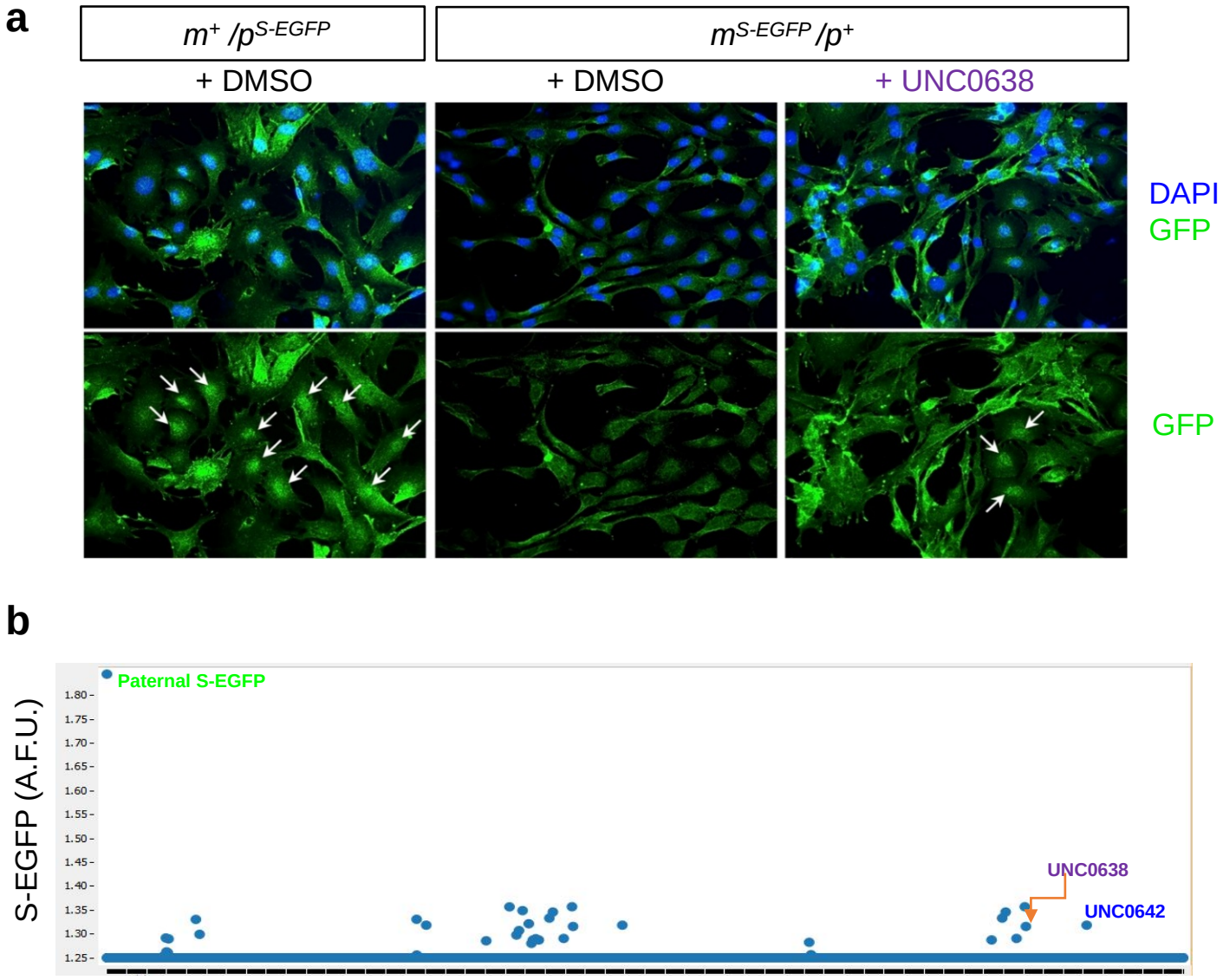
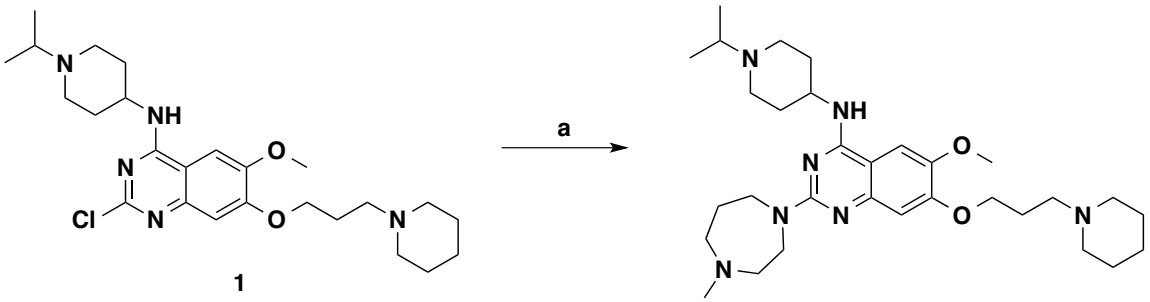
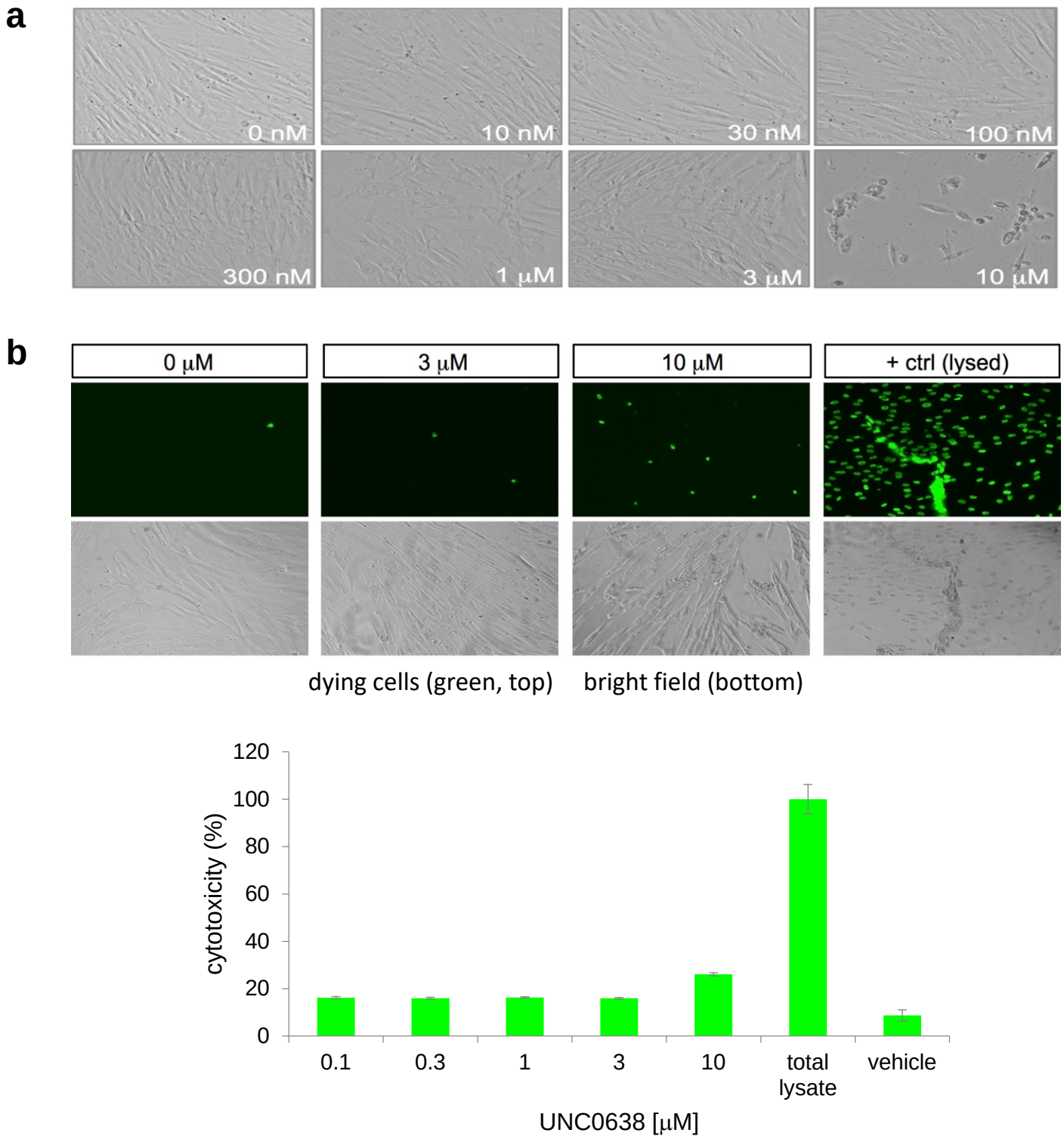


