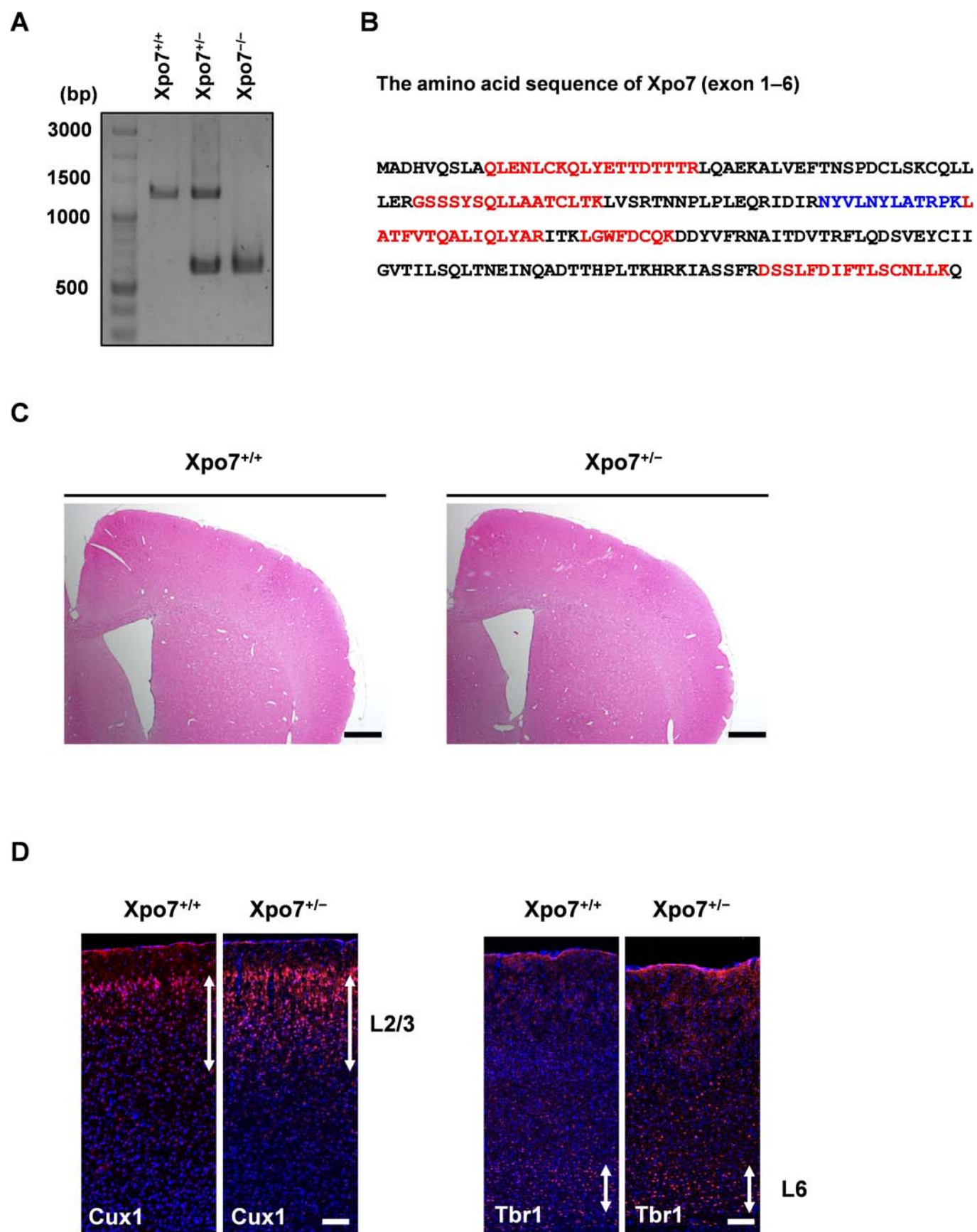
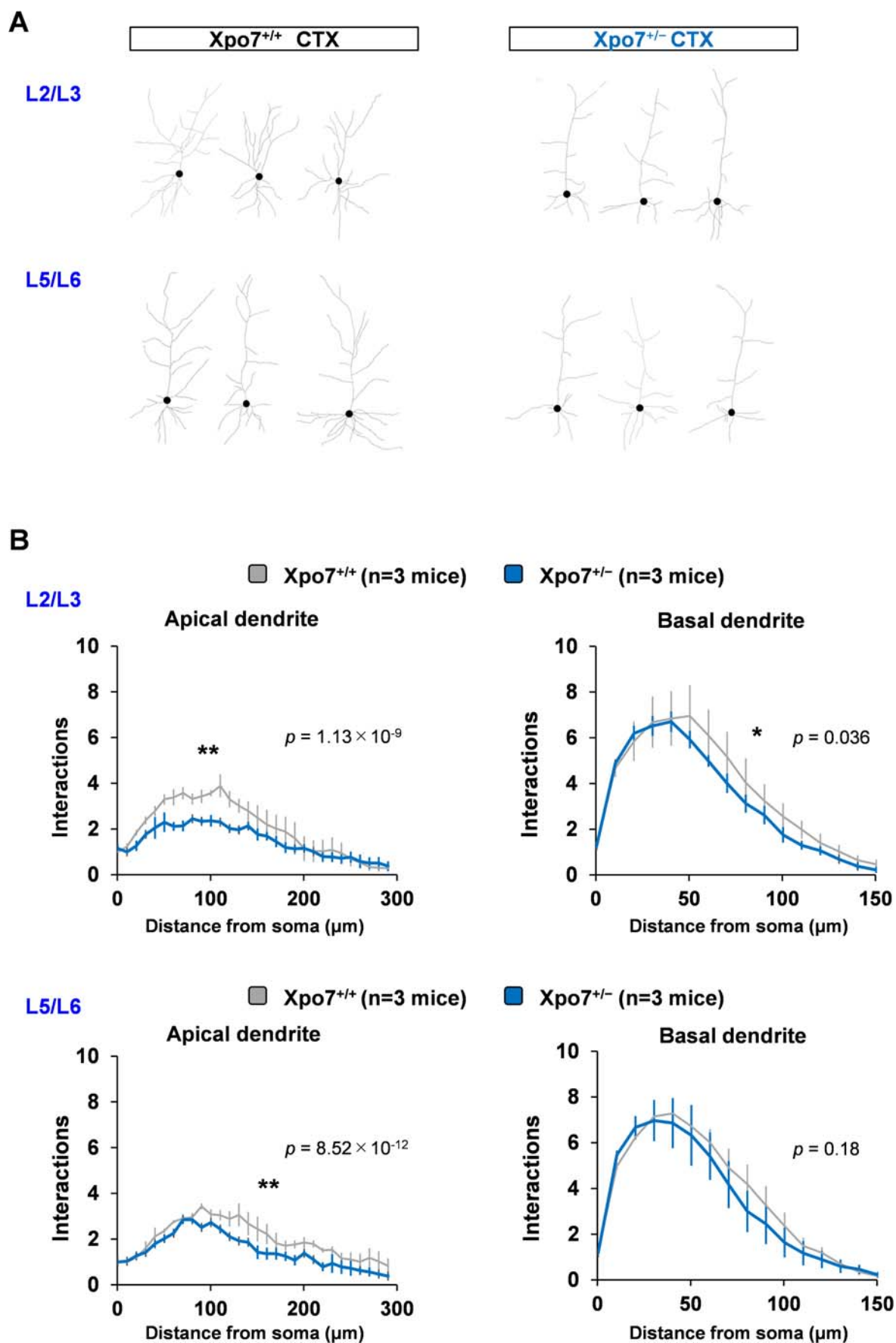


