

Supplementary Figure 1. Snf2h is robustly expressed in cerebellar neurons, whereas Snf2l is predominant in postmitotic PCs. (a) Wild type (WT) brain sagittal sections labeled with Snf2h (red) at the indicated ages. The cerebellum is shown in right panels. Cx, cortex; OB, olfactory bulb; Hipp, hippocampus; CPu, caudate putamen; Th, thalamus; CB, cerebellum; BS, brain stem. P = postnatal day. Scale bar, 500µm (left panels); 100µm (right panels). (b) WT cerebellar sections co-labeled with Snf2h (red) and NeuroD1 (green), a marker of neural lineages, at the indicated ages. Boxed areas are enlarged on right panels. Arrows denote Snf2h+, NeuroD1+ Purkinje cells (PCs), while asterisks and circles denote NeuroD1+, Snf2h+ granule cells (GCs) within the iEGL and the IGL. EGL, external granular layer; IGL, internal granular layer; o, outer; I, inner; PCL, Purkinje cell layer. Scale bar, 100 µm (left panels); 20µm (right panels). (c) WT cerebellar sections co-labeled with Snf2l (red) and Calbindin (green), a marker of PCs, at the indicated ages. Note that Snf2l is not expressed in PCs at P0, but in a distinct Calbindin+ cell lineage (circles), while that at P7 and P21 Snf2l is robustly expressed in PCs (arrows). Inset at P21 shows Snf2l channel only. Scale bar, 20µm.



Supplementary Figure 2. Nestin-Cre efficacy to CNS and cerebellar progenitors. (a,b) ROSA-STOP-LacZ reporter mice were bred to Nestin-Cre mice and X-gal staining performed at the embryonic stages indicated. <u>Inset:</u> Cerebellar sections from ROSA-STOP-lacZ::Nestin-Cre reporter mice stained with X-Gal at P30, highlighting robust lacZ expression in PCs and GCs. Fb = forebrain; Hb = hindbrain; SC = spinal cord; RL = rhombic lip. (c) ROSA-STOP-EYFP reporter mice were bred to Nestin-Cre mice and P0 sagittal sections co-labeled with Snf2h (red) and YFP (green). DAPI (cyan) labels all nuclei. Note robust Snf2h expression in hindbrain areas. Scale bar, 200µm. (d,e) Confocal Z-stacks through the cerebellar vermis reveals robust co-localization of Snf2h (red) and YFP (green) in nearly all cerebellar progenitors at P0. DAPI (blue) labels all nuclei. Asterisks denote 3 of the 4 principal fissures of the developing cerebellum. Boxed areas are enlarged in e. Scale bars, 100μ m (d); 5μ m (e).



Supplementary Figure 3. PCP2-Cre efficacy to postmitotic PCs after ~P10. (a) ROSA-STOP-EYFP reporter mice were bred to PCP2-Cre mice and co-labeled for Calbindin (green) and YFP (red) at the times indicated through the sagittal or transversal cerebellum. Scale bar, 200 μ m. (b,c) PCP2-Cre activity was assessed by generating *Atrx* cKO-PCP2 and *Snf2h* cKO-PCP2 mutant mice and cerebellar sections co-labeled for Calbindin (green) and Atrx (red); or Snf2h (red), where target deletion was exclusive to PCs by P30 (arrows). Asterisks denote Atrx- or Snf2h-null PCs. Scale bar, 50 μ m (b); 10 μ m (c).



Supplementary Figure 4. *Snf2h* cKO-PCP2 mice do not display motor alterations. *Snf2h* cKO-PCP2 do not exhibit motor alterations in the (a) elevated platform or (b) pole test relative to controls (n=10-14; one-way ANOVA). Values are presented as the mean \pm SEM.