Supplementary Figure 1. Validation and active compound data plot from HCS. (**a**) Determination of depressing Snrpn-EGFP in UNC0638-treated $m^{S\text{-}EGFP}/p^{+}$ MEFs (right: nuclear EGFP signal (arrows)). Paternal expression of Srnpn-EGFP in $m^{+}/p^{S\text{-}EGFP}$ MEFs (left, positive control); vehicle-treated $m^{S\text{-}EGFP}/p^{+}$ MEFs (middle, negative control). (**b**) Highlighted 32 potential compounds derepressing Snrpn-EGPF over 125%. The chemical libraries are listed in **Supplementary Table 1** and 32 potential active compounds are listed in the **Supplementary Table 2**. All data were plotted by GENE-E (http://www.broadinstitute.org/cancer/software/GENE-E/index.html).

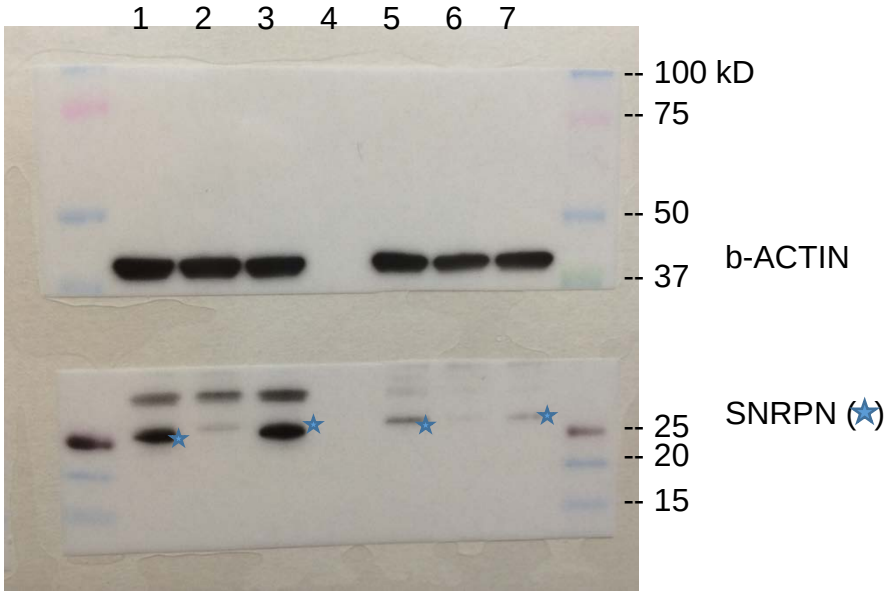


(a) 1-methyl homopiperazine, CF_3COOH, *i*-PrOH, 160°C, 72%.

Supplementary Figure 2. Synthesis of UNC617. N-(1-isopropylpiperidin-4-yl)-6-methoxy-2-(4-methyl-1,4-diazepan-1-yl)-7-(3-(piperidin-1-yl)propoxy)quinazolin-4-amine. A mixture of compound 1 (70 mg, 0.15 mmol), 1-methyl homopiperazine (34 mg, 0.30 mmol), and TFA (46 μL, 0.60 mmol) in i-PrOH (0.2 mL) in a sealed tube was heated by microwave irradiation to 160°C for 15 min. After concentration in vacuo, the crude product was purified by preparative HPLC with a gradient from 10% of MeOH in 0.1% TFA in H2O to 100% MeOH. The resulting product was basified with saturated aq. $NaHCO_3$ and extracted with CH_2Cl_2 to afford the title compound as a yellow solid (60 mg, 0.11 mmol, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 1H), 6.72 (s, 1H), 5.00 (d, J = 8.0 Hz, 1H), 4.11(t, J = 6.0 Hz, 2H), 4.05-4.01 (m, 1H), 3.96-3.94 (m, 2H), 3.87-3.83 (m, 5H), 2.89 (app. d, J = 12.0 Hz, 2H), 2.77-2.70 (m, 1H), 2.69-2.66 (m, 2H), 2.56-2.53 (m, 2H), 2.43 (t, J = 8.0 Hz, 2H), 2.38-2.26 (m, 9H) 2.15 (app. d, J = 12.0 Hz 2H), 2.06-1.95 (m, 4H), 1.60-1.50 (m, 6H), 1.42-1.39 (m, 2H), 1.05 (d, J = 4.0 Hz, 6H). ^{13}C HNMR (100 MHz, $CDCl_3$, 5 overlapping peaks) δ 158.5, 157.9, 153.9, 149.6, 145.1, 106.9, 102.6, 101.5, 67.3, 58.9, 57.3, 56.6, 55.7, 54.5(2C), 54.4(2C), 48.6, 47.7, 46.7, 45.8, 45.8, 32.5, 27.8, 26.4(2C), 25.9(2C), 24.4, 18.4(2C). HPLC: 98%; t_R 0.56 min. HRMS (TOF) calcd for C31H52N7O2 [M+H]+, 554.4177; found 554.4192.

