Expanded View Figures

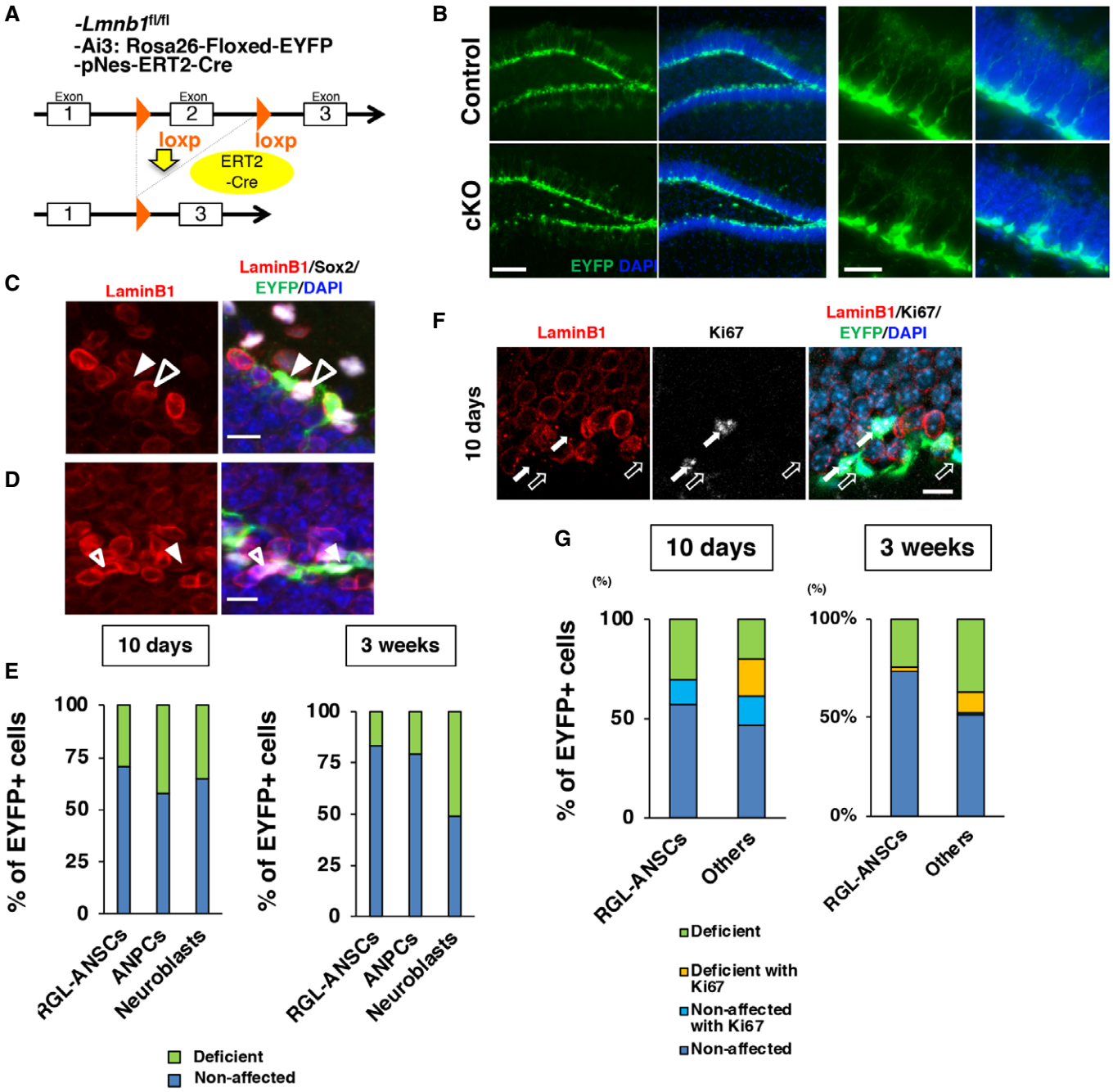

Figure EV1.

Figure EV1. Generation and evaluation of *Lmnb1* conditional knockout mouse line.

