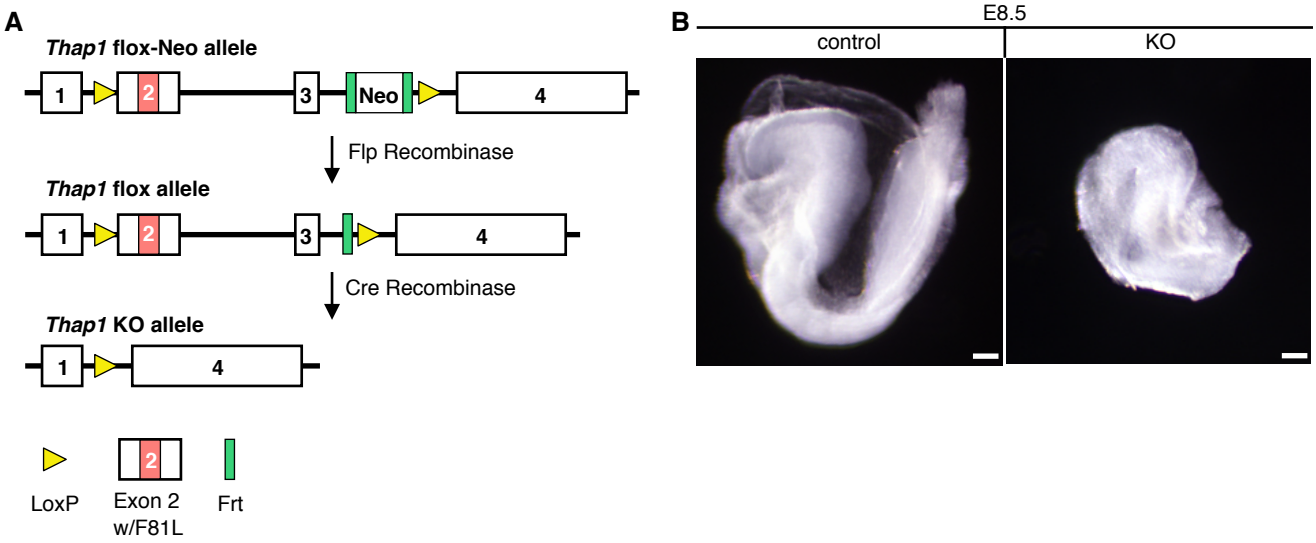
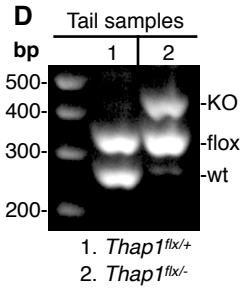
## Figure S1 - related Figure 1