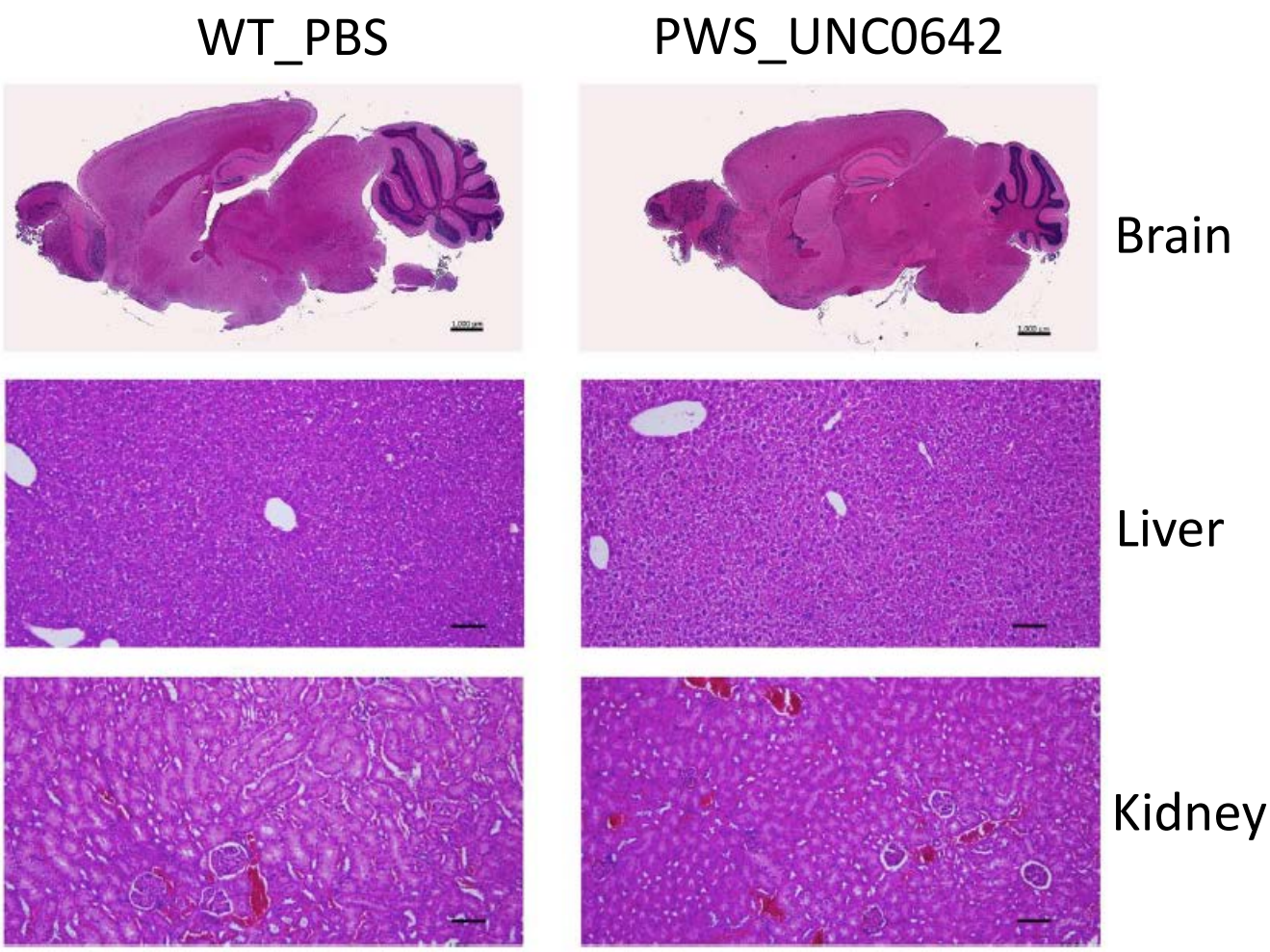


Supplementary Figure 3. Evaluation of drug toxicity. (**a**) Gross cell morphology at various dosage increments. Few cells are viable upon the exposure to 10 μM for 72-hr. (**b**) Quantification of cytotoxicity. Cytotoxicity is given as a percentage of cell death in drug-treated cells to cell death of completely lysed cells (bottom graph: ANOVA-Dunnett; $P < 0.05$[10 μM]; n = 4 per group, data are mean (%) ± s.e.m.).



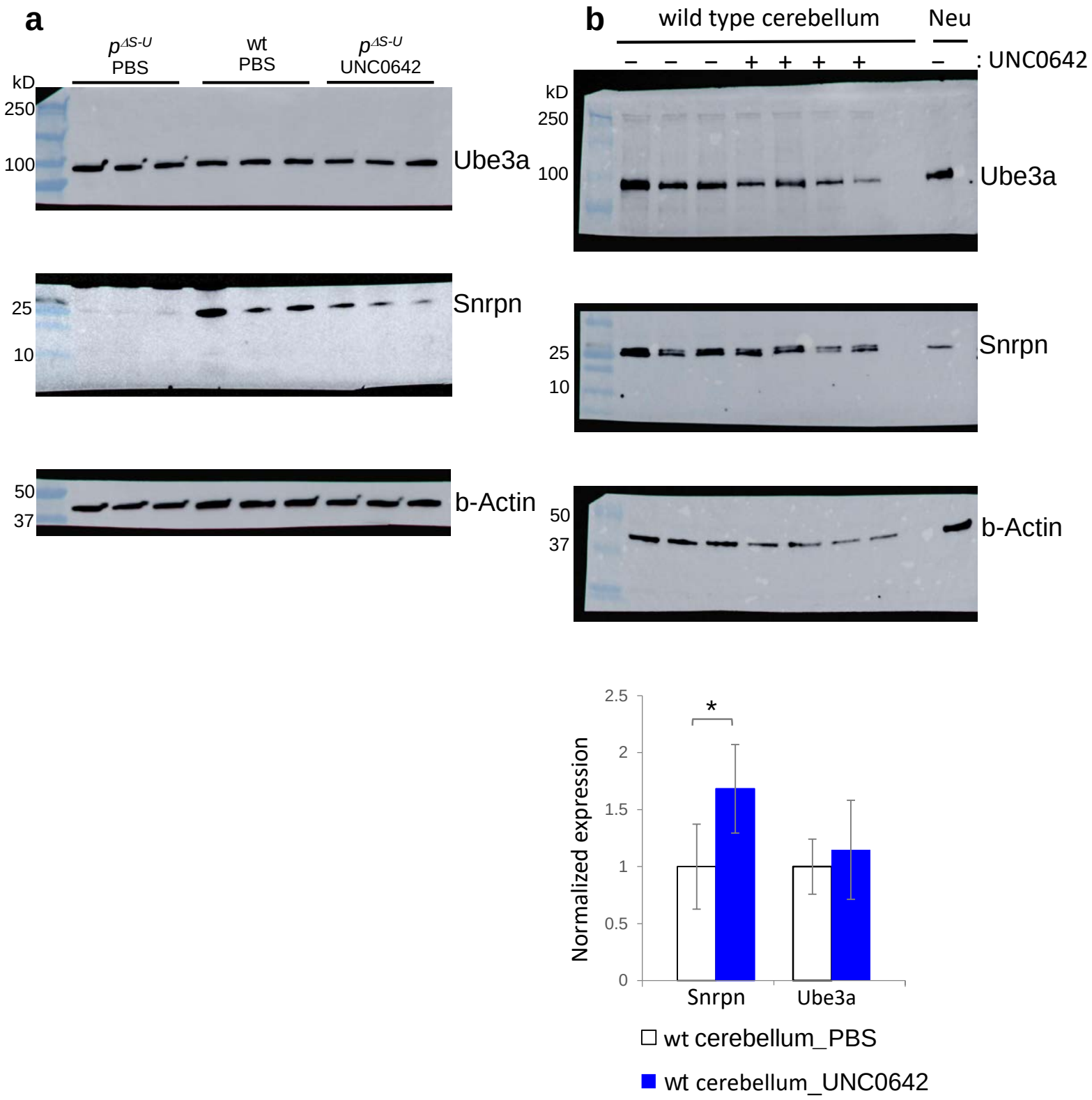
1. Liver from UNC0642-treated $m^{+}/p^{\Delta S\text{-}U}$
2. Liver from PBS-treated $m^{+}/p^{\Delta S\text{-}U}$
3. Liver from PBS-treated m^{+}/p^{+}
4. -
5. Mock-treated control human fibroblast
6. Mock-treated PWS human fibroblast
7. UNC0638-treated PWS human fibroblast

Supplementary Figure 4. Original western blots for figure 2e. Lane 1, 2, and 3 of the blot indicated western blot analysis of the drug treated liver from PWS mouse model. Lane 5, 6, and 7 of the blot represented figure 2e, indicating western blot analysis of the drug treated PWS fibroblast cells. Note. The membrane blots were trimmed after transferring.