Expanded View Figures

Figure EV1. Genotyping, Xpo7 expression analysis, and brain structure analysis of Xpo7 knockout mice.

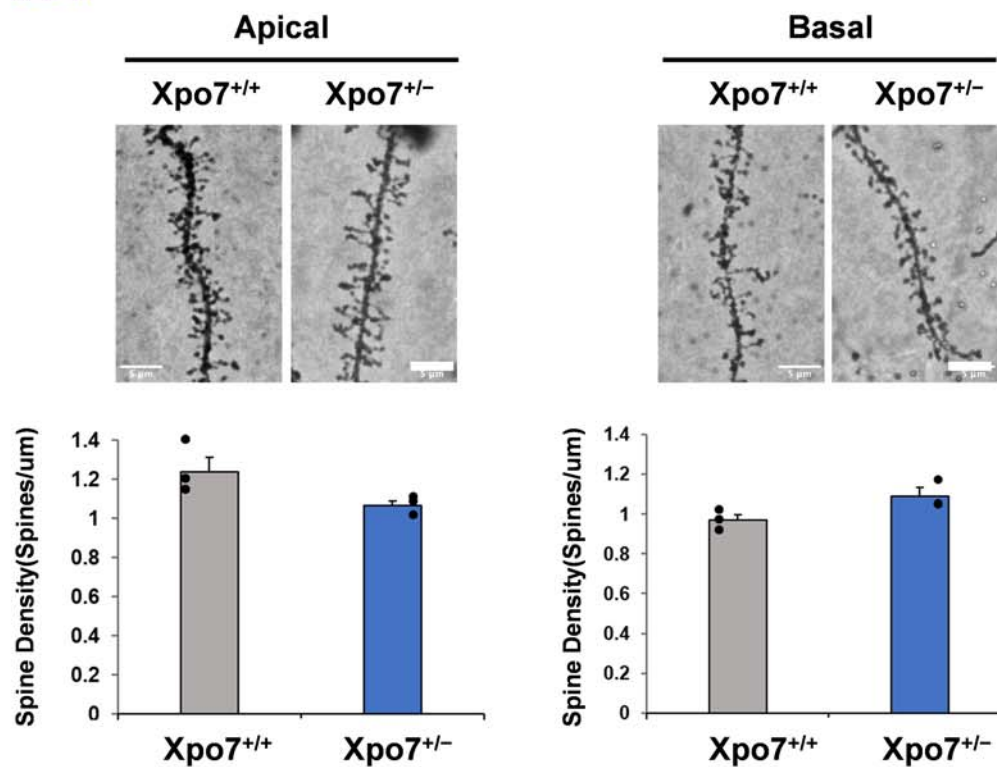
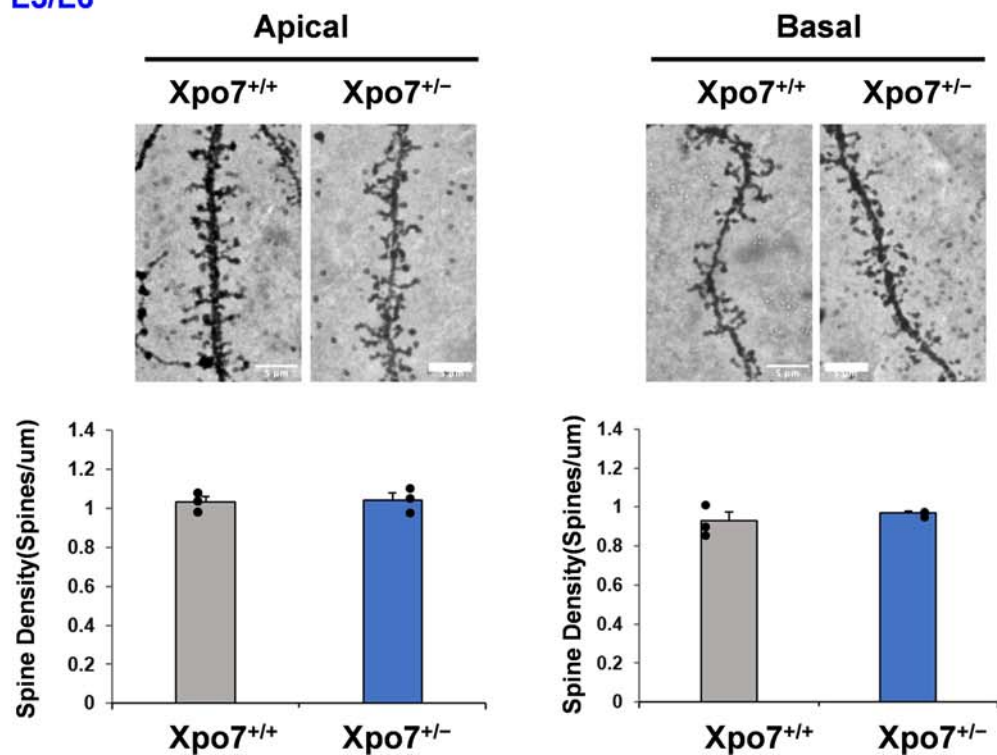
(A) The result of genotyping PCR of Xpo7 knockout mice. (B) The amino acid sequence of Xpo7 (exon 1–6). Six types of peptide fragments (red or blue) were detected from the sequence including 1–199 aa (exons 1–6) from Xpo7^{+/+} and Xpo7^{+/-} mice using LC-MS/MS, but not from Xpo7^{-/-} mice. (C) H&E staining of coronal section at the bregma of the brain at 3 months of age. Bar: 1 mm. (D) Immunostaining for layer-specific markers, Cux1 and Tbr1, reveals normal cortical layer organization in Xpo7^{+/-} mice at 3 months of age. Bar: 100 μ m.





