SUPPLEMENTARY INFORMATION

HDAC1 and HDAC2 Regulate Oligodendrocyte Differentiation By Disrupting β-Catenin-TCF Interaction

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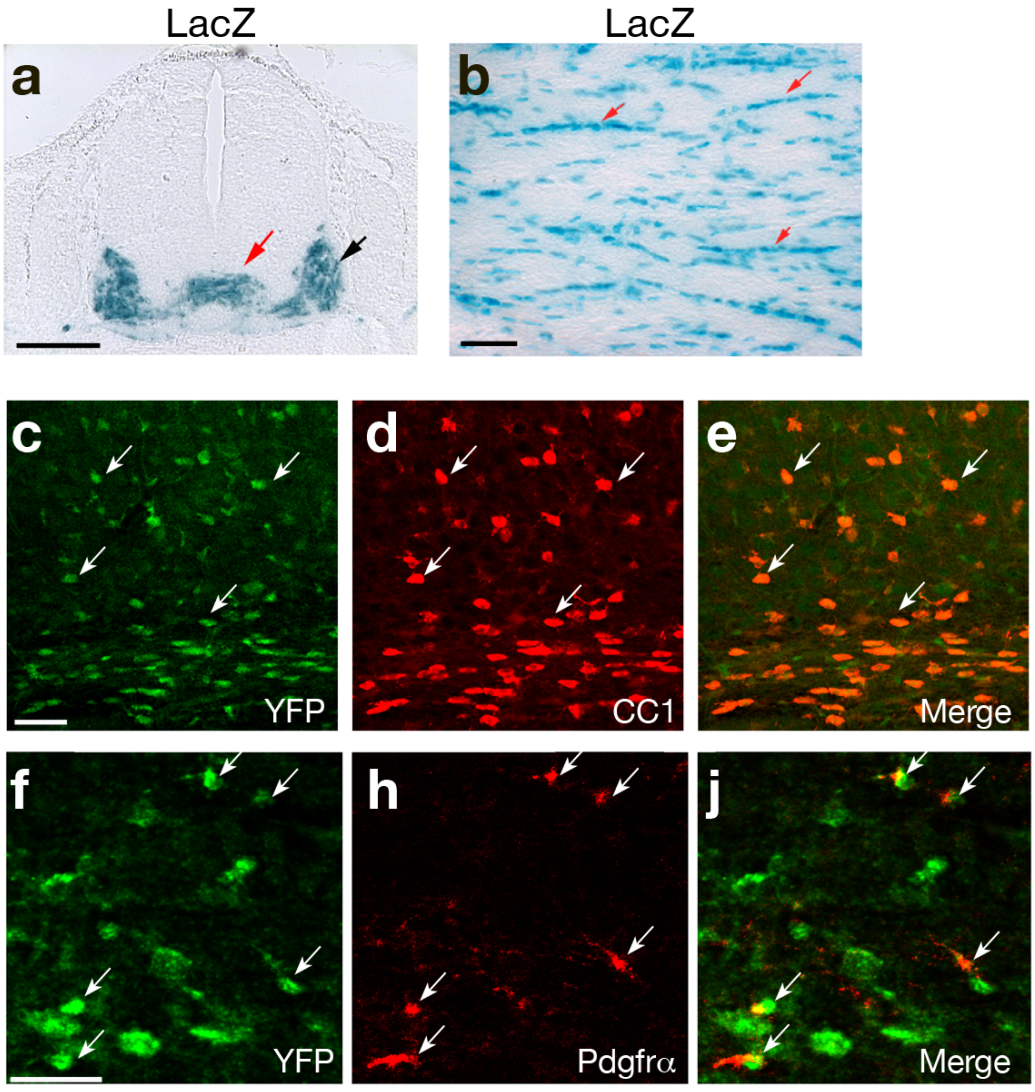
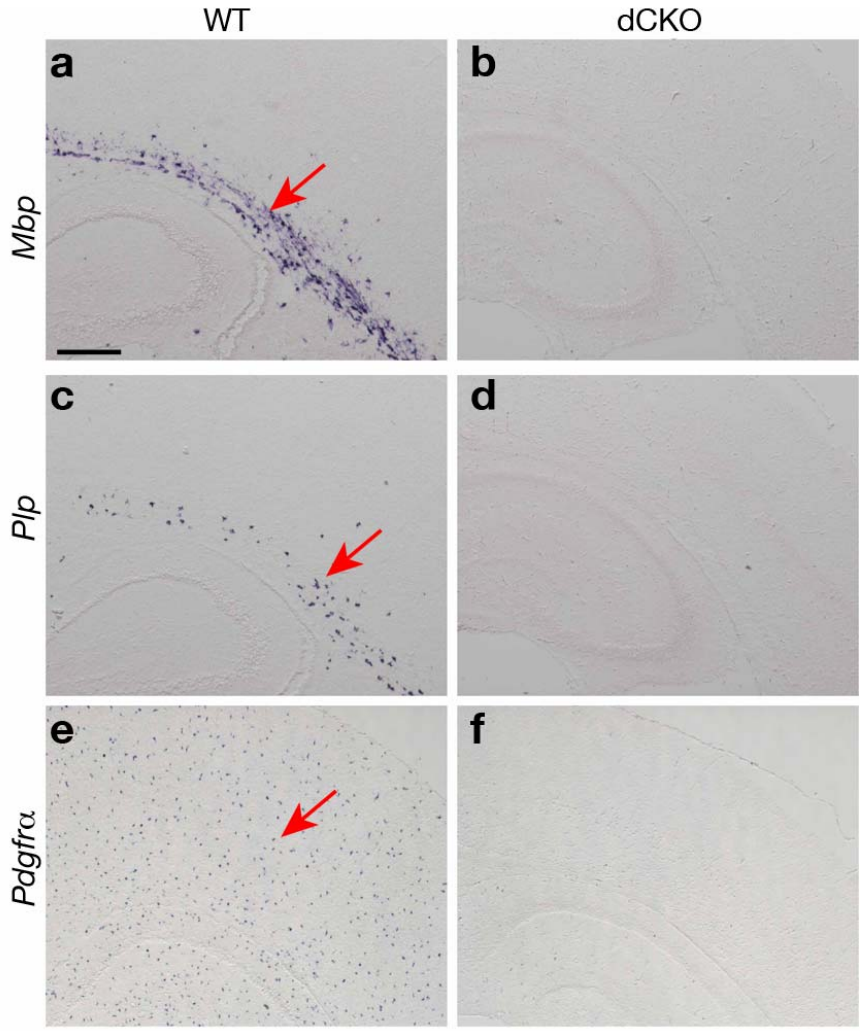