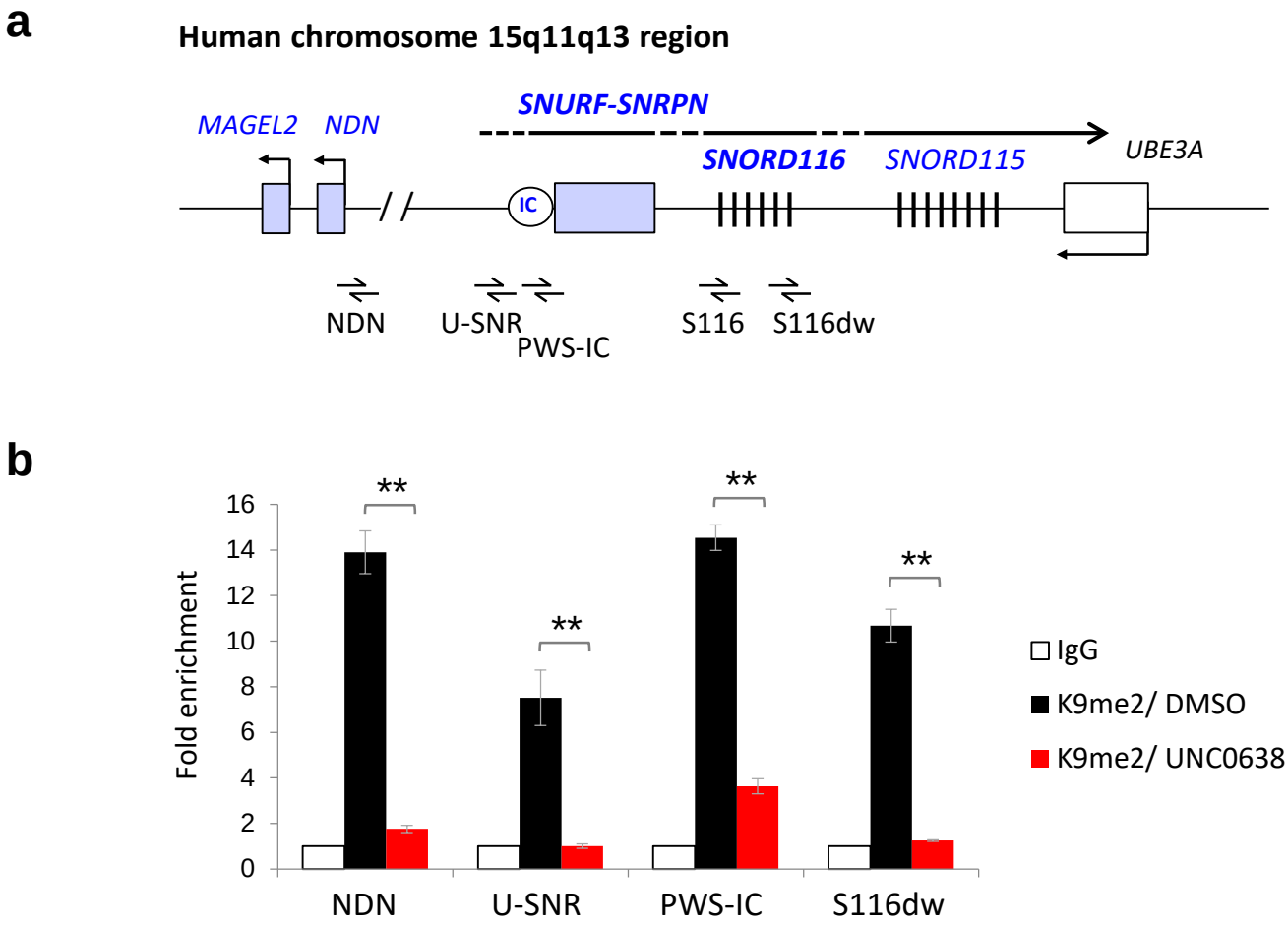
Supplementary Figure 5. Photomicrographs of UNC0642-treated PWS and vehicle-treated WT animals at age of 3 month-old. Hematoxylin and eosin stained sagittal sections of brain (scale bar, 1000 μm), liver and kidney (scale bar, 1000 μm). Histopathologic examination revealed no significant compound related lesions in any of the tissues examined (lung and heart, not shown).