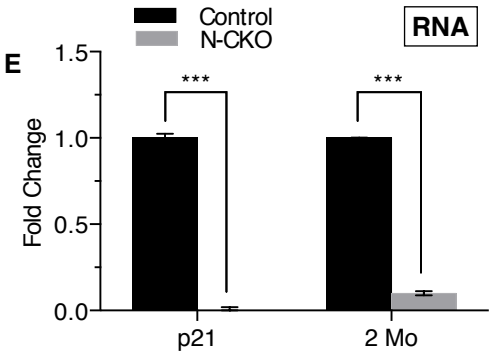


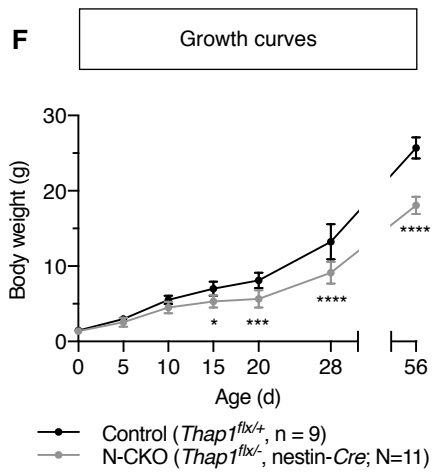

**C**

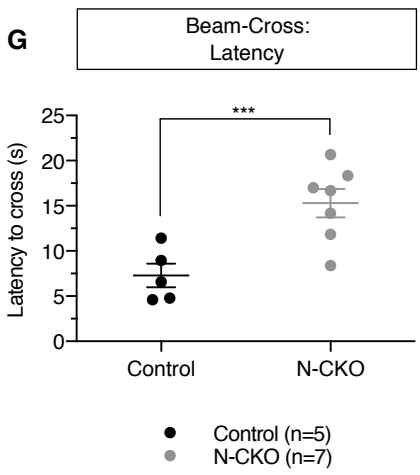
***Thap1* Mendelian Ratio**

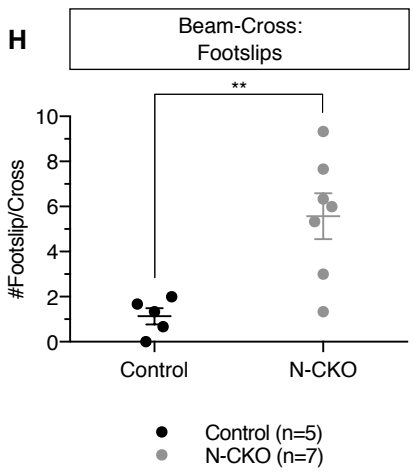
| Genotype | Observed | Ratio |
|---|---|---|
| *Thap1*$^{flx/+}$ | 51 | 24.9% |
| *Thap1*$^{flx/-}$ | 50 | 24.4% |
| *Thap1*$^{flx/+}$, nestin-*Cre* | 55 | 26.8% |
| *Thap1*$^{flx/-}$, nestin-*Cre* | 49 | 23.9% |

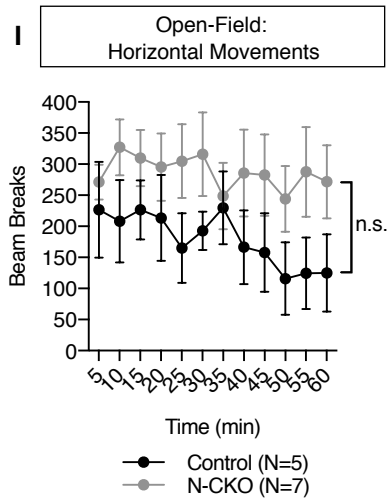


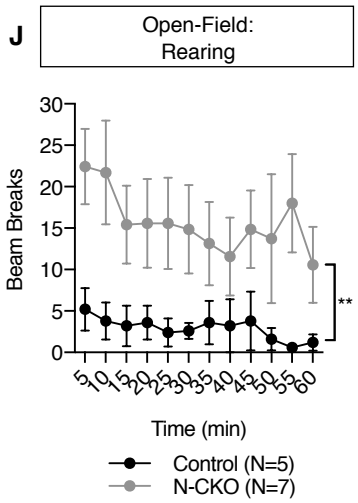



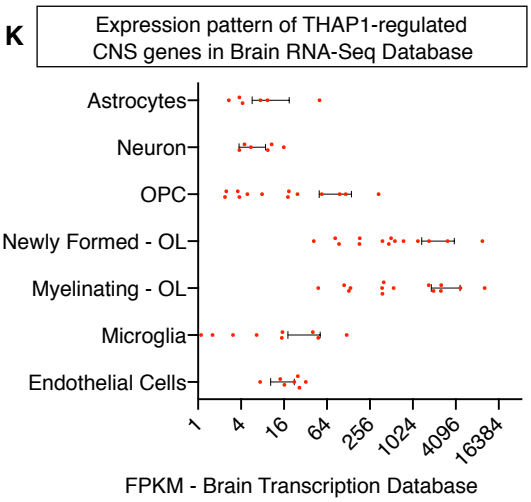



**Figure S1 - related to Figure 1: Germline Deletion of *Thap1* Results in Embryonic Lethality**

(A) Generation of *Thap1* null mice. Schematic representation of the strategy to generate *Thap1* null mice. Lox P sites were inserted flanking the 2nd and 3rd allele of *Thap1* locus using a Neomycin containing targeting construct to generate *Thap1-flx* allele that carries carries the DYT6 missense mutation F81L. Mice with *Thap1-flx* allele were intercrossed Flp-expressing mice to remove the neomycin cassette and generate *Thap1* $^{Flx/Flx}$ mice followed by crossing to Rosa-Cre line to generate germline *Thap1* knockout (*Thap1* $^{-/-}$).

