

Fig. S1. Expression pattern of SIRT1 during aNSC differentiation

(A) Markers expressed by cells at different developmental stages of adult neurogenesis (modified from Ming and Song, 2011).

(B,D) Immunostaining of SIRT1, GFAP, and Sox2 in the SGZ (B) and the hilus (D) of mouse adult hippocampus. Bold arrows in B, GFAP⁺/Sox2⁺ RGL aNSCs; arrowheads in D, GFAP⁺ astrocytes.

(C) Immunostaining of SIRT1, GFP, and Sox2 in the SGZ of adult *Gfap-Gfp* transgenic mice. Bold arrows, GFP⁺/Sox2⁺ RGL aNSCs.

(E,F,G) Additional examples of SIRT1 co-staining with different cell markers.

Scale bars, 25 μ m.

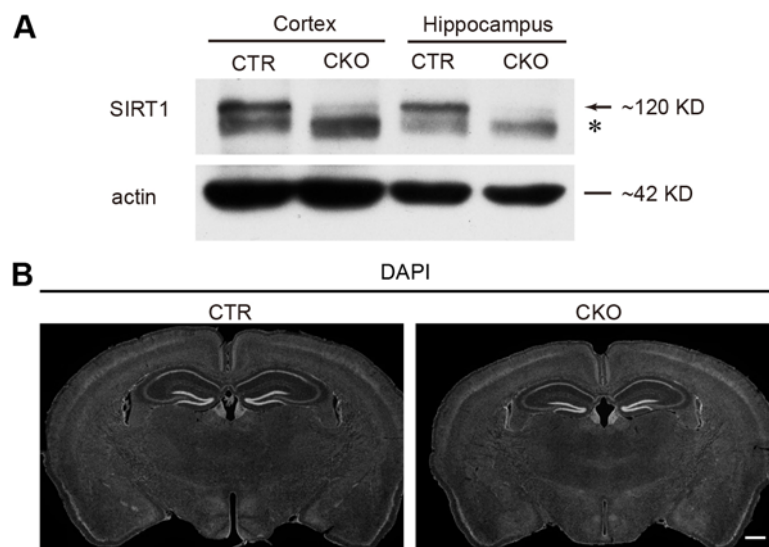


Fig. S2. Brain anatomy of *Nestin-Cre;Sirt1^{flx/flx}* conditional knockout (CKO)

mice

(A) A nonfunctional mutant SIRT1 protein (marked by *) was expressed in the cortex and hippocampus of CKO mice.

(B) DAPI-labeled coronal sections from a CKO mouse showing normal tissue structure as compared with a WT mouse. Scale bar, 500 μ m.

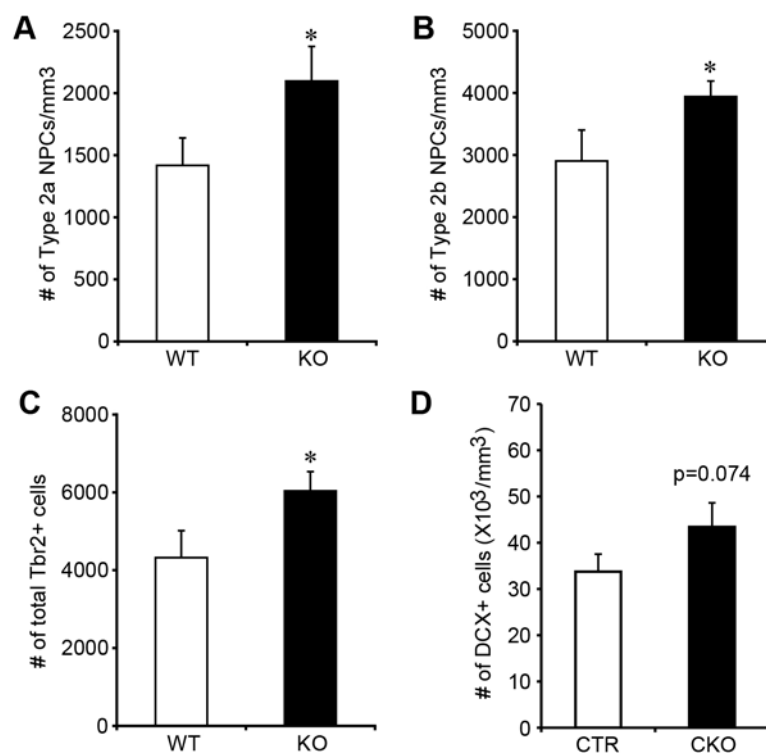


Fig. S3. Type 2 aNPCs and immature neurons were increased in SIRT1 deleted mice

(A,B,C) Number of Type 2a (Sox2⁺/Tbr2⁺) (A, * $P = 0.013$), Type 2b (Sox2⁻/Tbr2⁺) (B, * $P = 0.050$), and total Type 2 (Tbr2⁺) (C, * $P = 0.024$) cells in the SGZ of WT and SIRT1 KO mice (n = 5 pairs of mice, 9 to 12 sections per animal, paired *t*-test).