A A schematic illustration of *Lmnb1* conditional knockout mouse line (cKO).

B Induction of EYFP in ANSCPs 10 days after the administration of TAM in the SGZ of DG.

C, D Representative images of lamin B1 complete-loss cell (arrowhead) and non-EYFP ANPC (open arrowhead) (C), lamin B1 partial-loss cell (arrowhead), and non-EYFP ANPC (open arrowhead) (D).

E The fractions of EYFP+ cells with lamin B1 deficiency for each cell type 10 days or 3 weeks after TAM administration (Total number of counted cells, 10 days; RGL-ANSCs. 81 cells, ANPCs = 116 cells, Neuroblasts = 74 cells from 3 animals; 3 weeks, RGL-ANSCs = 39 cells, ANPCs = 59 cells, neuroblasts = 84 cells from 3 animals). Lamin B1-deficient cells are defined as having 30% or more reduced levels of lamin B1 intensity compared to the averaged intensity of the same type of control cells.

F A confocal image of lamin B1 deficiency in Ki67+ proliferating cells (arrows) 10 days after TAM infusion. Open arrows indicate lamin B1 deficient cells without Ki67.

G The fraction of lamin B1-deficient cells in Ki67+ proliferating cells. Ki67+ non-RGL cells (others cells) show lamin B1 deficiency whereas only a few Ki67+ RGL-ANSCs exhibit laminB1 deficiency, implying the necessity for cellular proliferation to deplete lamin B1 proteins (Total number of counted cells, 10 days; RGL-ANSCs. 115 cells, non-RGL cells = 196 cells, from 3 animals; 3 weeks; RGL-ANSCs. 42 cells, non-RGL cells = 142 cells, from 3 animals).

Data information: Scale bars, 200 μm in (B, left), 50 μm in (B, right), 10 μm (C, D, F).