Nature Medicine: doi:10.1038/nm.4257

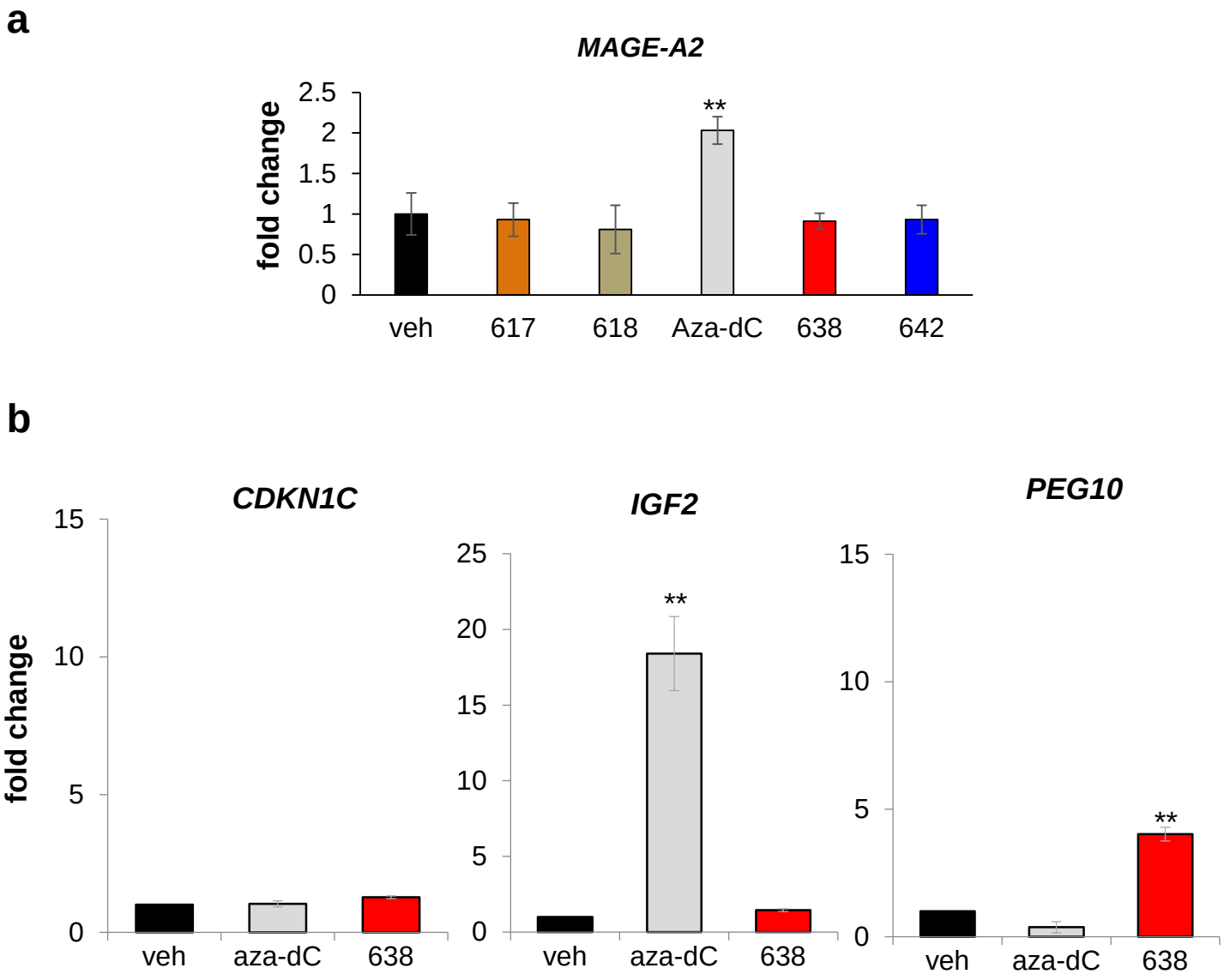


Supplementary Figure 6. Angelman syndrome UBE3A expression was not affected by UNC0642. (**a**) Original western blots for figure 4d. Note. The membrane blots were trimmed after transferring. (**b**) Normalized protein levels of UBE3A and SNPRN in cerebellum following *in vivo* treatment with PBS (-) or UNC0642 (+, 5 mg/kg, three daily *i.p.* injections). Neu, cultured primary cortical neurons, was included as internal control (*t*- test; * $P < 0.05$; n = 3 for PBS and n = 4 for UNC0642, data are mean ± s.e.m.). Note. The membrane blots were trimmed after transferring.

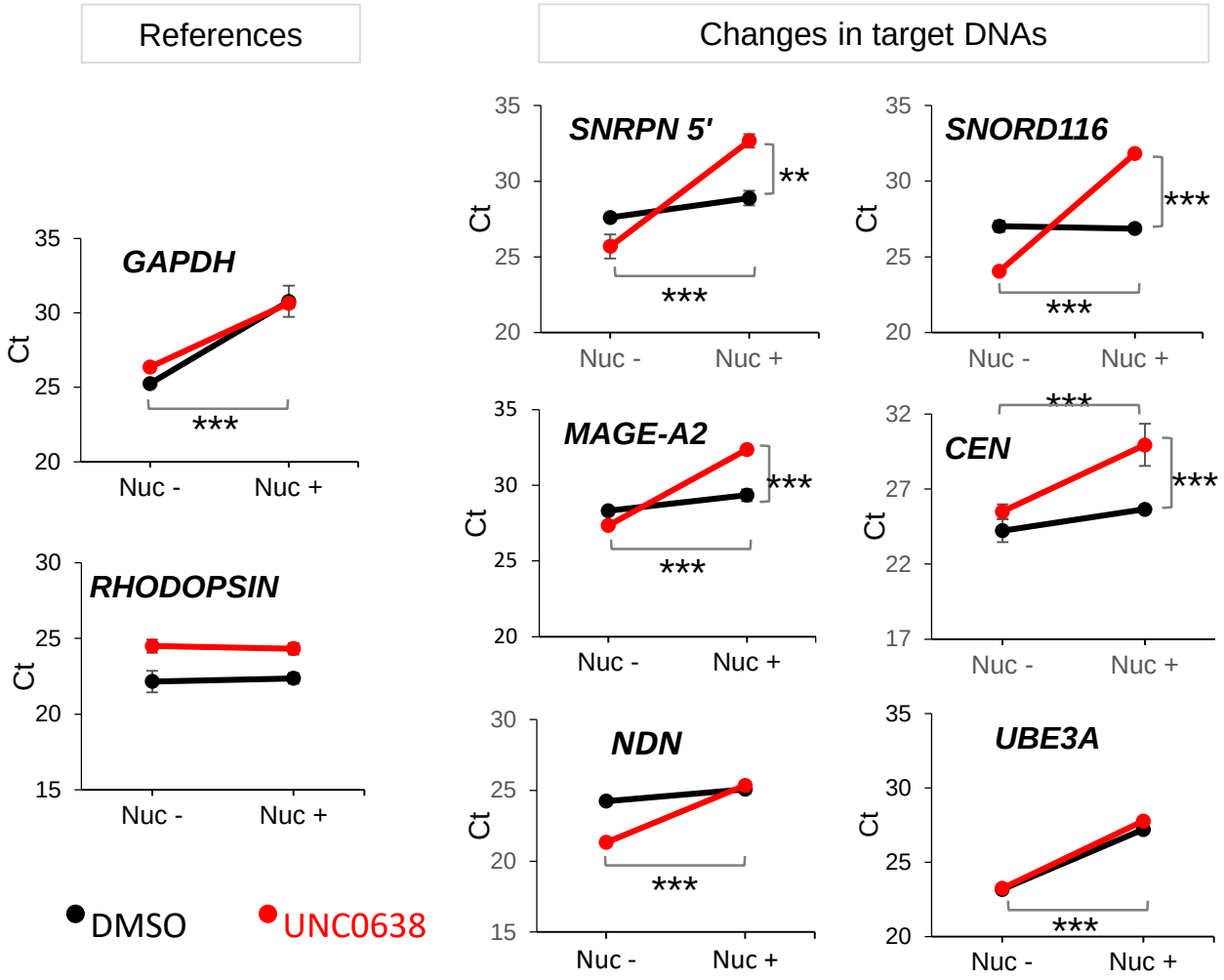
Supplementary Figure 7. Verification of ChIP assay in the PWS/AS cell lines. ChIP Experiments were performed on two or more independent cultures of human PWS or Angelman syndrome (AS) fibroblasts using H3K9me2, a heterochromatin marker, and acetyl-H3, an euchromatin marker. PWS cells have a paternal deletion of human 15q11-q13 and AS cells have a maternal deletion of 15q11-q13. The enrichment of Histone H3 acetylation (acetyl-H3) or H3K9me2 was determined by *q*PCR amplification (40 cycles) using a primer pair in the CpG island of *SNRPN* which overlaps with the PWS-IC. The allelic specific histone modifications of the PWS-IC is confirmed by the reciprocal pattern of H3K9me2 (filled red arrows) and H3 acetylation (black arrows) in PWS versus AS cells. UNC0638 and DNMT inhibitor (5-Aza-dC) reduced the level of H3K9me2 in treated PWS fibroblasts (open red arrows; 4μM UNC0638 or 10μM 5-Aza-dC, 72 hr).