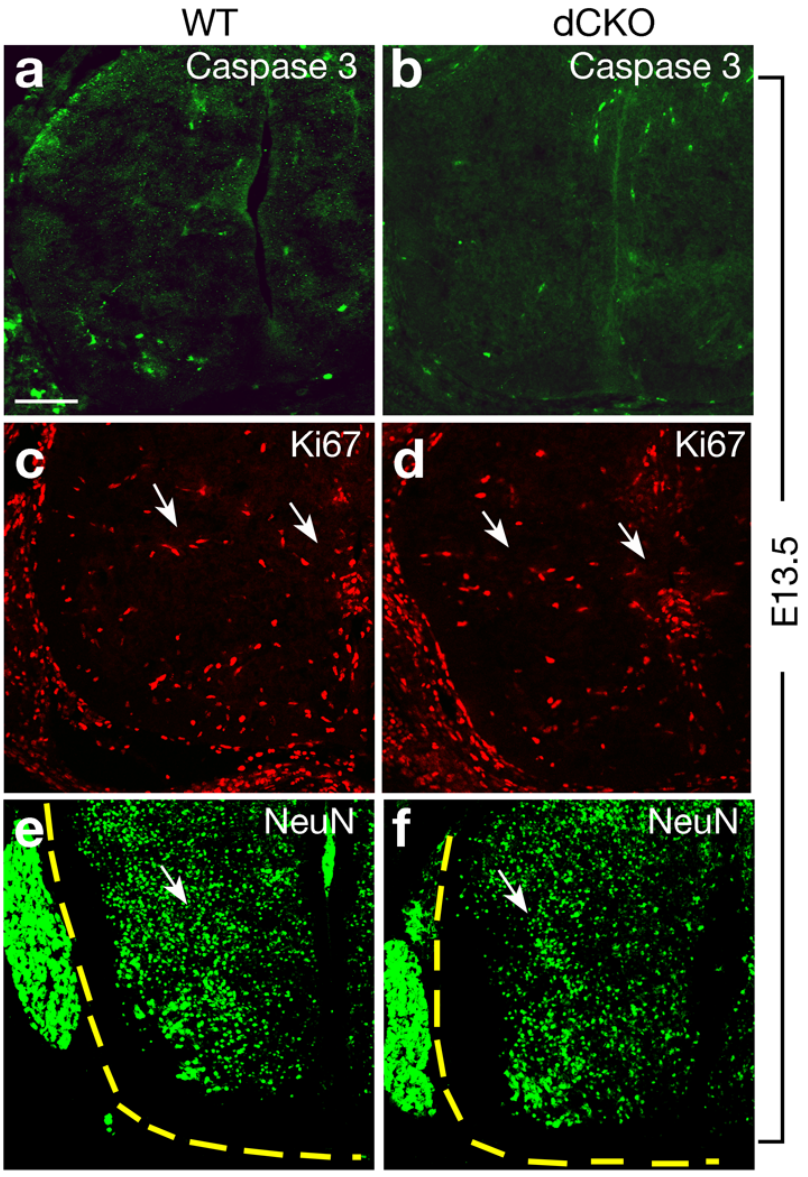
Supplementary Figure 1. Olig1-Cre directed reporter expression in oligodendrocytes and their progenitors

