



**Supplementary Figure S1.** SET8 expressions and H4K20me1 dynamic changes after X-ray or carbon ion radiation. (A) Relative SET8 mRNA expression was measured by qRT-PCR at indicated time points in A549 cells after 4 Gy X-ray irradiation. GAPDH was used as internal controls. (B) SET8 and H4K20me1 levels in A549 cells at indicated time points after 4 Gy X-ray radiation were measured by western blot assay. (C) Relative SET8 mRNA expression was measured by qRT-PCR at indicated time points in A549 cells after 2 Gy Carbon irradiation. (D) SET8 and H4K20me1 levels in A549 cells at indicated time points after 2 Gy Carbon radiation were measured by western blot assay. Significance was determined by unpaired *t*-test. \**P* < 0.05; \*\**P* < 0.01.

**Supplementary Table S1.** sgRNA used in CRISPR/Cas9 knockout experiments

Target	Sequence (5'-3')
Human-SET8-sg1	TTTAGGAGAACGTATTTACC
Human-SET8-sg2	GCACGTGACTACCTGCAGCT
Mouse-SET8-sg1	AGTATCTGAGCAAAACCTAC
Mouse-SET8-sg1	TCCGGAACTCCTCCGCACA

**Supplementary Table S2.** Oligonucleotide primers for qRT-PCR

Genes	Upstream primer (5'-3')	Downstream primer (5'-3')
SET8	CGCAAACCTACGGATTTC	CGATGAGGTC AATCTTCATT
GAPDH	GTCTCTCTGACTTCAACAGCG	ACCACCTGTTGCTGTAGCCAA

**Supplementary Table S3.** Gene expression signatures in SET8-KO A549 cells

Seq_id	(VC) fpkm	(KO)3_7_fpkm	log2FC(KO/VC)	Regulate	Description
ENSG00000264148	0	49.1764	5.61989422	up	-
ENSG00000236991	0.330355	3.76492	3.510530124	up	-
ENSG00000088448	41.5497	364.193	3.131793228	up	ankyrin repeat domain 10 [Source:HGNC Symbol;Acc:20265]
ENSG00000185437	0	8.08694	3.015593908	up	SH3 domain binding glutamic acid-rich protein [Source:HGNC Symbol;Acc:10822]
ENSG00000228950	0	7.66067	2.937470575	up	-
ENSG00000271267	0	5.72202	2.51652454	up	-
ENSG00000232859	1.14869	6.19551	2.43123354	up	LYR motif containing 9 [Source:HGNC Symbol;Acc:27314]
ENSG00000172339	1.08544	5.63913	2.377192622	up	asparagine-linked glycosylation 14 homolog (S. cerevisiae) [Source:HGNC Symbol;Acc:28287]
ENSG00000213420	1.27423	5.78869	2.183611189	up	glypican 2 [Source:HGNC Symbol;Acc:4450]
ENSG00000131095	0.961888	4.15931	2.112403391	up	glial fibrillary acidic protein [Source:HGNC Symbol;Acc:4235]
ENSG00000185920	3.25398	13.6198	2.065428229	up	patched 1 [Source:HGNC Symbol;Acc:9585]
ENSG00000234160	0	3.97046	1.989306161	up	-
ENSG00000241769	1.82417	7.01286	1.942762742	up	-
