	KEGG_OLFACTORY_TRANSDUCTION	382	0.87655911	2.220534	0.010101	0.379592	0.371643	907	tags =57%, list =5%, signal =55%
	KEGG_REGULATION_OF_AUTOPHAGY	35	0.873492442	1.792825	0.014286	0.379592	0.371643	711	tags =26%, list =4%, signal =25%
	KEGG_CYTOSOLIC_DNA_SENSING_PATHWAY	55	0.845811102	1.791346	0.013699	0.379592	0.371643	711	tags =15%, list =4%, signal =14%
	KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	80	0.80033631	1.728304	0.013333	0.379592	0.371643	1356	tags =15%, list =7%, signal =14%
	KEGG_RIG_I_LIKE_RECEPTOR_SIGNALING_PATHWAY	71	0.782945458	1.703603	0.013333	0.379592	0.371643	711	tags =11%, list =4%, signal =11%
	KEGG_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	102	0.728217286	1.635741	0.012048	0.379592	0.371643	711	tags =8%, list =4%, signal =8%
	KEGG_AUTOIMMUNE_THYROID_DISEASE	50	0.772392257	1.61047	0.014085	0.379592	0.371643	711	tags =16%, list =4%, signal =15%
	KEGG_INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION	46	−0.629462771	−1.68449	0.030303	0.6	0.587436	3129	tags =37%, list =16%, signal =31%
	KEGG_GLYCOSAMINOGLYCAN_BIOSYNTHESIS_HEPARAN_SULFATE	26	−0.68319187	−1.55322	0.028571	0.6	0.587436	2165	tags =35%, list =11%, signal =31%
	KEGG_INOSITOL_PHOSPHATE_METABOLISM	54	−0.55819397	−1.53354	0.032258	0.6	0.587436	5610	tags =54%, list =29%, signal =38%
	KEGG_ECM_RECEPTOR_INTERACTION	84	−0.553498609	−1.60807	0.04	0.62	0.607018	5657	tags =55%, list =29%, signal =39%
	KEGG_PHOSPHATIDYLINOSITOL_SIGNALING_SYSTEM	76	−0.556455883	−1.59193	0.037037	0.62	0.607018	5610	tags =57%, list =29%, signal =40%
	KEGG_NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY	131	0.618667475	1.444146	0.046512	0.664286	0.650376	1356	tags =10%, list =7%, signal =9%

RPN1, ribophorin I; KEGG, Kyoto Encyclopedia of Genes and Genomes.

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