Olig1-Cre mice were intercrossed to ROSA reporter strains Rosa-LacZ or RosaYFP containing the floxed STOP at the ROSA26 locus. **a**) In the Cre/lacZ or YFP-positive progeny of such intercrosses, β-galactosidase activity is restored in cells that express Cre. Daughter cells can be followed at later stages of development by incubation with the substrate X-gal. At E12.5 LacZ (β-galactosidase activity) was detected in OPCs and motor neurons as indicated by red and black arrows, respectively. **b**) At P14, LacZ (β-galactosidase activity) was detected in oligodendrocytes, which form typical intrafascicular linear arrays in the corpus callosum (arrows). **c-j**) Cortical sections of brains from intercross of RosaYFP;Olig1Cre were immunostained with antibodies to YFP and CC1 (**c-e**) or Pdgfrα (**f-j**). Co-localization of YFP reporter (GFP+) and CC1 or Pdgfrα was indicated by arrows. Scale bars in **a**, 200 μm; in **b** and **c-e**, **f-j**, 100 μm.



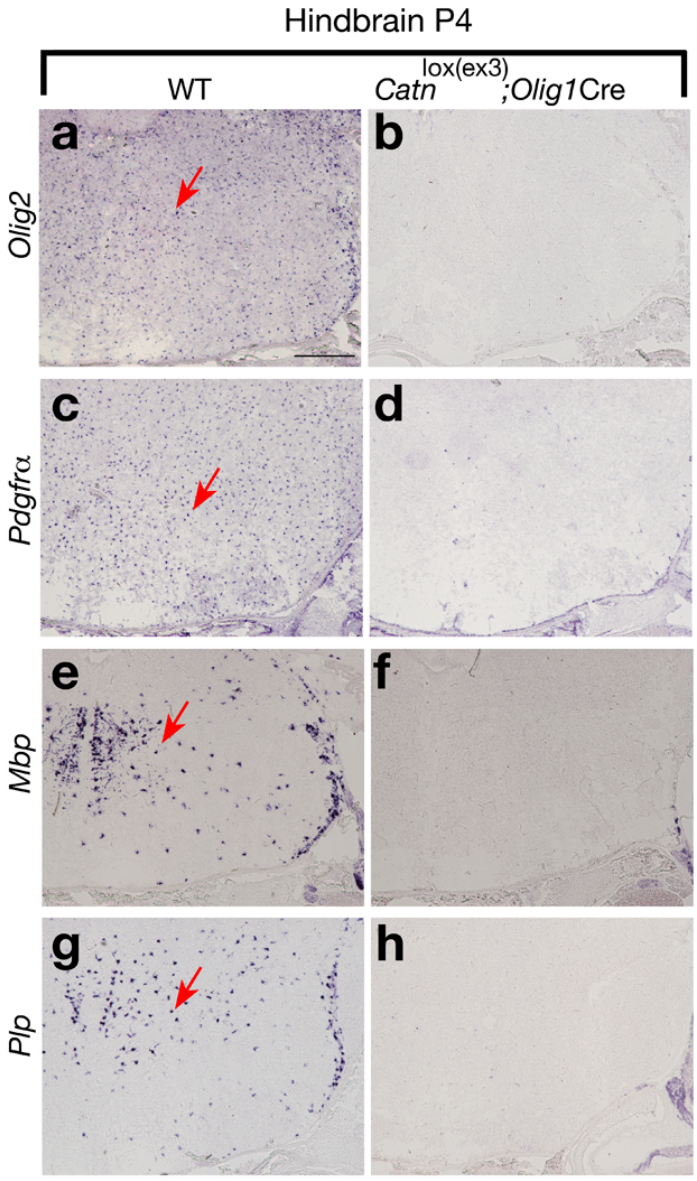
Supplementary Figure 2. Absence of oligodendrocyte lineage markers in the postnatal brain of *HDAC* dCKO mutants

Expression of mRNA transcripts for the oligodendrocyte lineage markers *Pdgfrα, Plp,* and *Mbp* was analyzed in situ on frozen sections of brains taken from wild-type and dCKO animals at P10 as indicated. Arrows in **a,c** and **e,f** indicated the cerebral white matter region and cortex, respectively. Note there is absent of these oligodendrocyte lineage markers in the brain of dCKO animals. Scale bar in **a-f**, 200 μm.



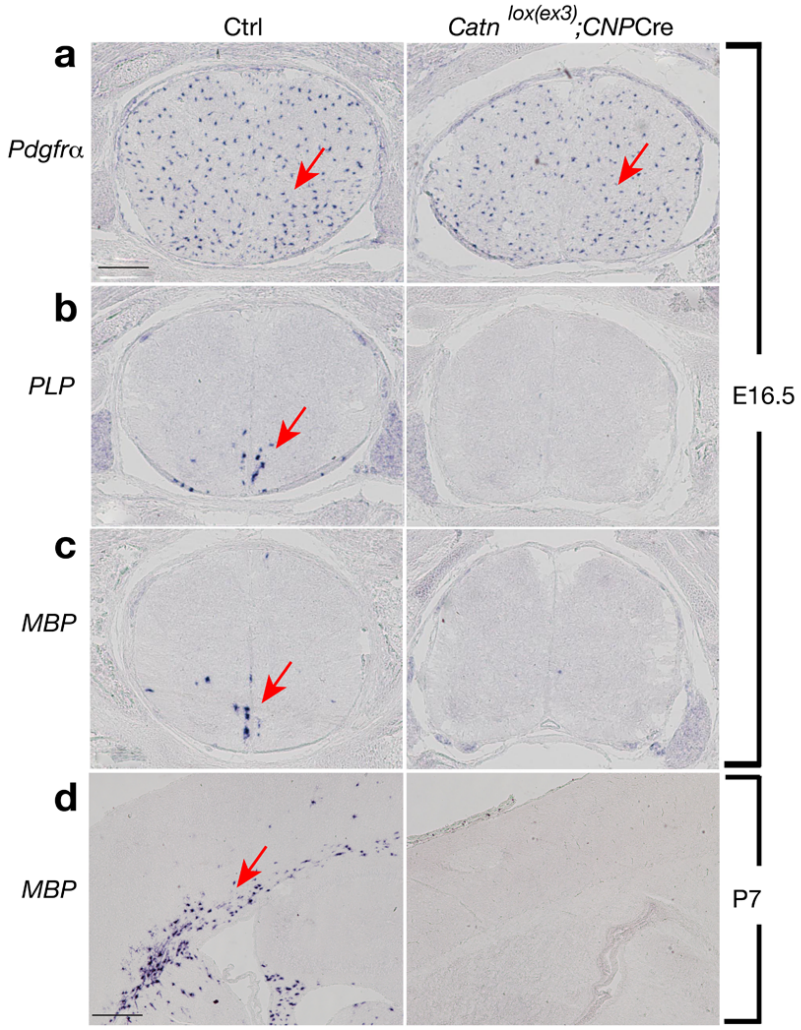
Supplementary Figure 3. Olig1-Cre mediated *HDAC1/2* deletion does not lead to abnormality in cell death, cell proliferation or neurogenesis in the spinal cord