◀ **Figure EV2. Dendrite analyses from the Golgi staining data revealed fewer dendrite branches in $Xpo7^{+/-}$ mice.**

(A) Representative neurons from L2/L3 and L5/L6 of the frontal cortex at three months of age. (B) Sholl analyses of apical and distal dendrites of L2/L3 neurons and L5/L6 neurons of the frontal cortex at three months of age. * $P < 0.05$, ** $P < 0.01$ ($N = 3$ mice. For each animal, 6–12 pyramidal neurons from either layers 2–3 or layers 5–6 were analyzed. Two-way repeated ANOVA test). Data are expressed as the mean $\pm$ s.e.m.

A**L2/L3****B****L5/L6**

**Figure EV3. Spine analyses from Golgi staining data revealed no significant change in spine densities per dendrite in $Xpo7^{+/-}$ mice.**

(A) Representative spines from L2/L3 neurons of frontal cortex at three months of age. The graphs show quantitative analysis of spine number. ($N = 3$ mice, 6–14 neurons/mice) Bar: 5 μm . Data are expressed as the mean $\pm$ s.e.m. (B) Representative spines from L5/L6 neurons of frontal cortex at three months of age. The graphs show quantitative analysis of spine number. ($N = 3$ mice, 6–14 neurons/mice) Bar: 5 μm . Data are expressed as the mean $\pm$ s.e.m.