(B) Germline deletion of *Thap1* results in embryonic lethality. *Thap1* $^{-/-}$ (Flx/-; Rosa Cre +) *are* developmentally arrested by stage E8.5. Shown are 2 representative embryos derived from *Thap1* $^{-/-}$ and littermate Control (Wt/Flx; Rosa Cre+).

(C) N-CKO mice are born in mendelian ratio. Genotypes of offspring obtained from the cross of *Thap1*$^{wt/-}$*; Nes-Cre* mice and *Thap1*$^{flox/flox}$ mice. Shown in the table are the numbers of mice of various genotypes obtained by crosses of *Thap1*$^{wt/-}$*; Nes-Cre* mice and *Thap1*$^{flox/flox}$ mice. The expected numbers of mice were calculated according to the total number of mice born based on the expected Mendelian 1:1:1:1 ratio.

(D-E) Loss of *Thap1* expression in N-CKO CNS. (D) PCR showing genotyping for the *Thap1* locus from tail DNA samples derived from (Flx/-) and littermate control (Wt/Flx) mice. (E) qRT-PCR showing the loss THAP1 mRNA expression derived from Cortex of Flx/-; Nes Cre+ relative to Cortex from littermate Control (Wt/Flx; Nes Cre+) at ages P21 and P60.

(F) Growth curve of N-CKO mice. N-CKO (Flx/-; Nes Cre+) mice are measurably smaller (~ 30 % smaller body weight at ages p28 and beyond; 2 - way Annova $p<.001$) than their littermate controls (Wt/Flx; Nes Cre+).

(G-J) P56 N-CKO (Flx/-; Nes Cre+, N= 7) mice exhibit motor deficits relative to littermate control (Wt/Flx; N=5).

(G-H) Beam-Cross assay: N-CKO mice take (G) longer time crossing the balance beam (Latency to Cross: Control = 7.28s ± 2.91 ; N-CKO= 15.30s ± 4.15 ; One-way ANOVA: $p< 0.001$) and (H) show more footslips during the assay as measured (Average footsteps per crossing: Control = 1.13 ± 0.8 ; N-CKO= 5.57 ± 2.7 ; One-way ANOVA: $p=0.003$).

(I-J) During the Open-field test, N-CKO mice show no significant changes in the (I) horizontal locomotor movements but exhibit increased (J) rearing activity compared to the control cohort (Two-way ANOVA: $p=0.0025$).

(K) Overrepresentation of THAP1-regulated genes in mature OL population. Expression levels (FPKM) (y - axis) of all N-CKO OL enriched genes from brain transcriptome was plotted for different brain cell population (x - axis). THAP1-regulated OL genes are enriched (> 10 fold) specifically within maturing OL.