WT and dCKO embryos at E13.5 were collected, sectioned and subjected to immunostain using anti-Caspase 3 (**a,b**), anti-Ki67 (**c,d**) and anti-NeuN (**e,f**) antibodies as indicated. No significant alteration in terms of cells death, cell proliferation or neurogenesis was detected between WT and dCKO mice. Scale bar in **a-f**, 100 μm.



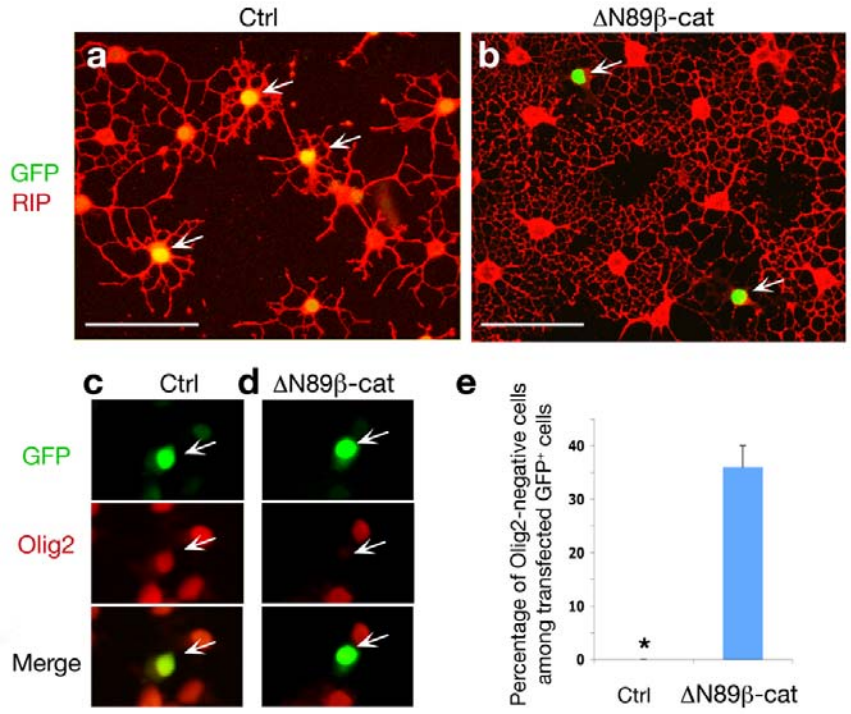
Supplementary Figure 4. Activation of canonical Wnt signaling in oligodendrocyte lineage cells inhibits oligodendrocyte differentiation in hindbrain

a-h) In situ hybridization of frozen transverse sections of hindbrains taken from wild-type (WT) and *Catn*$^{lox(ex3)}$*;Olig1Cre* mice at P4 using probes to *Olig2, Pdgfrα, Mbp,* and *Plp* as indicated. Arrows indicate the in situ labeled cells. Scale bar in **a-h**, 200 μm.