Supplementary Figure 5. *Snf2h* cKO-Nes mice display normal *N-Myc* and *CyclinD1* mRNA expression in the neonatal cerebellum, as well as normal astrocyte proliferation in the neonatal period. (a) *In situ* hybridization through the cerebellar vermis from *Snf2h* cKO-Nes and control mice for *N-myc* and *Cyclin-D1* at P0. Scale bar, 200 μ m. (b) Confocal Z-stacks from *Snf2h* cKO-Nes and control littermates that were BrdU-birthdated at E18.5, a time of astrocyte (GFAP+ lineage) expansion, and co-labeled for BrdU (green) and GFAP (red) at P7. DAPI (blue) stains all nuclei. Boxed areas are enlarged on bottom panels. Circles denote BrdU+, GFAP+ astrocytes within the white matter. Scale bar, 100 μ m (top panels); 20 μ m (bottom panels).



Supplementary Figure 6. En1 compensation is dependent on Snf2l dosage in Snf2h cKO-Nes mouse strains. (a) Immunoblots for Snf2l and En1 from $Snf2l^{/+}::Snf2h$ cKO-Nes, Snf2h cKO-Nes, and control cerebellar extracts at P5. Note that En1 levels are decreased upon deletion of one Snf2l allele in the Snf2h cKO-Nes background relative to Snf2h cKO-Nes and WT controls. However, both Snf2h cKO-Nes and Snf2l^{/+}::Snf2h cKO-Nes mice have upregulated Snf2l levels relative to WT controls. Actin served as loading control. (b) ChIP-qPCR from WT cerebellar extracts for the En2 locus reveals Snf2h enrichment throughout the gene at P7 and P21, whereas Snf2l was not enriched at neither time point. R4, 5kb away from TSS; R3, 1kb away from TSS; R2, 5'-UTR; R1, intronic primer pair. *P<0.05, student's t-test. Samples were analyzed in quadruplicates in three independent experiments per time point. Values are presented as the mean \pm SEM.



Supplementary Figure 7. *Snf2h* cKO-PCP2 cerebella develop normally, but have progressive PC death. (a) *In situ* hybridization through the cerebellar vermis from *Snf2h* cKO-PCP2 and control mice at P90 for *Pax6*, a marker of differentiated GCs, and *Patched-1* and *Gli-1*, downstream targets of the *Shh* signaling pathway. Scale bar, 100µm. (b) Quantitation of PCs through the cerebellar vermis from *Snf2h* cKO-PCP2, cDKO-PCP2 mice and control littermates at the indicated ages. Note the progressive loss of PCs by P300 in the mutant strains. **P*<0.05, ***P*<0.01, student's t-test. Values are presented as the mean \pm SEM. 3 mice were analyzed per genotype and time point. (c) Whole mount top view images from *Snf2h* cKO-PCP2, cDKO-PCP2 mice and control brains at P40. Note the normal morphology of the mutant brains.



Supplementary Figure 8. siSnf2h knockdown alters nuclear morphology prior to pCaspase activation, while GFP-H1e mobility is unaffected by Snf2l knockdown. (a) Neuro2A cells co-transfected with siScrambled + pEGFP (to label transfected cells), or siSnf2h + pEGFP. EGFP (green) and pCaspase (gray) co-labeling reveals that pEGFP+ cells show pCaspase-ir only 96 hrs after siSnf2h KD (arrows). DAPI (gray) stains all nuclei. Scale bar, 2μ m. (b) Neuro2A cells treated with siScrambled or siSnf2h and immunolabeled with Snf2h (red). DAPI (gray) stains all nuclei. Confocal Z-stacks reveal that Snf2h^{low}-expressing cells (circles) display a more diffuse DAPI+ staining throughout the nucleus, as well as decreased DAPI+ heterochromatic foci relative to Snf2h^{high}-expressing cells (boxes). Scale bar, 2μ m. (c) GFP-H1e FRAP recovery curves from Neuro2A cells 48-hrs after siSnf2l transfection. Error bars were removed for clarity, n=20 FRAP movies per condition.

Supplementary Figure 9. Original scanned radiography films of western blots and RNA quality checks are provided for the corresponding panels.