(D) Quantitation of DCX⁺ cells in control and CKO mice (n = 6 pairs of mice, 9 to 12 sections per animal, $P = 0.074$).

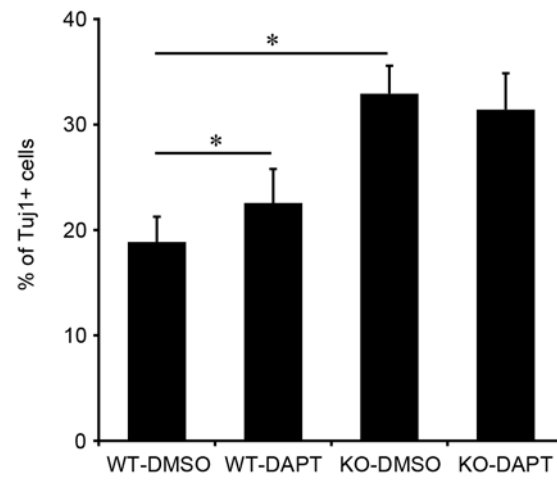


Fig. S4. SIRT1 affected lineage specification of aNSCs/aNPCs *in vitro*

Quantitation of Tuj1⁺ neurons among all cells labeled by DAPI (n = 5, paired

t-test, *P* = 0.014*, 0.012*).

Table S1. Primary antibodies used in immunostaining and Western blotting

Primary antibody	Species	Dilution	Source
SIRT1	Rabbit	1:100 or 1:500	Cell Signaling Technology
Sox2	Goat	1:100	Santa Cruz Biotechnology
NeuN	Mouse	1:1000	Millipore
Nestin	Mouse	1:200	Millipore
GFAP	Rabbit	1:500	Dako
GFAP	Mouse	1:500	Millipore
MCM2 (BM28)	Mouse	1:300	BD biosciences
DCX	Goat	1:200	Santa Cruz Biotechnology
GFP	Chicken	1:1000	Abcam
GFP	Rabbit	1:1000	Invitrogen
BrdU	Mouse	1:500	Millipore
Ki67	Rabbit	1:500	Abcam
Tbr2	Rabbit	1:200	Abcam
Actin	Mouse	1:5000	Abcam
Activated Notch1 (NICD)	Rabbit	1:700	Abcam
Tuj1	Mouse	1:1000	Covance

Table S2. Primers used for qPCR

Prime r	Forward	Reverse
<i>Dll4</i>	CTTGCTGTGGGTAAGATTTGGC	AGATGACCCGGTAAGAGTAGC
<i>Mfng</i>	GGCTCCTGTCTCTACGATACC	GATGAAGATGTCGCCTAGCTG
<i>Mib1</i>	ATTGGCATTTCGATGGAAATGTG C	CTCTAACAGAACCCGTTCACTT C
<i>Hes5</i>	AGATGCTCAGTCCCAAGGAG	TAGCCCTCGCTGTAGTCCTG
<i>Heyl</i>	AAGCGCAGAGGGATCATAGAG	CCAATCGTCGCAATTCAGAAAG
<i>Hey2</i>	GTGGGGAGCGAGAACAATTAC	TGAGAGGTAGTTGTCGGTGAA

Table S3. Summary of SIRT1-regulated genes involved in metabolism, neurogenesis, cell proliferation, and Notch signaling