ENSG00000153291	1.65069	6.24826	1.92038528	up	solute carrier family 25, member 27 [Source:HGNC Symbol;Acc:21065]
ENSG00000254335	0	3.74532	1.905088988	up	cadherin 12 (N-cadherin 2) pseudogene 1 [Source:HGNC Symbol;Acc:37698]
ENSG00000230438	1.00366	3.68563	1.876640622	up	-
ENSG00000170899	1.78022	5.97155	1.746049911	up	glutathione S-transferase alpha 4 [Source:HGNC Symbol;Acc:4629]
ENSG00000104205	1.80144	5.94424	1.722341765	up	serum/glucocorticoid regulated kinase family, member 3 [Source:HGNC Symbol;Acc:10812]
ENSG00000139946	1.0563	3.48076	1.72038271	up	pellino E3 ubiquitin protein ligase family member 2 [Source:HGNC Symbol;Acc:8828]
ENSG00000137843	1.61001	5.23319	1.70062099	up	p21 protein (Cdc42/Rac)-activated kinase 6 [Source:HGNC Symbol;Acc:16061]
ENSG00000246273	6.43651	18.854	1.550520085	up	SBF2 antisense RNA 1 [Source:HGNC Symbol;Acc:27438]
ENSG00000176371	3.07709	8.49372	1.464829909	up	zinc finger and SCAN domain containing 2 [Source:HGNC Symbol;Acc:20994]
ENSG00000080298	1.3528	3.72538	1.461439027	up	regulatory factor X, 3 (influences HLA class II expression) [Source:HGNC Symbol;Acc:9984]
ENSG00000133794	5.24692	13.2361	1.334935398	up	aryl hydrocarbon receptor nuclear translocator-like [Source:HGNC Symbol;Acc:701]
ENSG00000111850	2.28058	5.72774	1.328565227	up	small integral membrane protein 8 [Source:HGNC Symbol;Acc:21401]
ENSG00000126070	4.95836	12.1416	1.292023623	up	eukaryotic translation initiation factor 2C, 3 [Source:HGNC Symbol;Acc:18421]
ENSG00000154781	6.58946	15.389	1.223667339	up	coiled-coil domain containing 174 [Source:HGNC Symbol;Acc:28033]
ENSG00000111490	5.02417	11.7049	1.220155423	up	TBC1 domain family, member 30 [Source:HGNC Symbol;Acc:29164]
ENSG00000112183	2.14386	4.84626	1.17666111	up	RNA binding motif protein 24 [Source:HGNC Symbol;Acc:21539]
ENSG00000162433	5.88931	13.2923	1.174420239	up	adenylate kinase 4 [Source:HGNC Symbol;Acc:363]
ENSG00000189144	3.3689	7.60021	1.173761677	up	zinc finger protein 573 [Source:HGNC Symbol;Acc:26420]
ENSG00000267100	1.88424	4.19986	1.156358501	up	ILF3 antisense RNA 1 (head to head) [Source:HGNC Symbol;Acc:27115]
ENSG00000147654	6.32929	13.8479	1.129551635	up	estrogen receptor binding site associated, antigen, 9 [Source:HGNC Symbol;Acc:3123]
ENSG00000180447	1.91579	4.12663	1.107024662	up	growth arrest-specific 1 [Source:HGNC Symbol;Acc:4165]
ENSG00000254870	17.3676	37.3119	1.103237423	up	ATP6V1G2-DDX39B readthrough (non-protein coding) [Source:HGNC Symbol;Acc:41999]