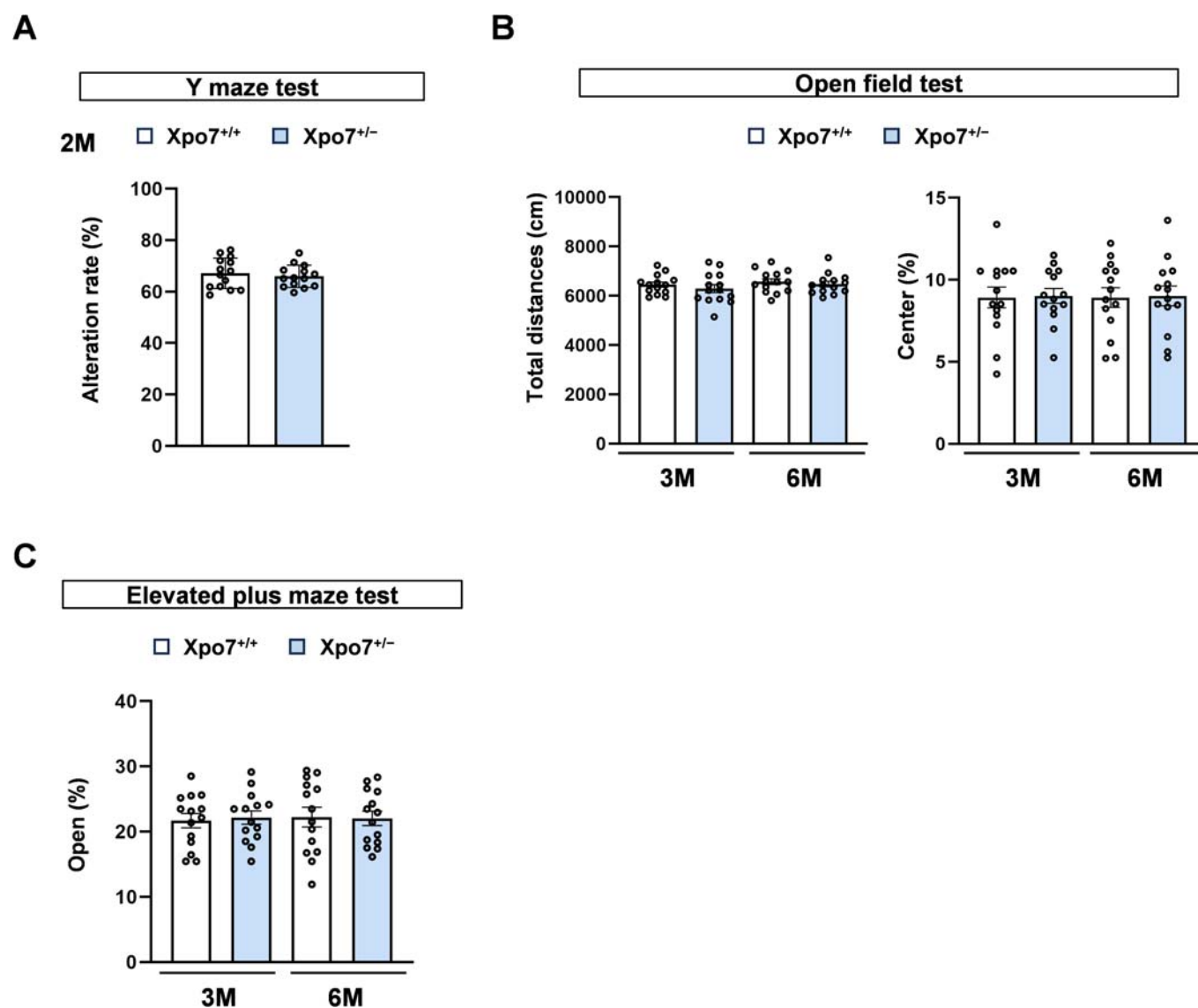
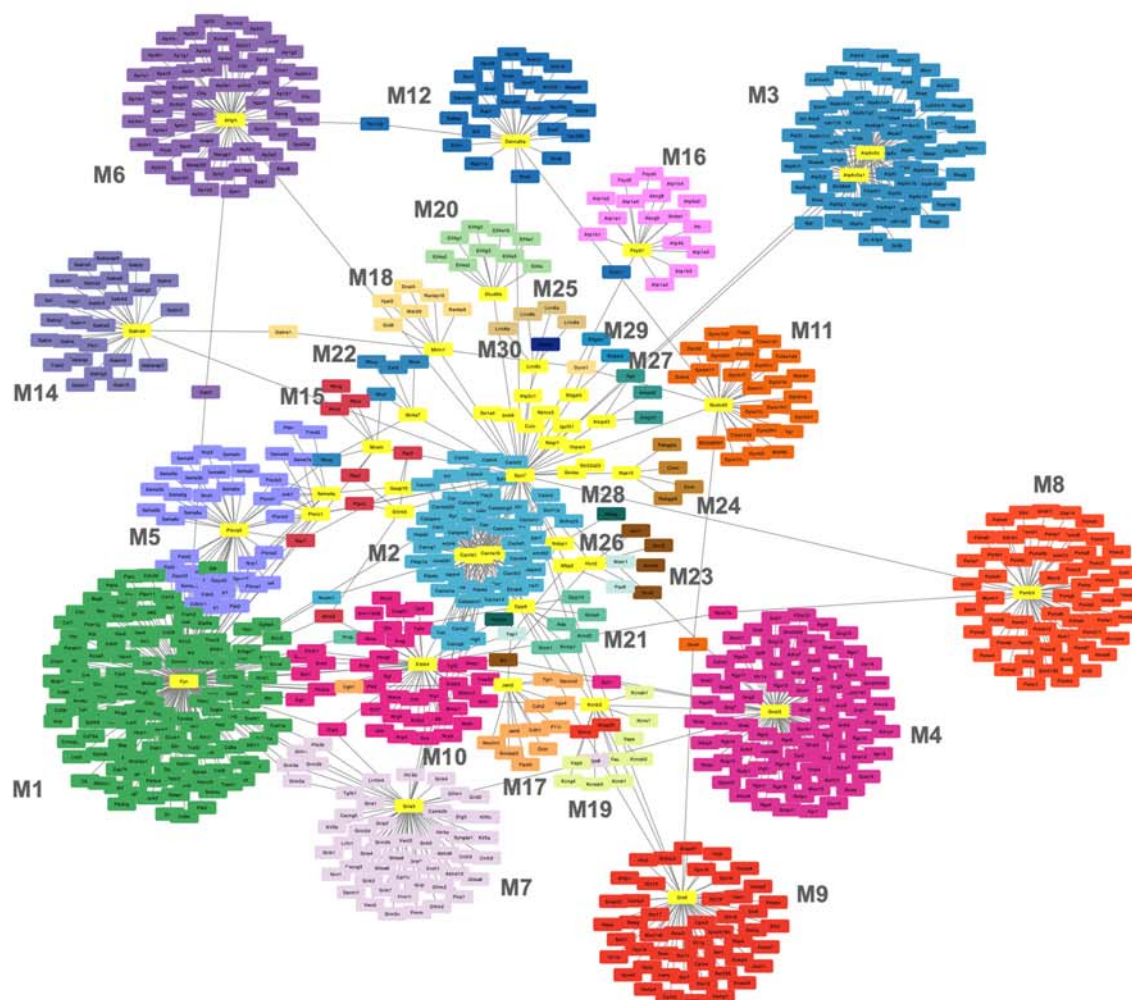