GO ID	GO term	Number of genes	P value	Genes
GO:0009893	Positive regulation of metabolic process	42	1.6E-04	<i>Ablim3, Apoa4, Bmp3, Camk1d, Camk4, Cbfa2t2, Cdkn1c, Cebpb, Ciita, Eng, Erbb4, Fgfr3, Foxc2, Gfi1b, Ghr, Gnal, Hand2, Hes5, Heyl, Hivep3, Hnf4a, Il22, Il2rb, Itch, Itga8, Klf2, Lck, Mbl2, Med13, Mesp1, Mlxipl, Nkx2-5, Npas2, Pbx2, Pf4, Plp1, Pou4f2, Sox10, Sox7, Sry, Taf9, Tnfrsf13c</i>
GO:0010604	Positive regulation of macromolecule metabolic process	39	1.62E-04	<i>Ablim3, Bmp3, Camk4, Cbfa2t2, Cdkn1c, Cebpb, Ciita, Eng, Erbb4, Fgfr3, Foxc2, Gfi1b, Ghr, Hand2, Hes5, Heyl, Hivep3, Hnf4a, Il22, Il2rb, Itch, Itga8, Klf2, Lck, Mbl2, Med13, Mesp1, Mlxipl, Nkx2-5, Npas2, Pbx2, Pf4, Plp1, Pou4f2,</i>

				<i>Sox10, Sox7, Sry, Taf9, Tnfrsf13c</i>
GO: 0010557	Positive regulation of macromolecule biosynthetic process	30	5.1E-04	<i>Ablim3, Bmp3, Camk4, Cbfa2t2, Cdkn1c, Cebpb, Ciita, Eng, Erbb4, Foxc2, Hand2, Hes5, Heyl, Hivep3, Hnf4a, Il22, Itga8, Klf2, Med13, Mesp1, Mlxipl, Nkx2-5, Npas2, Pbx2, Pou4f2, Sox10, Sox7, Sry, Taf9, Tnfrsf13c</i>
GO: 0031328	Positive regulation of cellular biosynthetic process	32	5.42E-04	<i>Ablim3, Apoa4, Bmp3, Camk4, Cbfa2t2, Cdkn1c, Cebpb, Ciita, Eng, Erbb4, Foxc2, Gnal, Hand2, Hes5, Heyl, Hivep3, Hnf4a, Il22, Itga8, Klf2, Med13, Mesp1, Mlxipl, Nkx2-5, Npas2, Pbx2, Pou4f2, Sox10, Sox7, Sry, Taf9, Tnfrsf13c</i>
GO: 0009891	Positive regulation of biosynthetic process	32	7.52E-04	<i>Ablim3, Apoa4, Bmp3, Camk4, Cbfa2t2, Cdkn1c, Cebpb, Ciita, Eng, Erbb4, Foxc2, Gnal, Hand2, Hes5, Heyl, Hivep3, Hnf4a, Il22, Itga8, Klf2, Med13, Mesp1, Mlxipl, Nkx2-5, Npas2, Pbx2, Pou4f2, Sox10, Sox7, Sry, Taf9, Tnfrsf13c</i>

GO: 0045935	Positive regulation of nucleobase containing compound metabolic process	30	8.06E-04	<i>Ablim3, Bmp3, Camk4, Cbfa2t2, Cdkn1c, Cebpb, Ciita, Eng, Erbb4, Foxc2, Gnal, Hand2, Hes5, Heyl, Hivep3, Hnf4a, Il22, Itga8, Klf2, Med13, Mesp1, Mlxipl, Nkx2-5, Npas2, Pbx2, Pou4f2, Sox10, Sox7, Sry, Taf9</i>
GO: 0022008	Neurogenesis	35	2.75E-07	<i>Ache, Bcl11a, Camk1d, Cbfa2t2, Ccr4, Cdkn1c, Cebpb, Celsr1, Clic5, D0H4S114, Dct, Dll4, Epha4, Exoc4, Fgfr3, Hand2, Helt, Hes5, Hey2, Heyl, Itga1, Kalrn, Kcnj10, Mesp1, Mib1, Nkx2-5, Nkx2-9, Plp1, Pmp22, Pou4f2, Prdm6, Robo2, Sox10, Syne1, Tnik</i>
GO: 0050767	Regulation of neurogenesis	20	2.67E-06	<i>Ache, Bcl11a, Camk1d, Cbfa2t2, D0H4S114, Dct, Dll4, Epha4, Fgfr3, Hes5, Hey2, Heyl, Kalrn, Mib1, Nkx2-5, Pmp22, Robo2, Sox10, Syne1, Tnik</i>
GO: 0048699	Generation of neurons	30	1.13E-05	<i>Ache, Bcl11a, Camk1d, Cbfa2t2, Ccr4, Cdkn1c, Cebpb, Celsr1, Clic5,</i>