Supplementary Figure 8. Enrichment of H3K9me2 at different PWS candidate gene loci (**a**) The positions of PCR primer pairs used for chromatin assays across the 15q11-q13 region including NDN (the promoter region of *NDN)*; U-SNR (the region at the most upstream of untranslated exons of SNRPN; PWS-IC (the region overlap with the CpG island of *SNRPN* and PWS-IC); and *S116dw* (the 3′ region of *SNORD116* cluster). *S116* (the 5' region of *SNORD116* cluster) is shown in Fig 4b-d. (**b**) ChIP-qPCR analysis of H3K9me2 in PWS imprinted domain. The levels of H3K9me2 association with the silent maternal copy of PWS genes are shown. Reduction of H3K9me2 by UNC0638 occurred at the examined sites across PWS imprinted domain. Especially, UNC0638 caused the reduction of H3K9me2 at *NDN* loci. (*t*- test; ** $P < 0.01$; n = 3 per group, data are mean ± s.e.m.)



Supplementary Figure 9. Changes in silent genes at the presence of G9a inhibitors. (a) MAGE-A2 transcript was not increased in the PWS cells treated with the G9a inhibitors. DNA methyltransferase inhibitor (5-Aza-dC), however, increased *MAGE-A2* transcription (*t*- test; ** $P < 0.01$; n = 3 per veh and n = 4 per drugs, data are mean ± s.e.m.) **(b)** Other imprinting loci (*CDKN1C,* Chr11p15.5; *IGF2,* Chr11p15.5; *PEG10,* Chr7q21) in the human PWS fibroblast at the presence of UNC0638 or 5-Aza-deoxycitidine. UNC0638 induced transcriptional increases of *PEG10,* while 5-Aza-dC induced *IGF2.* (*t*- test; ** $P < 0.01$; n = 3 per veh and n = 4 per UNC0638, data are mean ± s.e.m.)



Supplementary Figure 10. **Chromatin state at the silent maternal PWS region is H3K9me2 dependent**. The chromatin accessibility of genomic loci across PWS region assessed by genomic qPCR. The increase of Ct (threshold cycle), i.e. lower amount of target DNA indicates high susceptibility to nuclease (MNases) digestion and more open chromatin, as for the case of constitutively active *GAPDH* in Reference (left). UNC0638 elevated chromatin accessibilities in *SNRPN5'*, *SNORD116*, *MAGE-A2*, *CEN*, and *NDN*, but not in *UBE3A* (two way ANOVA analysis; GAP: Drug/P > 0.05, F=0.998; Nuc/*** P < 0.0001, F=308.7; Interaction/P > 0.05, F=1.182; RHO: Drug/P > 0.05, F=1.932; Nuc/P > 0.05, F=0.039; Interaction/P > 0.05, F=0.629; SN5': Drug/** P < 0.01, F=16.29; Nuc/*** P < 0.0001, F=166.9; Interaction/P < 0.0001, F=129.3; SNO116: Drug/*** P < 0.0001, F=58.96; Nuc/*** P < 0.0001, F=865.8; Interaction/P < 0.0001, F=935.4; MAGE: Drug/*** P < 0.0001, F=105.9; Nuc/*** P < 0.0001, F=916.6; Interaction/P < 0.0001, F=398.7; CEN: Drug/*** P < 0.0001, F=44.17; Nuc/*** P < 0.0001, F=48.8; Interaction/P < 0.005, F=12.82; NDN: Drug/*** P < 0.0001, F=130.6; Nuc/*** P < 0.0001, F=443.3; Interaction/P < 0.0001, F=191.4; UBE3A: Drug/P > 0.05, F=2.046; Nuc/*** P < 0.0001, F=6569; Interaction/P > 0.05, F = 0.00004873; n = 3 per group and 7 per target, data are mean ± s.e.m.).

Supplementary Table 1. Summary of small molecule libraries.

Library	No.	Description	Potential actives
NCC1	446	NIH Clinical Collection 1 - most anti-cancer drugs	
NCC2	320*	NIH Clinical Collection 2 - most anti-cancer drugs	
X-901	271	NIMH CNS drugs	
SMART	320	CNS penetrating drugs / IRSF	
Roth	456	CNS and GPCR targeting / Roth Lab Library, UNC	
Tocris Mini	1120	Biologically active compounds / Commercial / Tocris	
PKIS**	367	GlaxoSmithKline kinase inhibitors	
Prestwick	1120	FDA, EMA approved drug / Commercial / Prestwick Chemicals	
LOPAC	1280	Pharmacologically active compounds / Commercial / Sigma	
Spectrum	2400	Biologically active compounds / Commercial / MicroSource	
Epigenetic collection A	959	UNC synthetic epigenetic compounds / random collection	
Epigenetic collection B	73	UNC synthetic epigenetic compounds / random collection	
UNC.Epigenetic collection C	25	UNC synthetic epigenetic compounds / random collection	UNC0638 UNC0642
Subtotal	**9157**		
Selected compounds	295	Selectively chosen compounds that were tested to validate or repeat	
Total	**9452**		

NCC: NIH Clinical Collection, IRSF: International Rett Syndrome Foundation.
* NCC2 collection originally contains 281 compounds, however, we added 39 PDSP compounds to make arrayed 96-well drug plates
** PKIS. The GlaxoSmithKline Published Kinase Inhibitor Set

Supplementary Table 2. The list of initial active compounds potentially increasing over 125% of AFU in Snprn-EGFP.

Name of compounds	AFU	SEM	True/ False	Note
UNC0638	1.331	0.047	T	G9a inhibition
UNC0642	1.331	0.032	T	G9a inhibition
(d,l)-Tetrahydroberberine	1.357	0.04	F	DA antagonist / intrinsic fluorescence
6-Hydroxydopamine hydrochloride	1.247	0.051	F	Selective catecholaminergic neurotoxin
7-Methoxychlorpromazine hydrochloride	1.331	0.119	F	Potential anticoagulant
7-Nitroindazole	1.282	0.02	F	Neuronal nitric oxide synthase inhibition
Amphotericin B	1.349	0.045	F	Antifungal drug
Bestatin	1.254	0.045	F	Protease inhibitor
Bezafibrate	1.298	0.028	F	Fibrate drug
Cefaclor	1.253	0.064	F	Cephalosporin antibiotic
Chlordiazepoxide	1.258	0.062	F	Sedative/hypnotic drug
Clozapine	1.299	0.072	F	Atypical antipsychotic drug
Flufenamic acid	1.25	0.026	F	Anthranilic acid derivatives
Fluphenazine HCl	1.254	0.032	F	Typical antipsychotic drug
Furosemide	1.357	0.047	F	Treatment of hypertension and edema
Gabazine	1.321	0.02	F	GABAa antagonist
Iodipamide	1.318	0.044	F	Contrast medium.
Iohexol	1.257	0.026	F	Contrast medium.
Mebendazole	1.286	0.043	F	Treating infections by worms
Meclozine dihydrochloride	1.28	0.023	F	Antihistamine
Myricetin	1.287	0.084	F	Flavonoid class of polyphenolic compounds / intrinsic fluorescence
Palonosetron HCl	1.292	0.054	F	5-HT3 antagonist

Supplementary Table 2. The list of initial active compounds potentially increasing over 25% of AFU in Snprn-EGFP (*continued*).