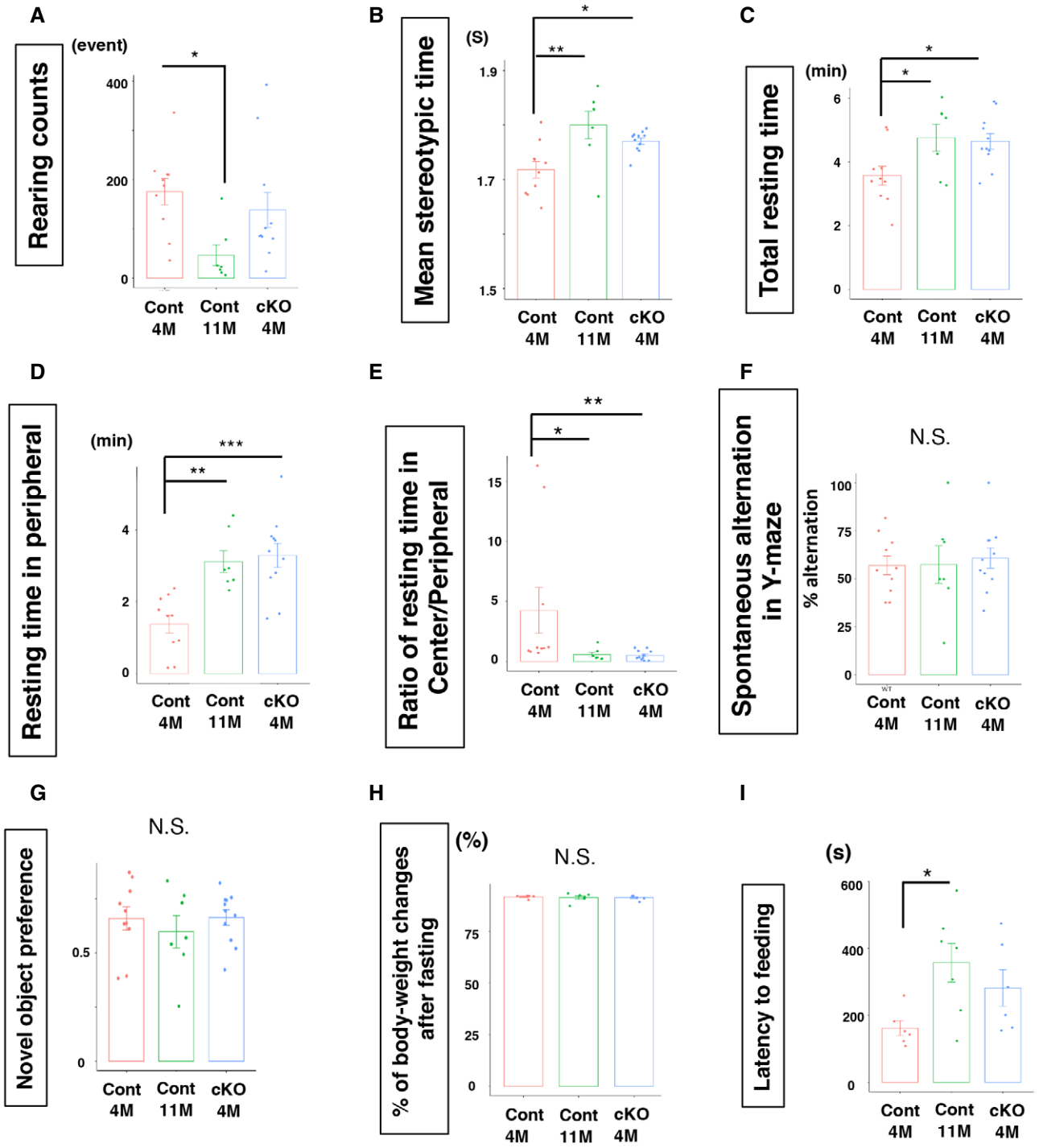

Figure EV2.

Figure EV2. Increased age-related behavior in Lmnb1-cKO mice.

A Rearing counts during the OF test. $F_{2,25} = 3.95$, $^{*}P = 0.032$, ANOVA followed by Tukey–Kramer (*n*: WT = 10, WT-old = 7, Lmnb1-cKO = 11 for the OF test).

B Average time spent on stereotypic behavior. $F_{2,\ 25)} = 7.15$, $P = 0.0035$, ANOVA followed by Tukey–Kramer, $^{*}P < 0.05$, $^{**}P < 0.01$ (*n*: WT = 10, WT-old = 7, Lmnb1-cKO = 11 for the OF test).

C Total resting time in the OF. $F_{(2,\ 25)} = 4.65$, $P = 0.018$, ANOVA followed by Tukey–Kramer, $^{*}P < 0.05$ (*n*: WT = 10, WT-old = 7, Lmnb1-cKO = 11 for the OF test).

D Total resting time in the peripheral area. $F_{2,25} = 12.34$, $P = 0.00019$, ANOVA followed by Tukey–Kramer, $^{**}P < 0.01$, $^{***}P < 0.001$ (*n*: WT = 10, WT-old = 7, Lmnb1-cKO = 11 for the OF test).

E Ratio of resting time between center and peripheral area. Kruskal–Wallis test followed by Dunn test, $^{*}P < 0.015$, $^{**}P < 0.01$ (*n*: WT = 10, WT-old = 7, Lmnb1-cKO = 11 for the OF test).

F No significant changes in spontaneous alternation in Y-maze test. $F_{2,25} = 0.12$, $P = 0.89$, ANOVA (*n*: WT = 10, WT-old = 7, Lmnb1-cKO = 11).

G Preference to novel object was not different among three groups $F_{2,25} = 3.39$, $P = 0.45$, ANOVA) (*n*: WT = 10, WT-old = 7, Lmnb1-cKO = 11 for the OF test).

H Proportional body weight loss after 24-h food deprivation for the NSF test $F_{2,25} = 6.11$, $P = 0.94$, ANOVA) (*n*: WT = 6, WT-old = 7, *Lmnb1*-cKO = 6).

I Latency to feed in NSF test. Kruskal–Wallis test followed by Steel test, $^{*}P = 0.038$, (*n*: WT = 6, WT-old = 7, *Lmnb1*-cKO = 6).