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Seq_id	(VC) fpkm	(KO)3_7_fpkm	log2FC(KO/VC)	Regulate	Description
ENSG00000143622	14.5221	30.7865	1.08404777	up	Ras-like without CAAX 1 [Source:HGNC Symbol;Acc:10023]
ENSG00000168283	5.71889	12.116	1.083106422	up	BMI1 polycomb ring finger oncogene [Source:HGNC Symbol;Acc:1066]
ENSG00000178537	8.94604	18.9266	1.081094153	up	solute carrier family 25 (carnitine/acylcarnitine translocase), member 20 [Source:HGNC Symbol;Acc:1421]
ENSG00000047617	6.34087	13.2084	1.058703012	up	anoctamin 2 [Source:HGNC Symbol;Acc:1183]
ENSG00000160404	9.5724	19.6562	1.038031853	up	torsin family 2, member A [Source:HGNC Symbol;Acc:11996]
ENSG00000116711	2.30078	4.72253	1.037436921	up	phospholipase A2, group IVA (cytosolic, calcium-dependent) [Source:HGNC Symbol;Acc:9035]
ENSG00000183579	1.75972	3.58008	1.024645935	up	zinc and ring finger 3 [Source:HGNC Symbol;Acc:18126]
ENSG00000197415	5.96185	12.0142	1.010908603	up	ventricular zone expressed PH domain-containing 1 [Source:HGNC Symbol;Acc:25735]
ENSG00000198088	17.2525	8.51158	-1.019306564	down	nucleoporin 62kDa C-terminal like [Source:HGNC Symbol;Acc:25960]
ENSG00000179046	10.0612	4.93927	-1.026432646	down	tripartite motif family-like 2 [Source:HGNC Symbol;Acc:26378]
ENSG00000085117	16.3935	8.02257	-1.030987524	down	CD82 molecule [Source:HGNC Symbol;Acc:6210]
ENSG00000270882	13.1691	6.38904	-1.043485676	down	-
ENSG00000167535	11.2491	5.40623	-1.057114786	down	calcium channel, voltage-dependent, beta 3 subunit [Source:HGNC Symbol;Acc:1403]
ENSG00000187764	5.71625	2.7422	-1.059735217	down	sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4D [Source:HGNC Symbol;Acc:10732]
ENSG00000115421	11.6833	5.54962	-1.073986933	down	poly(A) polymerase gamma [Source:HGNC Symbol;Acc:14982]
ENSG00000115947	25.359	11.9667	-1.083472494	down	origin recognition complex, subunit 4 [Source:HGNC Symbol;Acc:8490]
ENSG00000168143	4.12583	1.93689	-1.090942355	down	family with sequence similarity 83, member B [Source:HGNC Symbol;Acc:21357]
ENSG00000137868	4.36322	2.03399	-1.101080632	down	stimulated by retinoic acid 6 [Source:HGNC Symbol;Acc:30650]
ENSG00000184517	11.179	5.18427	-1.108578378	down	ZFP1 zinc finger protein [Source:HGNC Symbol;Acc:23328]
ENSG00000166025	8.62556	3.98626	-1.113582313	down	angiominin like 1 [Source:HGNC Symbol;Acc:17811]
ENSG00000164506	6.06679	2.79463	-1.118276086	down	syntaxin binding protein 5 (tomosyn) [Source:HGNC Symbol;Acc:19665]
ENSG00000131374	8.96638	4.11688	-1.122974246	down	TBC1 domain family, member 5 [Source:HGNC Symbol;Acc:19166]
ENSG00000157514	13.3161	6.03102	-1.142697685	down	TSC22 domain family, member 3 [Source:HGNC Symbol;Acc:3051]
ENSG00000204396	11.6324	5.11676	-1.184846314	down	von Willebrand factor A domain containing 7 [Source:HGNC Symbol;Acc:13939]
ENSG00000114861	7.03474	3.06923	-1.196620342	down	forkhead box P1 [Source:HGNC Symbol;Acc:3823]
ENSG00000164808	46.0156	20.0548	-1.198175461	down	KIAA0146 [Source:HGNC Symbol;Acc:28971]
ENSG00000281181	16.7705	7.1703	-1.225820316	down	-
ENSG00000167081	8.3093	3.50186	-1.246605537	down	pre-B-cell leukemia homeobox 3 [Source:HGNC Symbol;Acc:8634]
ENSG00000214174	4.86578	2.03253	-1.259394446	down	archaelysin family metallopeptidase 2 pseudogene 1 [Source:HGNC Symbol;Acc:26491]
ENSG00000072195	8.30099	3.33036	-1.317605271	down	SPEG complex locus [Source:HGNC Symbol;Acc:16901]
ENSG00000109458	3.66758	1.44769	-1.34107573	down	GRB2-associated binding protein 1 [Source:HGNC Symbol;Acc:4066]
ENSG00000075043	5.86368	2.26188	-1.374283981	down	potassium voltage-gated channel, KQT-like subfamily, member 2 [Source:HGNC Symbol;Acc:6296]