Name of compounds	AFU	SEM	True/ False	Note
Phenylbenzene-omega-phosphono-alpha-amino acid	1.251	0.021	F	Glycine antagonist
Puromycin dihydrochloride	1.29	0.013	F	Aminonuclease antibiotic
Ricinine	1.316	0.039	F	An alkaloid extracted from the seeds
Salbutamol	1.257	0.038	F	β2-adrenergic receptor agonist
Salsolinol hydrobromide	1.291	0.01	F	Metabolite of acetaldehyde and dopamine.
Selegiline hydrochloride	1.333	0.034	F	Substituted phenethylamine
Synephrine	1.286	0.021	F	An alkaloid, occurring naturally in some plants and animals
Terbutaline hemisulfate	1.307	0.083	F	β2-adrenergic receptor agonist
Tetracaïne hydrochloride	1.346	0.048	F	Potent local anesthetic of the ester group
Tiaprofenic acid	1.287	0.097	F	Non-steroidal anti-inflammatory drug (NSAID)

Supplementary Table 3. List of epigenetic compounds selectively chosen for individual unsilencing test.

Name	Target / MOA	Effectiveness in this study
5-Aza deoxcytidine	DNA methyltransferase / Inhibition	O
BIX01294	G9a / Inhibition	X
S-Adenosyl methionine	G9a / Cofactor	X
Sinefungin	G9a / Pan inhibitor	X
4-Phenylbutyrate (PBA)	HDAC / Inhibition	X
Entinostat (MS-275)	HDAC / Inhibition	X
NSC 3852	HDAC / Inhibition	X
Vorinostat (SAHA)	HDAC / Inhibition	X
Scriptaid	HDAC / Inhibition	X
Splitomicin	HDAC / Inhibition	X
Trichostatin A (TSA)	HDAC / Inhibition	X
Valproic acid (VPA)	HDAC / Inhibition	X

Supplementary Table 4. Summary of general health and neurological screening analysis

mouse ID	Sex	Geno-type	Drug Tx	Age (week)	Weight (g)	Temp (ºC)	Body Posture	Tail Elevation	Pelvic Elevation	Hair Loss	Barber-ing
535-2	F	PWS	vehicle	12	17.6	38.8	normal	normal	normal	none	none
536-30	M	PWS	vehicle	12	19.6	38.9	normal	normal	normal	none	none
439-10	F	PWS	UNC0642	12	17.4	38.6	normal	normal	normal	none	none
439-30	F	PWS	UNC0642	12	19.9	38.8	normal	normal	normal	none	none
935-3	F	PWS	UNC0642	12	17.4	38.9	normal	normal	normal	none	none
935-10	F	PWS	UNC0642	12	15.1	39.2	normal	normal	normal	none	none
935-30	F	PWS	UNC0642	12	14.4	39.2	normal	normal	normal	none	none
574-10	F	PWS	UNC0642	14	15.9	38.3	normal	normal	normal	none	none
580-10	F	PWS	UNC0642	14	23.1	38.5	normal	normal	normal	none	none
580-30	F	PWS	UNC0642	14	16.7	38.6	normal	normal	normal	none	none
739-10	M	PWS	UNC0642	15	23.0	38.4	normal	normal	normal	none	none
739-20	M	PWS	UNC0642	15	23.0	37.7	normal	normal	normal	none	none
739-30	M	PWS	UNC0642	15	23.0	36.8	normal	normal	normal	none	none
431-10	F	WT	vehicle	12	20.2	37.6	normal	normal	normal	none	none
431-20	F	WT	vehicle	12	20.5	38.4	normal	normal	normal	none	none
431-30	F	WT	vehicle	12	21.4	37.1	normal	normal	normal	none	none
535-1	F	WT	vehicle	12	21	38.0	normal	normal	normal	none	none
536-20	F	WT	vehicle	12	19.1	37.9	normal	normal	normal	none	none
431-1	F	WT	vehicle	12	20	38.6	normal	normal	normal	none	none
431-2	F	WT	vehicle	12	20.1	38.4	normal	normal	normal	none	none
431-3	F	WT	vehicle	12	19.3	38.5	normal	normal	normal	none	none
933-10	M	WT	vehicle	14	30.9	37.8	normal	normal	normal	none	none
933-1	M	WT	vehicle	14	31.1	38.3	normal	normal	normal	none	none
933-3	M	WT	vehicle	14	31.4	37.6	normal	normal	normal	none	none
933-30	M	WT	vehicle	14	34.2	37.1	normal	normal	normal	none	none
436-1	M	WT	UNC0642	12	22.4	37.3	normal	normal	normal	none	none
436-2	M	WT	UNC0642	12	22.6	37.3	normal	normal	normal	none	none
436-3	M	WT	UNC0642	12	22.5	38.0	normal	normal	normal	none	none
436-10	F	WT	UNC0642	12	19.8	37.1	normal	normal	normal	none	none
436-30	F	WT	UNC0642	12	20.8	37.5	normal	normal	normal	none	none
439-3	F	WT	UNC0642	12	22.8	37.8	normal	normal	normal	none	none
935-1	F	WT	UNC0642	12	22.4	37.6	normal	normal	normal	none	none
574-1	F	WT	UNC0642	14	23.6	37.1	normal	normal	normal	none	none
580-1	F	WT	UNC0642	14	26.4	38.1	normal	normal	normal	none	none
159-1	F	WT	UNC0642	15	30.0	37.3	normal	normal	normal	none	none
159-2	F	WT	UNC0642	15	29.0	37.0	normal	normal	normal	none	none
159-3	F	WT	UNC0642	15	25.0	36.8	normal	normal	normal	H, E *	none

* Head and between ears

Nature Medicine: doi:10.1038/nm.4257

Supplementary Table 4. Summary of general heatlh and neurological screening analysis (*continued*)

mouse ID	Boli	Urine	Skin Color	Body Tone	Muscle/Fat	Convulsions	Tremor	Piloerection
535-2	0	0	normal	normal	normal	none	none	normal
536-30	1	1	normal	normal	normal	none	none	normal
439-10	0	0	normal	normal	normal	none	none	normal
439-30	1	0	normal	normal	normal	none	none	normal
935-3	0	0	normal	normal	normal	none	none	normal
935-10	0	0	normal	normal	normal	none	none	normal
935-30	1	0	normal	normal	normal	none	none	normal
574-10	2	0	normal	normal	normal	none	none	normal
580-10	1	0	normal	normal	normal	none	none	normal
580-30	3	0	normal	normal	normal	none	none	normal
739-10	1	1	normal	normal	normal	none	none	normal
739-20	2	0	normal	normal	normal	none	none	normal
739-30	2	1	normal	normal	normal	none	none	normal
431-10	1	1	normal	normal	normal	none	none	normal
431-20	0	1	normal	normal	normal	none	none	normal
431-30	2	0	normal	normal	normal	none	none	normal
535-1	1	1	normal	normal	normal	none	none	normal
536-20	1	0	normal	normal	normal	none	none	normal
431-1	0	1	normal	normal	normal	none	none	normal
431-2	0	0	normal	normal	normal	none	none	normal
431-3	1	0	normal	normal	normal	none	none	normal
933-10	0	1	normal	normal	normal	none	none	normal
933-1	0	0	normal	normal	normal	none	none	normal
933-3	1	1	normal	normal	normal	none	none	normal
933-30	2	0	normal	normal	normal	none	none	normal
436-1	1	0	normal	normal	normal	none	none	normal
436-2	1	0	normal	normal	normal	none	none	normal
436-3	1	0	normal	normal	normal	none	none	normal
436-10	1	0	normal	normal	normal	none	none	normal
436-30	0	1	normal	normal	normal	none	none	normal
439-3	1	1	normal	normal	normal	none	none	normal
935-1	1	0	normal	normal	normal	none	none	normal
574-1	1	1	normal	normal	normal	none	none	normal
580-1	1	0	normal	normal	normal	none	none	normal
159-1	1	0	normal	normal	normal	none	none	normal
159-2	2	0	normal	normal	normal	none	none	normal
159-3	2	0	normal	normal	normal	none	none	normal