Data information: Data are presented as mean ± SEM.

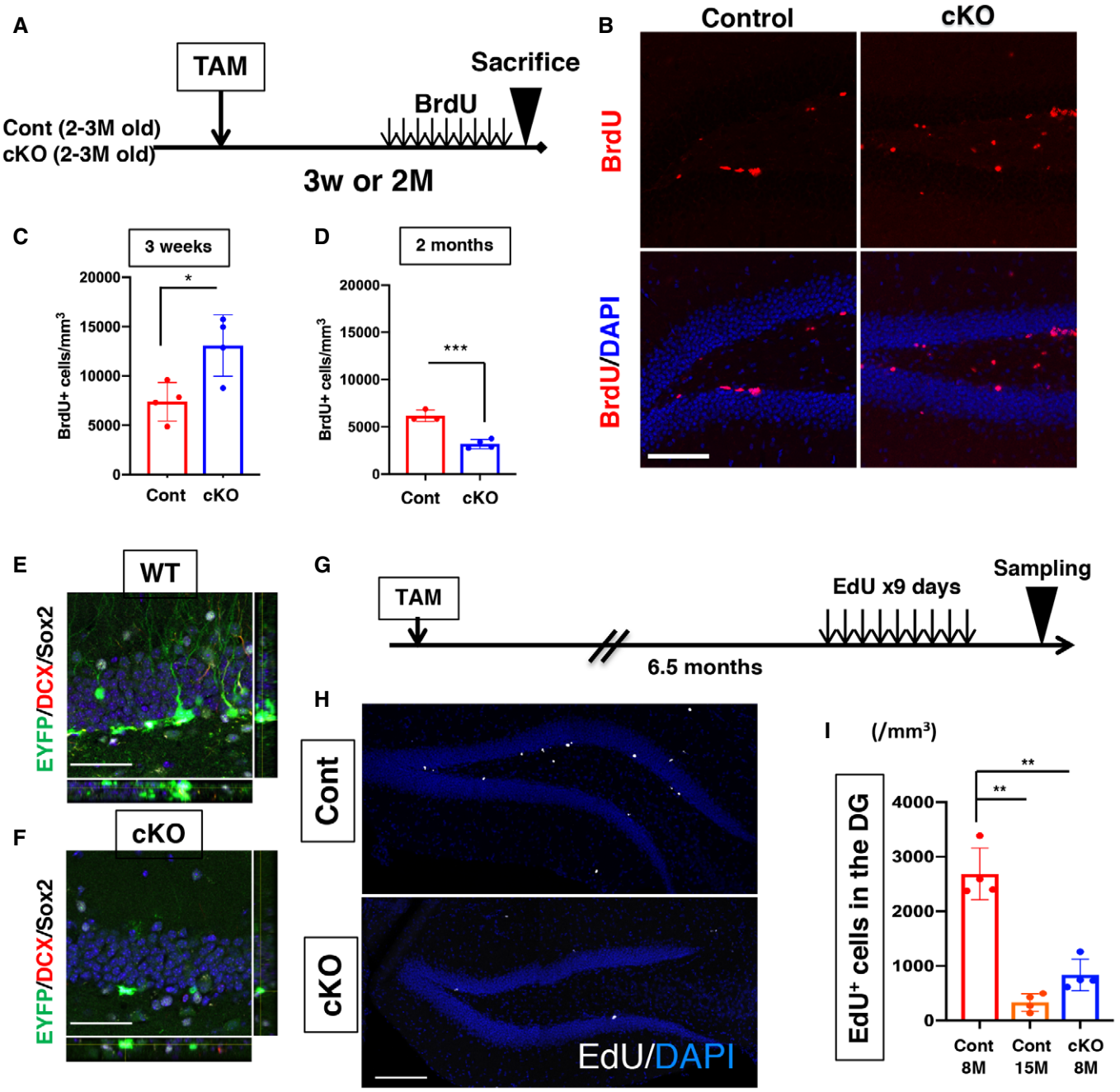

Figure EV3. Effects of lamin B1 loss on adult hippocampal neurogenesis.