Mouse Gene	Application	<u>5' to 3'</u>
Uncx-Ex2-F	qRT-PCR	GCGTTCAATGAGAGCCACTA
Uncx-Ex3-R	qRT-PCR	CCCTTTTTGGTGTTCTCCTTC
Rfx3-Ex3-F	qRT-PCR	GCTCAGGTGCAGTATGTGGA
Rfx3-Ex4-R	qRT-PCR	CTGGGCAGAACTTCCTTGAG
Cbp Ex2-F	qRT-PCR	ACACAGGTTTCCCCACAAAT
Cbp Ex3-R	qRT-PCR	CTAACTGGGGGGTTCACTCCA
Bmp4-Ex1-F1	qRT-PCR	TGATACCTGAGACCGGGAAG
Bmp4-Ex2-R	qRT-PCR	CCTGGGATGTTCTCCAGATG
En1-F1	qRT-PCR	TCACAGCAACCCCTAGTGTG
En1-R1	qRT-PCR	TATAGCGGTTTGCCTGGAAC
En2-F1	qRT-PCR	GACTCGGACAGCTCTCAAGC
En2-R1	qRT-PCR	GCCGCTTGTCCTCTTTGTTA
Pax6-Ex2F	qRT-PCR	TCAGCTTGGTGGTGTCTTTG
Pax6-Ex3R	qRT-PCR	AGCACCTGGACTTTTGCATC
Snf2h-Ex4F	qRT-PCR	ACACCGTAGAACGGAGCAAG
Snf2h-Ex5R	qRT-PCR	AGACTTGGGAACCAAAACCA
Math1-F2	qRT-PCR	GCTTCCTCTGGGGGGTTACTC
Math-R2	qRT-PCR	CTGTGGGATCTGGGAGATGT
Snf2l-Ex4-F	qRT-PCR	CCACAGGCGTACAGAACAAG
Snf2l-Ex5-R	qRT-PCR	GCGGTCCTCCTTTCACAT
Pcdhb6-F	qRT-PCR	CCCTCGATGCCTTAGTTGTC
Pcdhb6-R	qRT-PCR	CAAAATCCAGTGCCCCTTTA
Pcdhb17-F	qRT-PCR	AGCTACTCGCTGTTGCCTTC
Pcdhb17-R	qRT-PCR	GGTGAGCCTTGGTCTATTGC
En2-5kbpromo-F (R4)	ChIP-qPCR	TTTTTGGGTGCCATCTTCTC
En2-5kbpromo-R (R4)	ChIP-qPCR	CCCTCCAGGTGTTACAGAGG
En2-1kbpromo-F (R3)	ChIP-qPCR	GGTTCCTGTCACCAAGCTG
En2-1kbpromo-R (R3)	ChIP-qPCR	CGCAACCTGAGACACTTTCA
En2-I1-F (R1)	ChIP-qPCR	AGGCAGTTGGAAGGACACAC
En2-I1-R (R1)	ChIP-qPCR	CCTGAGGATGGCAGAGAGTT
En2-ATG-F (R2)	ChIP-qPCR	CACTTGAGGGGGGCTCTGTTA
En2-ATG-R (R2)	ChIP-qPCR	GGGAAAATTTCAGGCCACTT
En1-P4F-5kb (R4)	ChIP-qPCR	GGTGGGGATACACCCAGATA
En1-P4R-5kb (R4)	ChIP-qPCR	TGTGGAGAAGGCTTTGAGGT
En1-P3F (R3)	ChIP-qPCR	CTTCATGCCCTCTTAAGTCC
En1-P3R (R3)	ChIP-qPCR	CGGGACTTTGCGGATAAATA
En1-P2F-Ebox (R2)	ChIP-qPCR	AGTGTCAGCGCGAGTTCTG
En1-P2R-Ebox (R2)	ChIP-qPCR	TCTGACCAGCTCGGATCTTTG
En1-I1F (R1)	ChIP-qPCR	CGGGAGAGTCCAGTTTGAAG
En1-I1R (R1)	ChIP-qPCR	GTGCGTGCCAATAGCTGTAA

Supplementary Table 1. List of primer pairs used for RT-qPCR and qPCR-ChIP experiments.