				<i>D0H4S114, Dct, Dll4, Epha4, Fgfr3, Hand2, Helt, Hes5, Hey2, Heyl, Itgal, Kalrn, Mib1, Nkx2-5, Nkx2-9, Pmp22, Pou4f2, Robo2, Sox10, Syne1, Tnik</i>
GO: 0045664	Regulation of neuron differentiation	16	3.96E-05	<i>Ache, Bcl11a, Camk1d, Cbfa2t2, D0H4S114, Epha4, Hes5, Hey2, Heyl, Kalrn, Mib1, Nkx2-5, Pmp22, Robo2, Syne1, Tnik</i>
GO: 0042127	Regulation of cell proliferation	29	4.13E-04	<i>Btla, Cdkn1c, Dct, Dpp4, Eng, Erbb4, Fgfr3, Foxp2, Hand2, Hes5, Hey2, Hnf4a, Ido1, Il7, Itch, Itgal, Mlxipl, Ndr2, Nkx2-5, Nkx2-9, Pmp22, *Ptgs1, Slfn3, Sox10, Sox7, Tgm2, Tnfrsf13c, Tnmd, Tns3</i>
GO: 0007219	Notch signaling pathway	7	4.4E-05	<i>Dll4, Foxc2, Hes5, Hey2, Heyl, Mesp1, Mib1</i>
GO: 0045747	Positive regulation of Notch signaling pathway	4	1.28E-04	<i>Hes5, Hey2, Mesp1, Mfng</i>

GO analysis was carried out on putative SIRT1-regulated genes identified by screening microarray data. Significantly over-represented GO terms related to metabolism, neurogenesis, cell proliferation, and Notch signaling are summarized in this table.

Table S4. Summary of metabolic pathways with gene enrichment in ‘Pathway to Gene’ analysis of putative SIRT1-regulated genes based on microarray data

Pathway DB	Name	Hits	P value	Genes
Kegg	Metabolic pathways	19	0.0023	<i>Acacb, Alox5, Cda, Ckmt1, Cyp2j13, Dct, Galnt3, Glt28d2, Gyk, Hk3, Idol, Mdh1, Nnmt, Otc, Pank1, Pgap1, Prps111, Ptgs1, Uox</i>
Biocarta	Eicosanoid metabolism	2	0.0095	<i>Alox5, Ptgs1</i>
Kegg	Arachidonic acid metabolism	3	0.0265	<i>Alox5, Cyp2j13, Ptgs1</i>
Kegg	Pyruvate metabolism	2	0.0399	<i>Acacb, Mdh1</i>
Kegg	Fatty acid biosynthesis	1	0.0548	<i>Acacb</i>
Kegg	Arginine and proline metabolism	2	0.061	<i>Ckmt1, Otc</i>
Kegg	Pantothenate and CoA biosynthesis	1	0.1066	<i>Pank1</i>
Kegg	Glyoxylate and dicarboxylate metabolism	1	0.1191	<i>Mdh1</i>
Kegg	Nicotinate and nicotinamide	1	0.1674	<i>Nnmt</i>

	metabolism			
Kegg	Glycosylphosphatidylinositol (GPI) - anchor biosynthesis	1	0.1733	<i>Pgap1</i>
Kegg	Galactose metabolism	1	0.1791	<i>Hk3</i>
Kegg	O-glycan biosynthesis	1	0.1791	<i>Galnt3</i>
Kegg	Glycosaminoglycan biosynthesis	1	0.1849	<i>Hs3st5</i>
Kegg	Citrate cycle (TCA cycle)	1	0.2019	<i>Mdh1</i>
Kegg	Propanoate metabolism	1	0.2019	<i>Acacb</i>
Kegg	Fructose and mannose metabolism	1	0.2296	<i>Hk3</i>
Kegg	Amino sugar and nucleotide sugar metabolism	1	0.2718	<i>Hk3</i>
Kegg	Starch and sucrose metabolism	1	0.2718	<i>Hk3</i>
Kegg	Linoleic acid metabolism	1	0.277	<i>Cyp2j13</i>
Kegg	N-glycan biosynthesis	1	0.282	<i>Glt28d2</i>
Kegg	Glycerolipid metabolism	1	0.3214	<i>Gyk</i>
Kegg	Glycerophospholipid metabolism	1	0.4231	<i>Ache</i>
Kegg	Glycolysis/gluconeogenesis	1	0.5801	<i>Hk3</i>

TCA, Tricarboxylic acid.