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Seq_id	(VC) fpkm	(KO)3_7_fpkm	log2FC(KO/VC)	Regulate	Description
ENSG00000131746	9.23984	3.52582	-1.389909046	down	tensin 4 [Source:HGNC Symbol;Acc:24352]
ENSG00000156453	4.01672	1.50392	-1.417290071	down	protocadherin 1 [Source:HGNC Symbol;Acc:8655]
ENSG00000188517	6.04896	2.24749	-1.428372424	down	collagen, type XXV, alpha 1 [Source:HGNC Symbol;Acc:18603]
ENSG00000265096	8.69038	3.22807	-1.428747399	down	Uncharacterized protein [Source:UniProtKB/TrEMBL;Acc:J3KS61]
ENSG00000151689	9.40788	3.47631	-1.436312918	down	inositol polyphosphate-1-phosphatase [Source:HGNC Symbol;Acc:6071]
ENSG00000088756	4.70196	1.68862	-1.477417559	down	Rho GTPase activating protein 28 [Source:HGNC Symbol;Acc:25509]
ENSG00000104081	5.96943	2.12103	-1.492828154	down	Bcl2 modifying factor [Source:HGNC Symbol;Acc:24132]
ENSG00000118194	4.6428	1.62065	-1.518422578	down	troponin T type 2 (cardiac) [Source:HGNC Symbol;Acc:11949]
ENSG00000188266	6.21225	2.05372	-1.596876388	down	aminoglycoside phosphotransferase domain containing 1 [Source:HGNC Symbol;Acc:34403]
ENSG00000172927	9.72759	3.20937	-1.599792299	down	myeloma overexpressed (in a subset of t(11;14) positive multiple myelomas) [Source:HGNC Symbol;Acc:7563]
ENSG00000278932	9.65933	3.14891	-1.617070599	down	-
ENSG00000107614	3.78983	1.11699	-1.762516865	down	tRNA aspartic acid methyltransferase 1 [Source:HGNC Symbol;Acc:2977]
ENSG00000152076	3.91793	1.15134	-1.766777686	down	coiled-coil domain containing 74B [Source:HGNC Symbol;Acc:25267]
ENSG00000159788	5.99872	1.73903	-1.786371872	down	regulator of G-protein signaling 12 [Source:HGNC Symbol;Acc:9994]
ENSG00000232973	5.70581	1.57831	-1.85405111	down	CYP1B1 antisense RNA 1 [Source:HGNC Symbol;Acc:28543]
ENSG00000067141	4.28714	1.16488	-1.879834187	down	neogenin 1 [Source:HGNC Symbol;Acc:7754]
ENSG00000203326	25.5951	6.93345	-1.884222339	down	zinc finger protein 525 [Source:HGNC Symbol;Acc:29423]
ENSG00000163995	4.71407	1.25699	-1.907000009	down	actin binding LIM protein family, member 2 [Source:HGNC Symbol;Acc:19195]
ENSG00000280130	3.76176	0	-1.911407808	down	-
ENSG00000240364	3.86536	0	-1.950602786	down	ribosomal protein L31 pseudogene 59 [Source:HGNC Symbol;Acc:36975]
ENSG00000174640	4.63741	1.17475	-1.980965515	down	solute carrier organic anion transporter family, member 2A1 [Source:HGNC Symbol;Acc:10955]
ENSG00000133401	4.00349	0.995203	-2.008195463	down	PDZ domain containing 2 [Source:HGNC Symbol;Acc:18486]
ENSG00000278903	11.7426	2.82235	-2.056783067	down	-
ENSG00000204406	6.34622	1.49977	-2.081156265	down	methyl-CpG binding domain protein 5 [Source:HGNC Symbol;Acc:20444]
ENSG00000280987	8.10572	1.90811	-2.086795997	down	-
ENSG00000108387	7.70484	1.56887	-2.296039185	down	septin 4 [Source:HGNC Symbol;Acc:9165]
ENSG00000253492	5.21647	0	-2.383073861	down	cadherin 12 (N-cadherin 2) pseudogene 3 [Source:HGNC Symbol;Acc:37699]
ENSG00000184271	7.99757	1.44707	-2.466427003	down	POU class 6 homeobox 1 [Source:HGNC Symbol;Acc:9224]
ENSG00000249684	5.82118	0	-2.541311629	down	-
ENSG00000185324	207.869	31.9115	-2.703526292	down	cyclin-dependent kinase 10 [Source:HGNC Symbol;Acc:1770]
ENSG00000251141	12.3399	1.88182	-2.71313016	down	-
ENSG00000130208	6.13461	0.690214	-3.151855987	down	apolipoprotein C-I [Source:HGNC Symbol;Acc:607]
ENSG00000270808	9.54955	0	-3.255432751	down	-
ENSG00000257341	6.31322	0.598144	-3.399811274	down	-
ENSG00000266210	11.7633	0	-3.556220936	down	Metazoan signal recognition particle RNA [Source:RFAM;Acc:RF00017]
ENSG00000189283	15.9633	0.425823	-5.228361236	down	fragile histidine triad [Source:HGNC Symbol;Acc:3701]
ENSG00000277739	85.2919	0	-6.414336833	down	-