**Figure S2 - related to Figure 2**

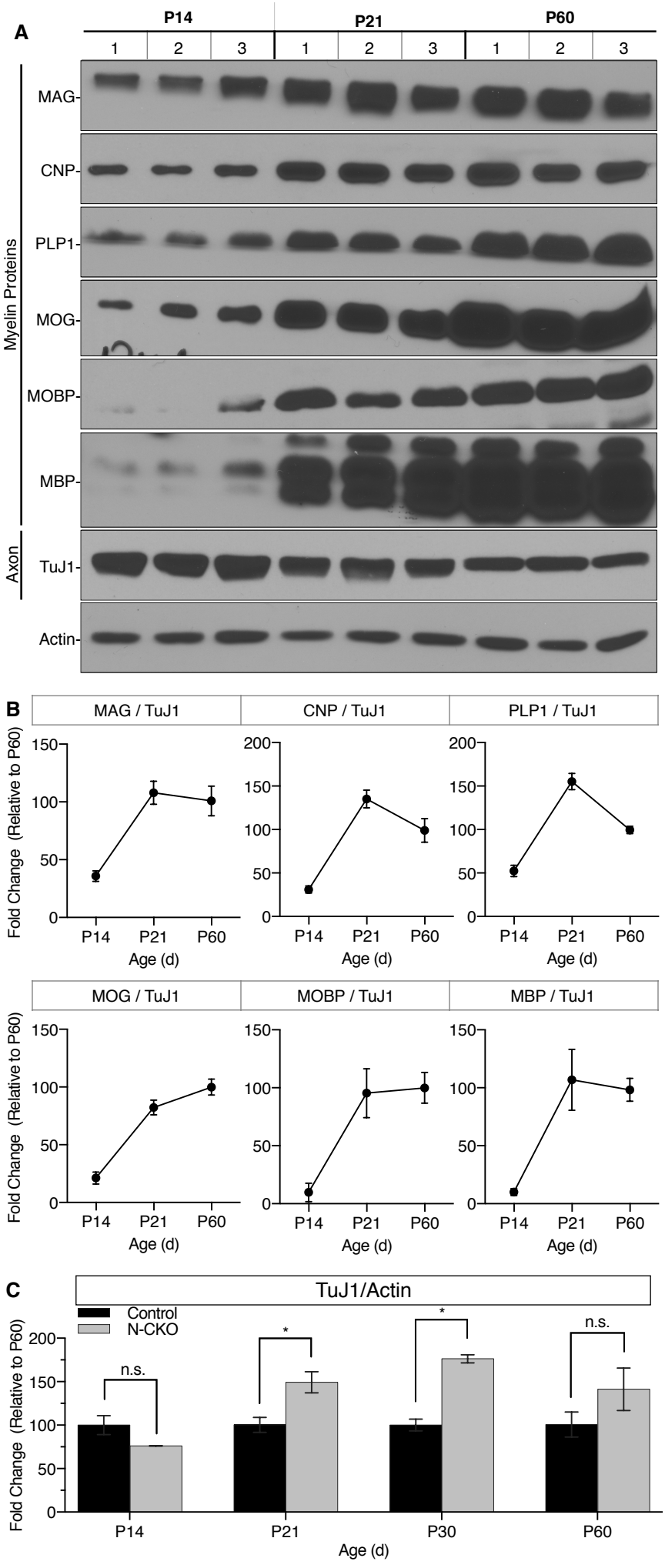


**Figure S2 - related to Figure 2: Kinetics of Myelin Protein Production in Developing Mouse CNS:**

(A) Western blot of the Myelin proteins (MAG, CNP, PLP1, MOG, MOB and MBP), axon protein β-III Tubulin (TuJ1) and loading control proteins (Actin, Calnexin) from mouse whole forebrain homogenate of Control (WT/Flx; Nes Cre+) mice from multiple stages of postnatal development (P14, P21 and P60) (N=3 for each age).

(B) Ratio of Myelin / Axon for various Myelin proteins during postnatal development as measured from intensity of the Western blot (Image J analysis) is represented as a percentage change to values at P60.

(C) N-CKO mice exhibit no significant reductions in axon levels (TuJ1) during juvenile CNS maturation, when normalized to the loading control , Actin. The graph represents the ratio ofTuJ1 / Actin as measured from intensity of the Western blot (Figure 1G) (Image J analysis) and represented as a percentage change to littermate controls (Wt/Flx; Nes Cre+) at the age of P14, P21, P30 and P60.