Supplementary Table 4. Summary of general health and neurological screening analysis (*continued*)

mouse ID	Whiskers	Whisker Stop	Ear	Lacrimation	Palperbral Closure	Exopthalamus	Eye Reflex	Grasp Coordnt
535-2	normal	normal	normal	normal	normal	normal	normal	normal
536-30	normal	normal	normal	normal	normal	normal	normal	normal
439-10	normal	normal	normal	normal	normal	normal	normal	normal
439-30	normal	normal	normal	normal	normal	normal	normal	normal
935-3	normal	normal	normal	normal	normal	normal	normal	normal
935-10	normal	normal	normal	normal	normal	normal	normal	normal
935-30	normal	normal	normal	normal	normal	normal	normal	normal
574-10	normal	normal	normal	normal	normal	normal	normal	normal
580-10	normal	normal	normal	normal	normal	normal	normal	normal
580-30	normal	normal	normal	normal	normal	normal	normal	normal
739-10	normal	normal	normal	normal	normal	normal	normal	normal
739-20	normal	normal	normal	normal	normal	normal	normal	normal
739-30	normal	normal	normal	normal	normal	normal	normal	normal
431-10	normal	normal	normal	normal	normal	normal	normal	normal
431-20	normal	normal	normal	normal	normal	normal	normal	normal
431-30	normal	normal	normal	normal	normal	normal	normal	normal
535-1	normal	normal	normal	normal	normal	normal	normal	normal
536-20	normal	normal	normal	normal	normal	normal	normal	normal
431-1	normal	normal	normal	normal	normal	normal	normal	normal
431-2	normal	normal	normal	normal	normal	normal	normal	normal
431-3	normal	normal	normal	normal	normal	normal	normal	normal
933-10	normal	normal	normal	normal	normal	normal	normal	normal
933-1	normal	normal	normal	normal	normal	normal	normal	normal
933-3	normal	normal	normal	normal	normal	normal	normal	normal
933-30	normal	normal	normal	normal	normal	normal	normal	normal
436-1	normal	normal	normal	normal	normal	normal	normal	normal
436-2	normal	normal	normal	normal	normal	normal	normal	normal
436-3	normal	normal	normal	normal	normal	normal	normal	normal
436-10	normal	normal	normal	normal	normal	normal	normal	normal
436-30	normal	normal	normal	normal	normal	normal	normal	normal
439-3	normal	normal	normal	normal	normal	normal	normal	normal
935-1	normal	normal	normal	normal	normal	normal	normal	normal
574-1	normal	normal	normal	normal	normal	normal	normal	normal
580-1	normal	normal	normal	normal	normal	normal	normal	normal
159-1	normal	normal	normal	normal	normal	normal	normal	normal
159-2	normal	normal	normal	normal	normal	normal	normal	normal
159-3	normal	normal	normal	normal	normal	normal	normal	normal

Supplementary Table 5. Summary of comprehensive blood chemistry and hematological analysis

	Normal range	(Unit)	WT_UNC0642		PWS_UNC0642	
BUN	20.0-88.0	mg/dl	25.03	± 2.67	25.5	± 2.69
Creatine	0.5-1.6	mg/dl	0.6	± 0.30	0.43	± 0.09
BUN/creatine ratio			66.8	± 25.23	61	± 10.61
Phophorus	5.6-9.2	mg/dl	7.67	± 0.29	6.43	± 0.30
Calcium	7.9-10.5	mg/dl	11.3	± 0.95	9.7	± 0.46
Total protein	4.5-6.0	g/dl	6.1	± 0.95	5.77	± 0.35
Albumin	3.0-4.0	g/dl	2.97	± 0.52	2.63	± 0.15
Globulin		g/dl	2.7	± 0.00	3.13	± 0.33
alb/glob ratio			0.9	± 0.00	0.87	± 0.09
Glucose	190-280	mg/dl	267.67	± 56.16	254.33	± 29.72
Cholesterol	0-0	mg/dl	82.5	± 6.12	95.67	± 2.19
ALT (GPT)	10 - 89	U/l	28.67	± 6.12	24.67	± 4.06
AST (GOT)	10 - 380	U/l	52	± 18.00	46.5	± 7.76
ALP	0 - 185	U/l	88.33	± 6.01	67.67	± 9.17
GGT	0 - 0	U/l	n.d.		n.d.	
Total bilirubin	0.2 - 0.8	mg/dl	0.5	± 0.06	0.43	± 0.15
Sodium	143 - 150	mEq/l	147	± 1.53	151.33	± 0.67
Pottasium	3.8 - 10.0	mEq/l	7.37	± 1.57	7.2	± 0.67
Chloride	0 - 0	mEq/l	111.67	± 0.33	115.67	± 0.88
Na/K ratio			21.67	3.84	21.67	± 2.19

BUN, blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, Alkaline phosphatase; GGT, gamma-glutamyl transferase; n.d., not detected; n=3 per group

Supplementary Table 5. Summary of comprehensive blood chemistry and hematological analysis (*continued*)

	Normal range	(Unit)	WT_UNC0642		PWS_UNC0642	
Red blood cell	7.14-12.20	[M/UL]	10.62	± 0.388	9.303	± 1.651
Hb conc.	10.8-19.2	[G/dL]	16.3	± 0.529	14.03	± 2.547
Hematocrit	37.2-67.2	[%]	65.1	± 2.042	47.97	± 8.772
Mean corpuscular vol	42.6-56.0	[fL]	61.33	± 1.859	51.43	± 0.371
Mean corpuscular Hb	11.7-16.8	[pg]	15.37	± 0.524	15.1	± 0.231
Mean corpuscular Hb conc.	29.1-38.0	[g/dL]	25.03	± 0.033	29.3	± 0.503
Reticulocyte		[K/uL]	228	± 63.10	335.5	± 163.2
Platelet	565-2159	[K/uL]	1044	± 59.92	679.3	± 226.4
White blood cell	3.9-13.96	[K/uL]	4.967	± 0.639	5.467	± 3.743
Neutrophil	0.42-3.09	[K/uL]	1.063	± 0.295	0.557	± 0.393
Lymphocyte	2.88-11.15	[K/uL]	3.55	± 0.559	4.723	± 3.302
Monocyte	0.00-0.94	[K/uL]	0.227	± 0.024	0.063	± 0.030
Eosinophil	0.01-0.5	[K/uL]	0.126	± 0.042	0.123	± 0.027
Basophil	0.00-0.14	[K/uL]	0	± 0.000	0	± 0.000

Hb. Hemoglobin, n=3 per group