A Schematic of BrdU treatment and collection of brain tissue.
B Representative images of BrdU staining in the DG 3 weeks after TAM administration. BrdU-positive cells were markedly increased in cKO mice.
C Quantification of BrdU+ cells 3 weeks after TAM administration (*P = 0.021, t-test, n = 4).
D Quantification of BrdU+ cells 2 months after TAM administration (***P = 0.0007, t-test, n = 3 for Control, 4 for cKO).
E, F Orthogonal views of confocal images to identify cell type of EFYP+ cells.
G Schematic of EdU treatment and collection of brain tissue.
H Representative images of EdU-click staining in the DG. EdU-positive cells were markedly reduced in cKO mice.
I Quantification of EdU-positive cells in the DG indicates that lamin B1 loss induces the prominent reduction of new cell generation in the DG similar to Cont-15M mice. **P < 0.01, ANOVA (P = 0.0009) followed by Tukey–Kramer test (n = 4 for each genotype).

Data information: Data are presented as mean ± SD. Scale bars, 100 μm in (B), 50 μm in (E, F), and 200 μm in (H).

Figure EV4. Lamin B1 is essential for the survival of adult-born cells.

A Quantification of EYFP+ NeuN+ neurons 2 months after TAM administration. *$P = 0.042$, *t*-test, $n = 4$).

B Schematic of BrdU treatment and collection of brain tissue.

C Representative images of BrdU staining 10 days or 2 months after TAM treatment. Scale bar = 250 μm.

D Quantification of BrdU-positive cells in each time point. Number of BrdU-positive cells was significantly higher at day 10 (*$P = 0.049$, *t*-test) or 3 weeks (*$P = 0.019$, *t*-test) after TAM in cKO mice, but not at 2 months ($P = 0.12$, *t*-test, $n = 3$ animals). Data represent mean ± SD.

E The survival ratio of BrdU+ cells from 10 days to 2 months after TAM treatment (*$P = 0.015$, *t*-test, $n = 3$). Data represent mean ± SD.

F Representative images of active caspase3 2 months after TAM treatment. Scale bar = 20 μm.

G–I Significant difference in the density of active caspase3 was observed 2 months after TAM treatment, but not 3 weeks or 6.5 months after TAM treatment (3 weeks, $P = 0.86$, $n = 3$, *t*-test; 2 months, *$P = 0.028$, $n = 5$-6, *t*-test; 6.5 months, $P = 0.09$, $n = 4$, ANOVA). Data are presented as mean ± SD.

J Experimental schema. RV:pSox2-Cre-GFP was injected into the DG of *Lmnb1*fl/fl:Ai3 or *Lmnb1*+/+:Ai3 mice and the morphology of EYFP+ newborn neurons was assessed at 21dpi. Scale bar = 20 μm.

K Dendritic reconstruction of RV-labeled neurons derived from WT and cKO mice. Scale bars = 20 μm.

L, M Total dendrite length (L) and total numbers of branches (M) were quantified (65 cells for control, 35 cells for cKO from 3 animals per genotype; total length, *$P = 0.0147$; number of branches, $P = 0.099$, Mann–Whitney test). Data are presented as mean ± SEM.

N Sholl analysis of neurite length. **$P < 0.01$, *$P < 0.05$ (*t*-test) (65 cells for control, 35 cells for cKO from 3 animals per genotype). Data are presented as mean ± SEM.