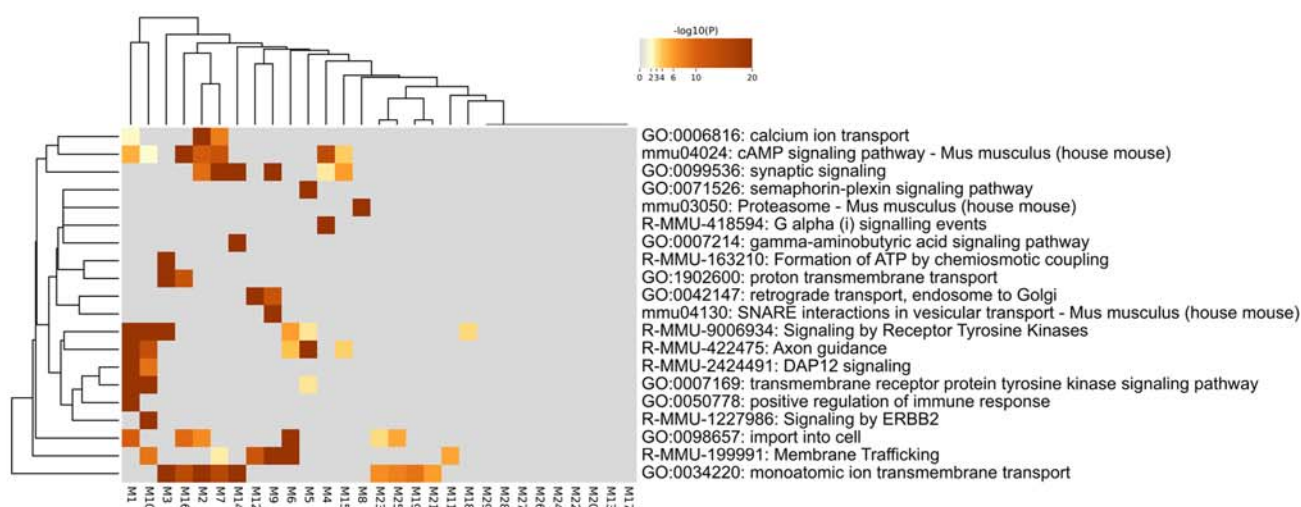