## Figure S3 - related to Figure 3 - 5

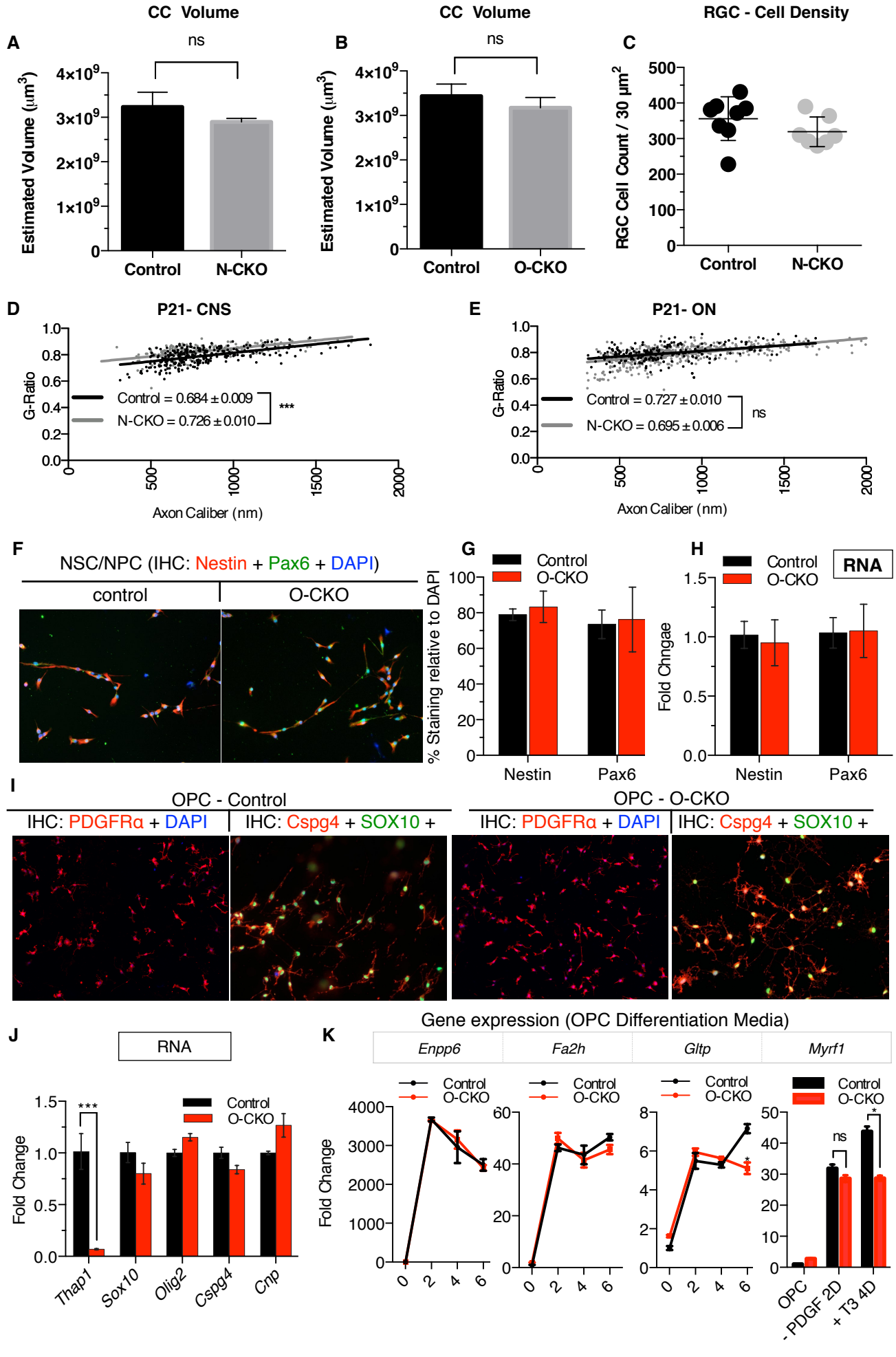


**Figure S3 - related to Figure 3 - 5: Derivation of OPC from SVZ-NSC.**

(A-B) No significant changes in the CC volume of adult *Thap1* null mice. (A) Final volume of CC, as assessed using Cavalieri's estimator is represented as $\mu m^3$ (y-axis) for control (*Thap1*$^{flx/+}$; nestin-*Cre*$^{+}$; N=3) and N-CKO (*Thap1*$^{flx/-}$; nestin-*Cre*$^{+}$; N=3) mice (P90 - Control = 3.23 $mm^3$ ± 0.148 ; N-CKO = 2.89 $mm^3$ ± 0.09 ± 0.04; T-test p=0.09).
(B) Final volume of CC, as assessed using Cavalieri's estimator is represented as $\mu m^3$ (y-axis) for control (*Thap1*$^{+/+}$; N=3) and O-CKO (*Thap1*$^{flx/flx}$; Olig2-*Cre*$^{+}$; N=3) mice (P90 - Control = 3.43 mm3 ± 0.15 ; O-CKO = 3.17 mm3 ± 0.17; T-test p=0.27).
(C) Conditional deletion of THAP1 in the CNS has no effect on the RGC neurons in the optic nerve. The average numbers of retinal ganglion cell bodies, that give rise to optic nerve axons was estimated from Brn3a + cell counts taken as an average from 5 serial sections (30 µm2 thick) from control (Wt/Flx; Nes Cre+) and N-CKO (Flx/-; Nes Cre+) retina (N=3) (WT = 319 ± 38 RGC/30 µm2; N-CKO = 365 ± 57 RGC/30 µm2 ).
(D-E) Characterization of myelin thickness (G-ratio) for N-CKO mice in CNS. The G-ratio (ratio of the inner axonal diameter to total (including myelin) outer diameter) for control (*Thap1*$^{+/+}$; nestin-*Cre*$^{-}$; N=5) and N-CKO (*Thap1*$^{flx/-}$; nestin-*Cre*$^{+}$; N=5) mice at ages P21 from (B) CC (Control = 0.684 ± 0.009, O-CKO = 0.7550 ± 0.008 t-test p<0.001) and (C) ON (Control = 0.727 ± 0.01, O-CKO = 0.695 ± 0.006 t-test p = 0.592).