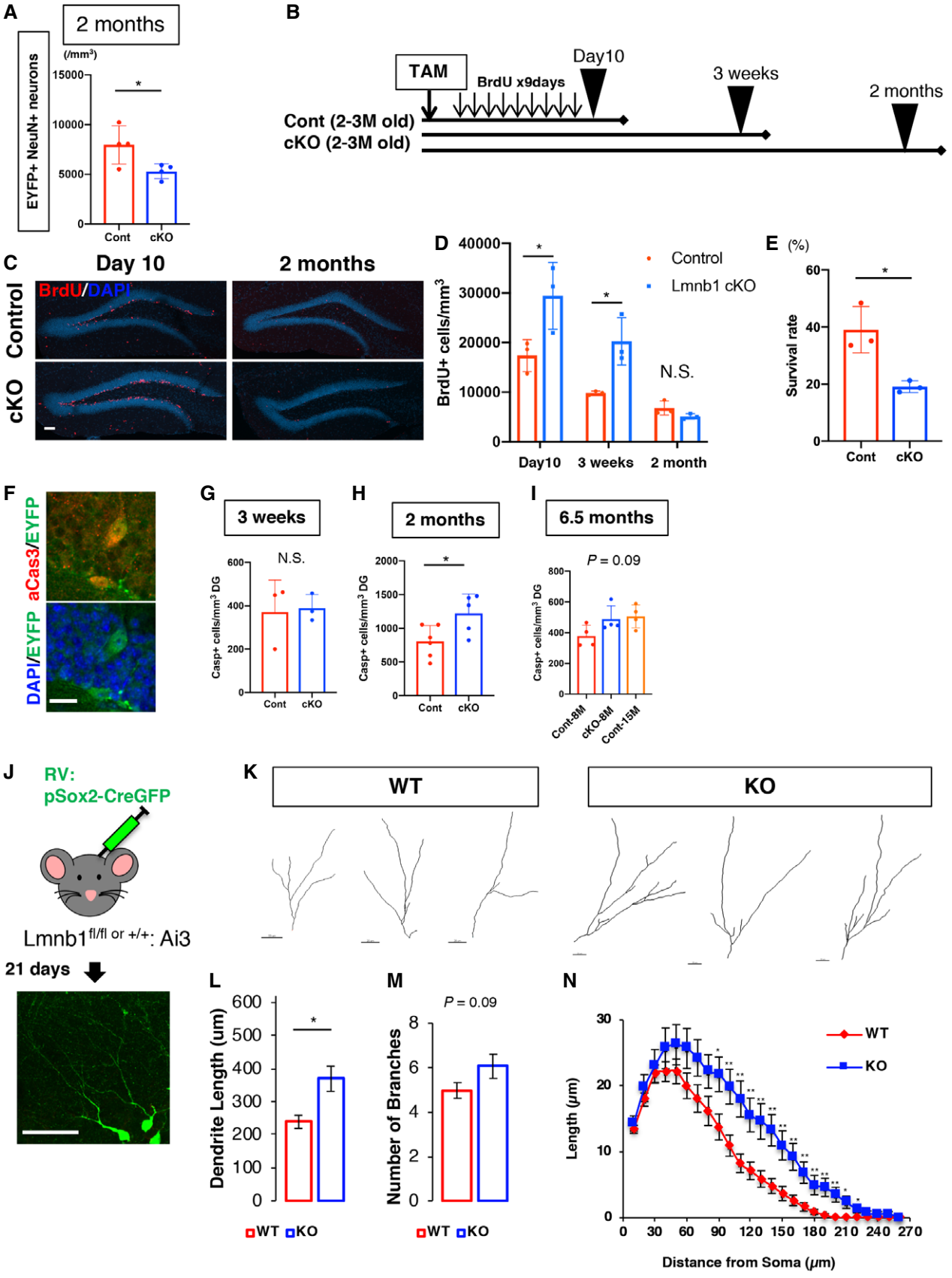

Figure EV4.