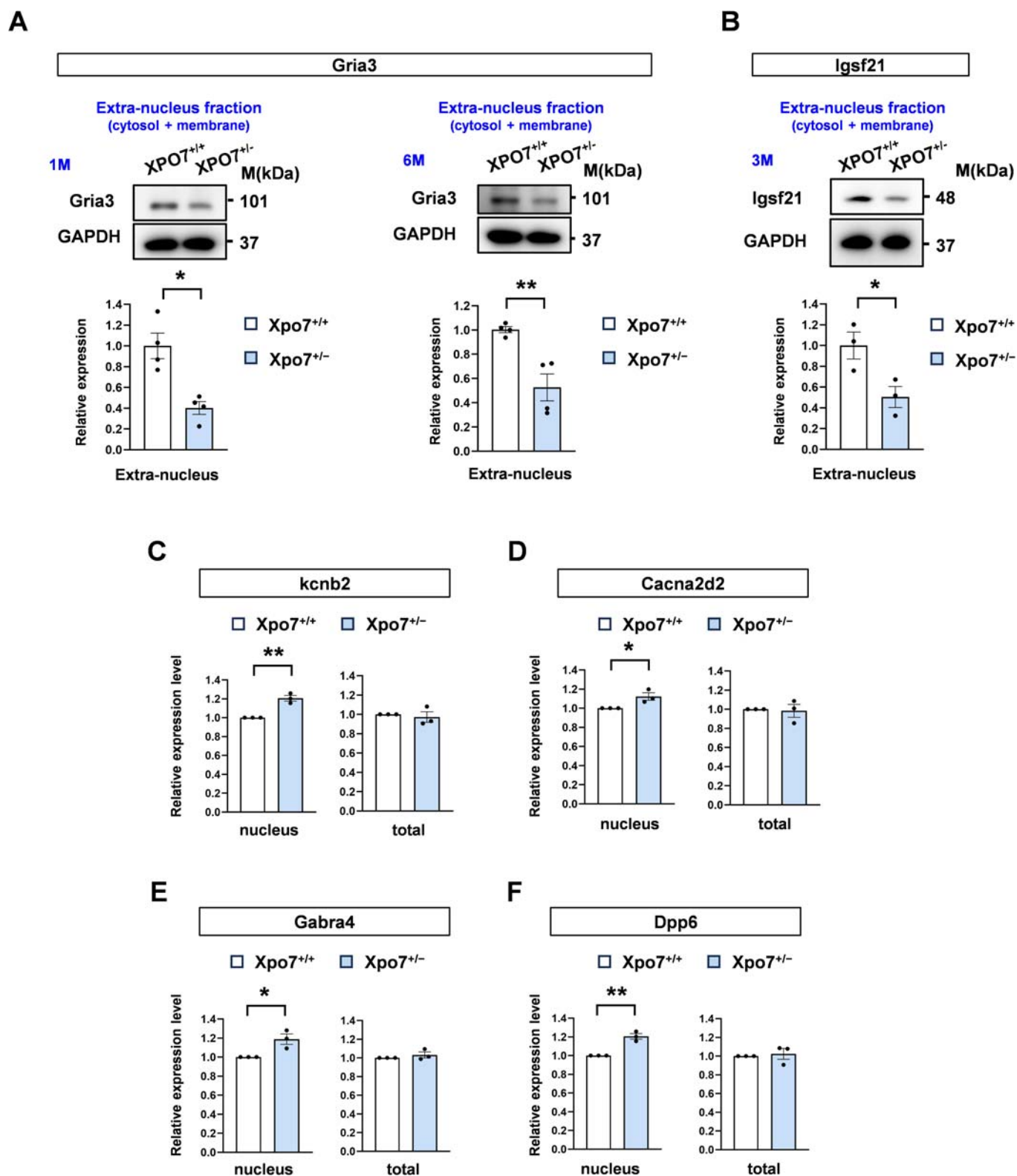
Figure EV4. Behavioral analysis of XPO7^{+/-} mice.