(F-H) Characterization of NSC derived from Control (*Thap1*$^{+/+}$) and O-CKO (*Thap1*$^{flx/-}$; Olig2-*Cre*$^{+}$) SVZ. (F) representative ICC images and (G) quantitation of ICC analyses for markers of NSC (PAX6 and NESTIN ) confirmed that NSC cells isolated from Control and THAP1 O-CKO cells. (H) qRT-PCR analysis confirming relative expression of *Nestin* and *Pax6* genes from control and THAP1 O-KO NSC.
(I-J) Derivation and characterization of OPC derived from Control and O-CKO NSC. (I) Staining for OPC specific markers ( PDGFr**α**, Sox10 and NG2) confirmed purity of OPC cells isolated from from wild type and THAP1 O-CKO NSC. (J) qRT-PCR analysis confirming relative expression of OL lineage specific genes (*Sox10, Olig2, Cspg4* and *Cnp*) genes from OPC derived from control and THAP1 O-cKO NSC.
(K) qRT-PCR analysis for immature OL marker *Ennp6* and OL enriched genes (*Fa2h, Gltp*) in differentiating OL by PDGF withdrawal (days 0, 2, 4 and 6) from Control (*Thap1*$^{+/+}$) and THAP1 null (*Thap1*$^{-/-}$) OPC. The relative expression for the OL pro-maturation gene *Myrf1* was measured from OPC and differentiating OL by PDGF withdrawal for 2 days and PDGF withdrawal + T3 for 4 days. The expression values for all gene is normalized to *Olig2* expression and represented as a fold change with respect to values from control OPC (0D).