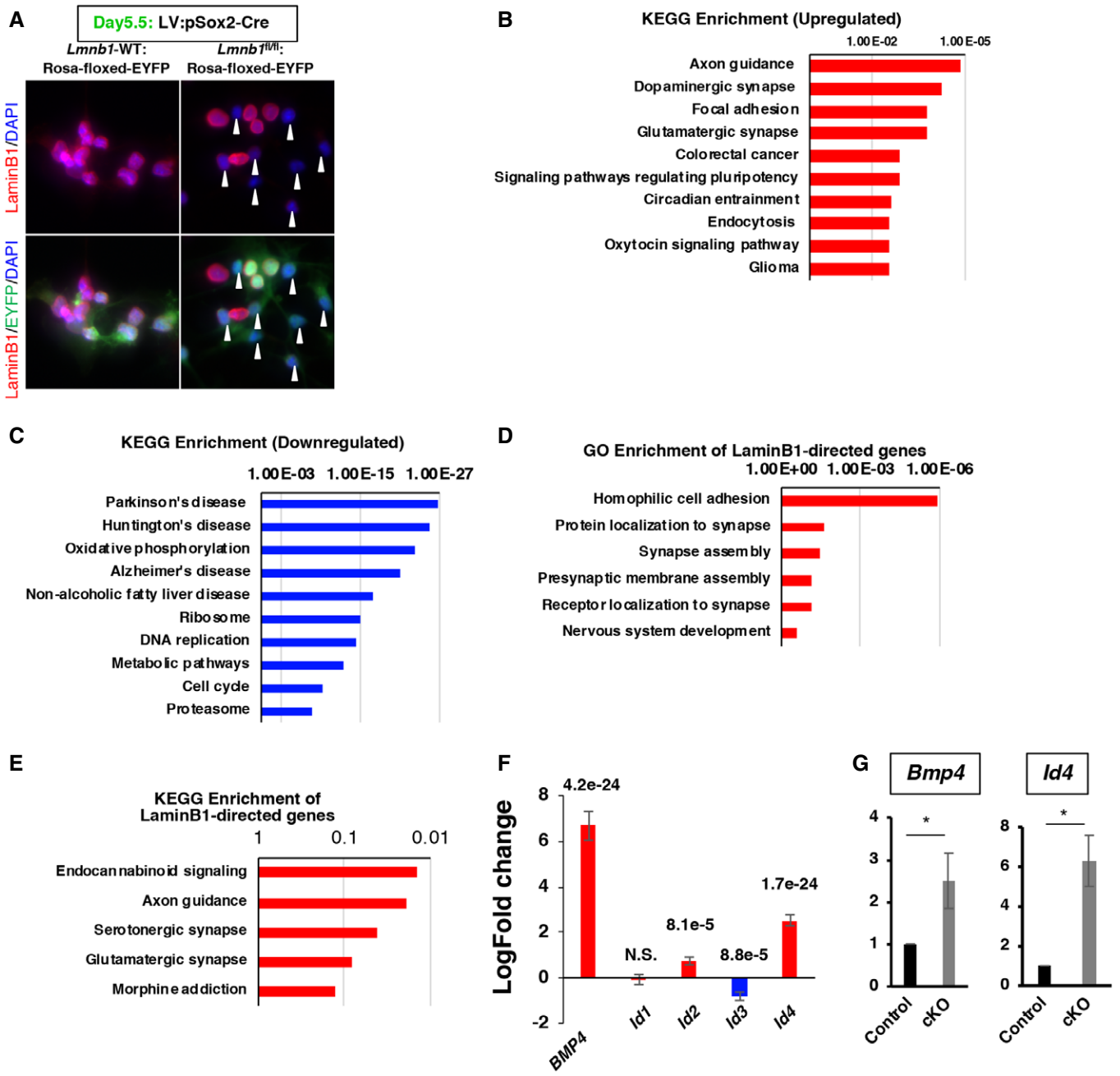

Figure EV5. Gene pathways regulated by lamin B1 in NPCs.

A Confirmation of lamin B1 depletion after the delivery of LV; pSox2-Cre. Closed white arrowheads indicate the depletion of lamin B1 immunoreactivity in right panels. Scale bar = 25 μm.

B, C GO and KEGG pathway enrichment analyses of differentially expressed genes.

D, E GO and KEGG enrichment analyses for lamin B1-directed upregulated genes.

F Fold change expression of *Bmp4* and *Id1-4* from the transcriptomic analysis in cKO-NPCs, $n = 3$, DEseq2 for statistical test. Data are presented as mean ± SEM.

G qRT–PCR validation of *Bmp4* and *Id4* upregulation in cKO-NPCs (*Bmp4*, $^*P = 0.022$; *Id4*, $^*P = 0.015$, one-sample *t*-test, $n = 3$). Data are presented as mean ± SD.