(A) Alteration ratios in the Y maze test with Xpo7^{+/+} and Xpo7^{+/-} mice at 2 months of age. There was no significant difference between the groups. ($N = 14$ for each group; Tukey's HSD test). Data are expressed as the mean $\pm$ s.e.m. (B) Total distances (left) and Time in center region (right) in the open-field test. There was no significant difference between the groups. ($N = 14$ for each group; Tukey's HSD test). Data are expressed as the mean $\pm$ s.e.m. (C) Time in the open arm regions in the elevated plus maze test. There was no significant difference between the groups. ($N = 14$ for each group; Tukey's HSD test). Data are expressed as the mean $\pm$ s.e.m.

A**B**

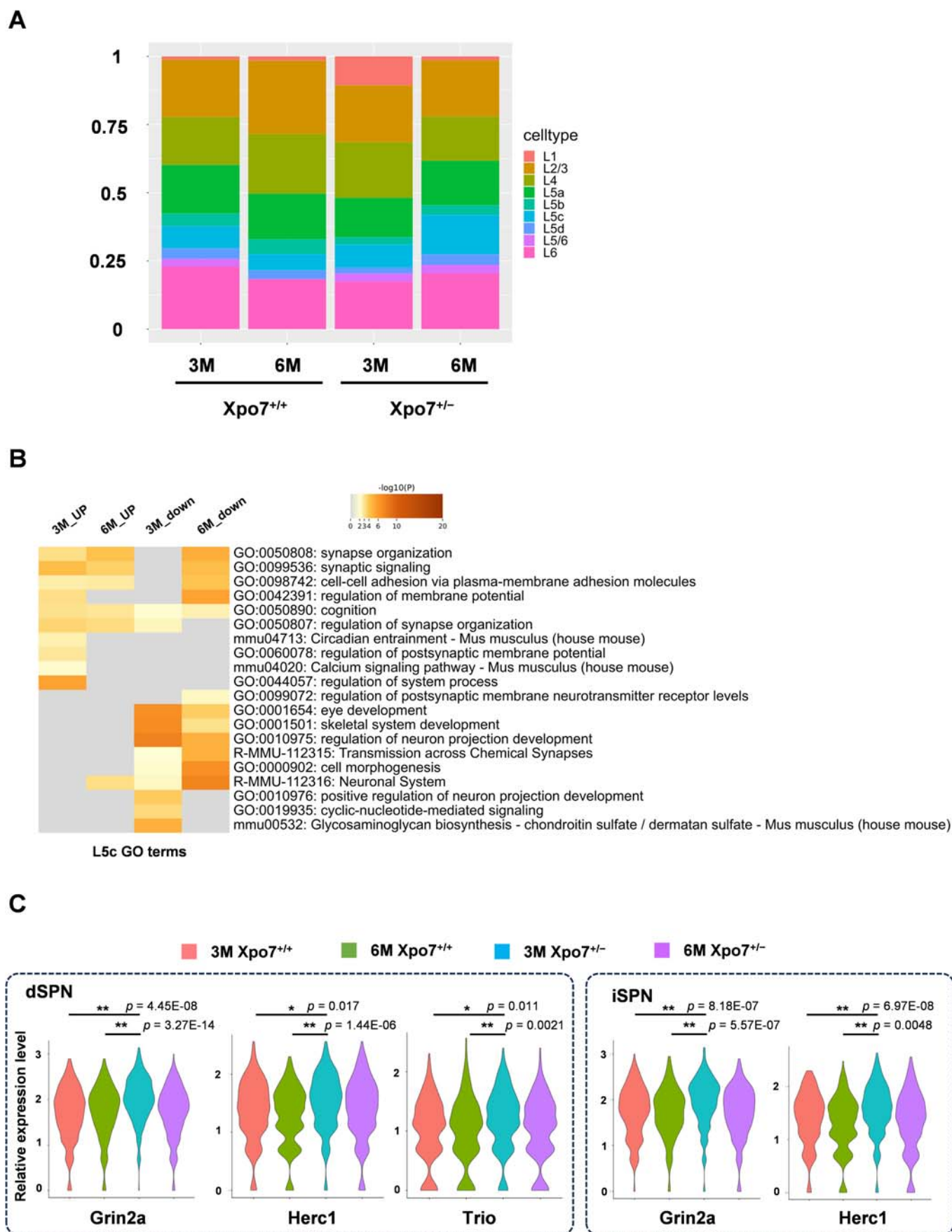
**Figure EV5. Protein interaction network analysis 45 Xpo7 direct-effect molecules.**