**Figure S4 - related to Figure 6**

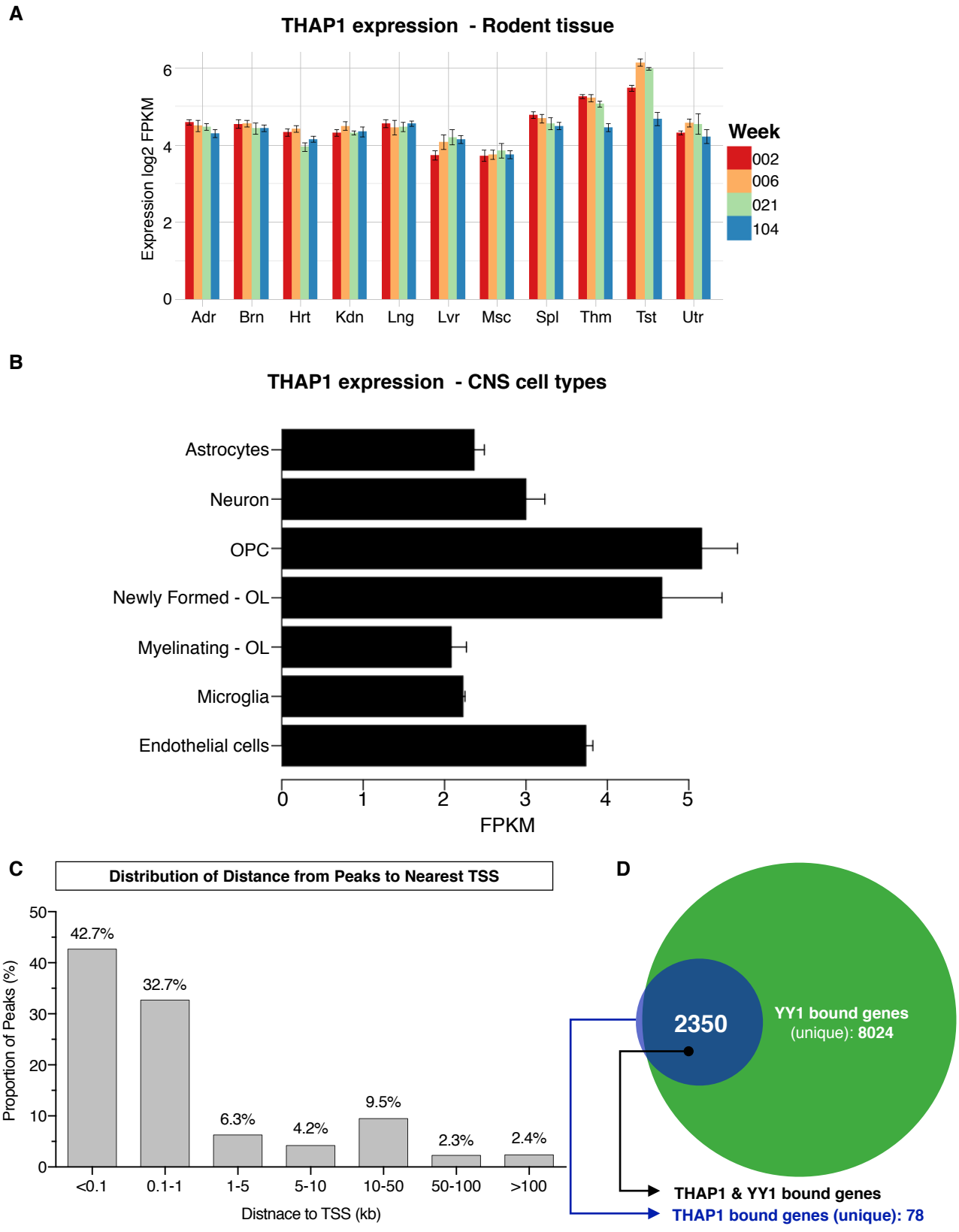


**Figure S4 - related to Figure 6: *Thap1* expression in rodent tissue.**

(A) THAP1 is expressed ubiquitously in all rodent tissues throughout development. RNA expression levels(FPKM) (y - axis for *Thap1* was assessed in developing rodent for 10 organs (adrenal gland, brain, heart, kidney, liver, lung, muscle, spleen, thymus, and testis or uterus) from ages 2 weeks through 104 weeks using RNA expression database from Rat BodyMap (http://pgx.fudan.edu.cn/ratbodymap/index.html).
(B) THAP1 is ubiquitously expressed in all CNS cell types. Expression levels (FPKM) (y - axis) of *Thap1* from brain transcriptome was plotted for different brain cell population (x - axis).
(C) Majority (> 70 %) of THAP1 associated peaks are distributed within 1kb of TSS. The y-axis represents the proportion of total peaks distribution relative to TSS (x-axis; represent in kilo bases). Peak distribution was determined using CHIP-Enrich (Experimental procedures)
(D) YY1 in associated with 97 % of THAP1 bound genes as shown in the Venn diagram in the schematic.