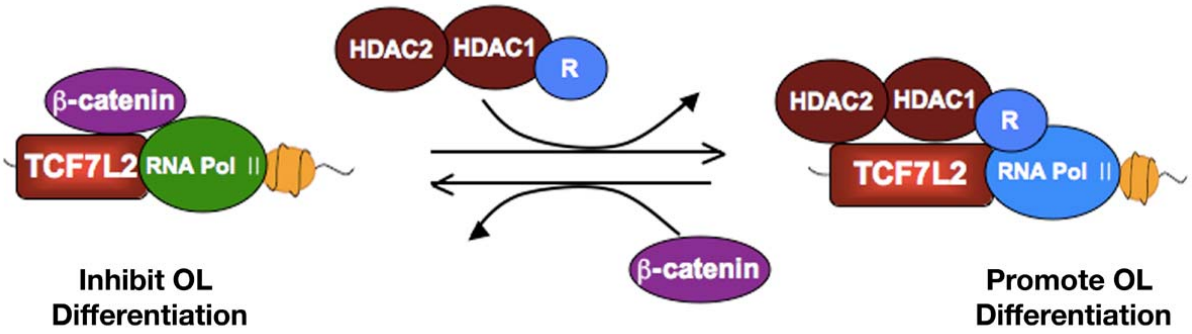
Supplementary Figure 5. Activation of canonical Wnt signaling in *CNP*$^{+}$ oligodendrocyte lineage cells inhibits oligodendrocyte differentiation

In situ hybridization of frozen transverse sections of spinal cord (**a-c**) and forebrain (**d**) taken from wild-type (WT) and *Catn*$^{lox(ex3)}$*;CNP-Cre* (β-catenin gain-of-function) mice at E16.5 and P7 using probes to *Pdgfrα, Plp* and *Mbp* as indicated. Arrows indicate in situ labeled signals. Notably, oligodendrocyte differentiation markers *Plp* and *Mbp* were not detected in the CNP-Cre mediated β-catenin gain-of-function animals. Scale bar in **a-d**, 200 μm.



Supplementary Figure 6. Constitutive expression of an active form of β-catenin inhibits Olig2 expression

a,b) Immunostain of hippocampus-derived adult neural progenitor cells (HCN) four days after being transfected with ΔN89 β-catenin and control pCIG vectors (GFP) using antibodies to RIP. Arrows indicate ΔN89β-catenin expressing cells (**b**) and pCIG vectors (GFP) cells **(a)**, respectively. **c,d**) HCN cells transfected with control GFP and ΔN89 β-catenin as indicated. HCN cells express Olig2 homogeneously in the presence of IGF-1. Absence or severe reduction of Olig2 expression was observed in ΔN89β-catenin transfected cells (arrows; **d**). **e**) Histograph shows the percentage of Olig2-negative cells among control and ΔN89β-catenin-transfected cells. Data are derived from three independent experiments. Error bars shown are the mean ± S.D. (*p<0.01, Student *t*-test).



Supplementary Figure 7. A schematic model for the convergence of β-catenin and HDAC proteins on TCF7L2 to regulate oligodendrocyte differentiation

HDAC1 and HDAC2 interact with each other and are the catalytic core components to multiple large transcriptional complexes. The complex might be bridged by co-repressors (R) such as Groucho-type repressors. HDAC1/2 and co-repressors compete with β-catenin to form a complex with TCF7l2 and therefore promote oligodendrocyte (OL) differentiation. On the other hand, β-catenin association with TCF7L2 disrupts the HDAC-TCF complex and inhibits OL differentiation. Hence, TCF7L2 functions as a key molecular switch for oligodendrocyte differentiation and a balance or ratio between HDAC1/2 and β-catenin on TCF7L2 transcriptional activity regulates the timing of oligodendrocyte differentiation.