(A) The 1-hop protein-protein interaction analysis with Xpo7 revealed 847 molecules. the Infomap algorithm revealed 28 modules (M1 - M28). (B) Gene Ontology (GO) analysis of (A). These analyses revealed that 45 XPO7 direct-effect molecules are associated with transmembrane transport (M10, M7, M12, M9, M6), immune response (M1), axon guidance (M1, M10, M6, M5, M15), synaptic signaling (M2, M7, M14, M9, M4, M15) and proteasome (M8).



◀ **Figure EV6. Detailed analysis of Xpo7-binding and Xpo7 haploinsufficiency-affected molecules.**

(A) Western blot analysis of Gria3 in the extranuclear fraction from the frontal cortex of Xpo7^{+/+} and Xpo7^{+/-} mice at 1 and 6 months of age. ** $P < 0.01$ (1 M $p = 0.0049$; 6 M $P = 0.0057$; $N = 4$ experiments; Tukey's HSD test). Data are expressed as the mean $\pm$ s.e.m. (B) Western blot analysis of Gria3 in the extranuclear fraction from the frontal cortex of Xpo7^{+/+} and Xpo7^{+/-} mice at 3 months of age. * $P < 0.05$ ($P = 0.039$; $N = 3$ experiments; Tukey's HSD test). Data are expressed as the mean $\pm$ s.e.m. (C-F) Relative expression of kcnb2, Cacna2d2, Gabra4, and DPP6 in nuclei and whole cells from the frontal cortex of Xpo7^{+/+} and Xpo7^{+/-} mice by LC-MS/MS analysis. * $P < 0.05$, ** $P < 0.01$ (kcnb2 $P = 0.0024$; Cacna2d2 $P = 0.035$; Gabra4 $P = 0.024$; Dpp6 $P = 0.0024$; $N = 3$ experiments, 3 mice per group/experiment; Tukey's HSD test). Data are expressed as the mean $\pm$ s.e.m. As described in Fig. 3, the LC-MS/MS analysis data were derived from pairs of mice at 1, 3, and 6 months of age.



**Figure EV7. Detailed analysis for single-nucleus RNA sequencing analysis.**

(A) The ratio of neurons in the frontal cortical layers by single-nucleus RNA sequencing analysis. (B) GO analysis of DEGs of L5c excitatory neurons. To evaluate the functional enrichment of a given gene list, the metascape performed an accumulative hypergeometric test or Fisher's exact test to calculate *P* values and enrichment factors for each ontology category. (C) Relative mRNA expression levels in dSPN and iSPN. Relative mRNA expression levels of *Grin2A*, *Herc1*, and *TRIO* *****P* < 0.01** (dSPN 3 M *Xpo7*^{+/+} *N* = 540 cells, 6 M *Xpo7*^{+/+} *N* = 544 cells, 3 M *Xpo7*^{+/-} *N* = 481 cells, 6 M *Xpo7*^{+/-} *N* = 319 cells; iSPN 3 M *Xpo7*^{+/+} *N* = 442 cells, 6 M *Xpo7*^{+/+} *N* = 487 cells, 3 M *Xpo7*^{+/-} *N* = 464 cells, 6 M *Xpo7*^{+/-} *N* = 250 cells; Wilcoxon rank-sum test).