**Figure S5 - related to Figure 6**

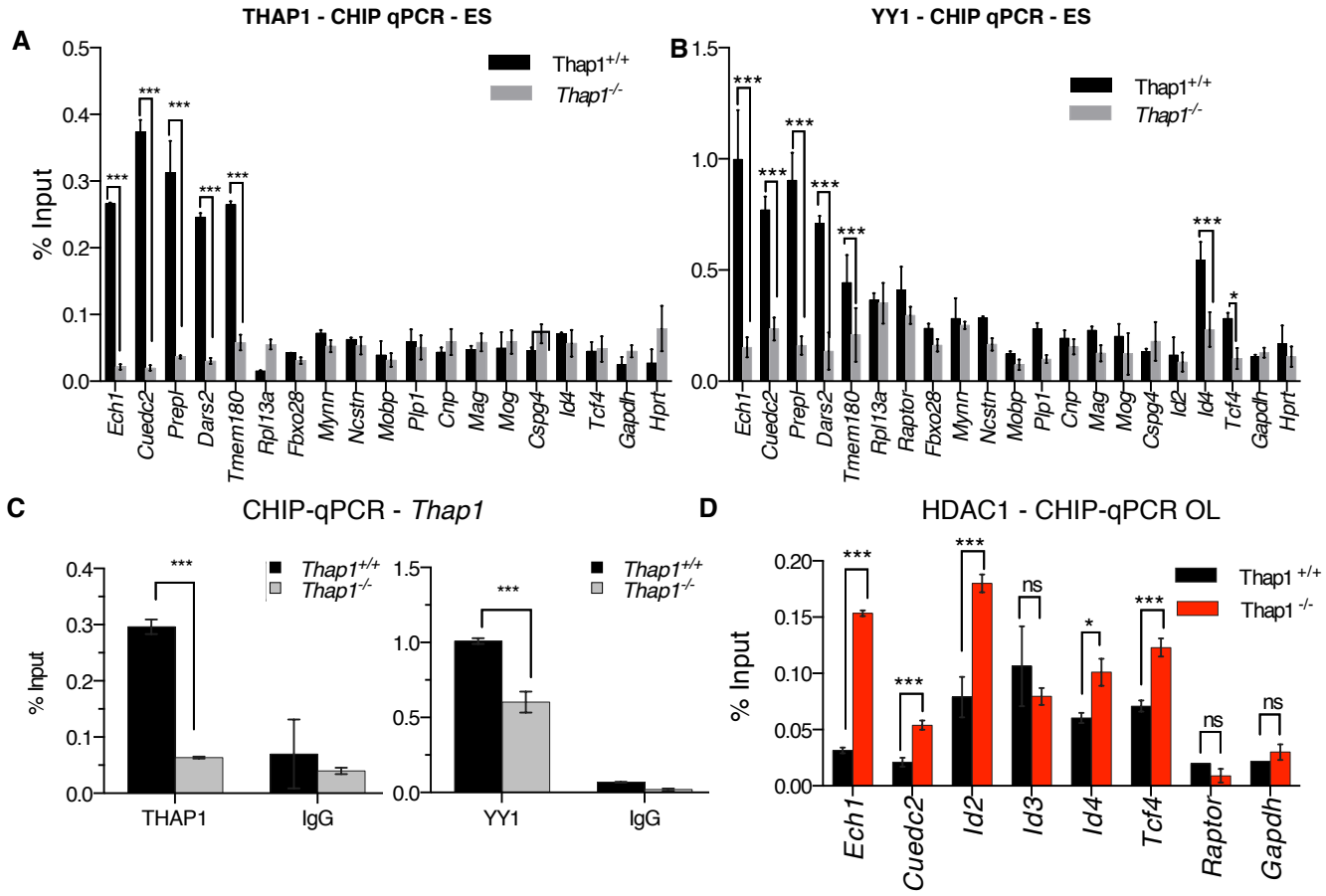


**Figure S5 - related to Figure 6: THAP1 regulates YY1 occupancy in mouse ES cells.**

(A-B) THAP1 regulates YY1 occupancy. qCHIP showing the binding, represented as % input (y-axis) of (A) THAP1 and (B) YY1 at 19 gene loci (x-axis) in *Thap1* null ES cells. Significance value determined using T-test (* = $p < 0.05$, ** = $P < 0.01$ and *** = $p<0.001$). The % input represents the final amount of immunoprecipitated chromatin / gene (assessed by q-PCR; see Experimental procedures) assessed as the percentage of total input chromatin from corresponding Control (*Thap1*$^{+/+}$) and *Thap1* null (*Thap1*$^{-/-}$) ES cells.

(C) qCHIP results for THAP1, YY1 and their respective isotype control IgG (Goat IgG or Rabbit IgG) for *Thap1* loci (x-axis) represented as % input (y-axis).

(D) qCHIP results for HDAC1 for all the *Ech1, Cuedc2, Id2, Id3, Id4, Tcf4, Raptor* and *Gapdh* (x-axis) represented as % input (y-axis).