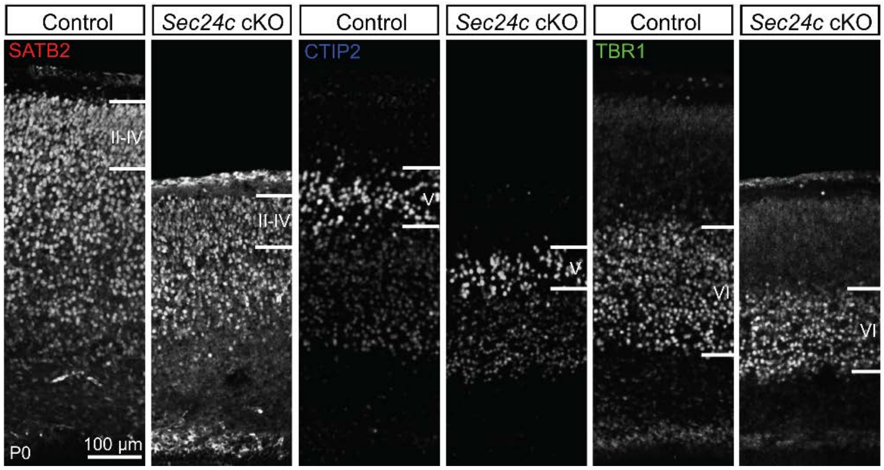
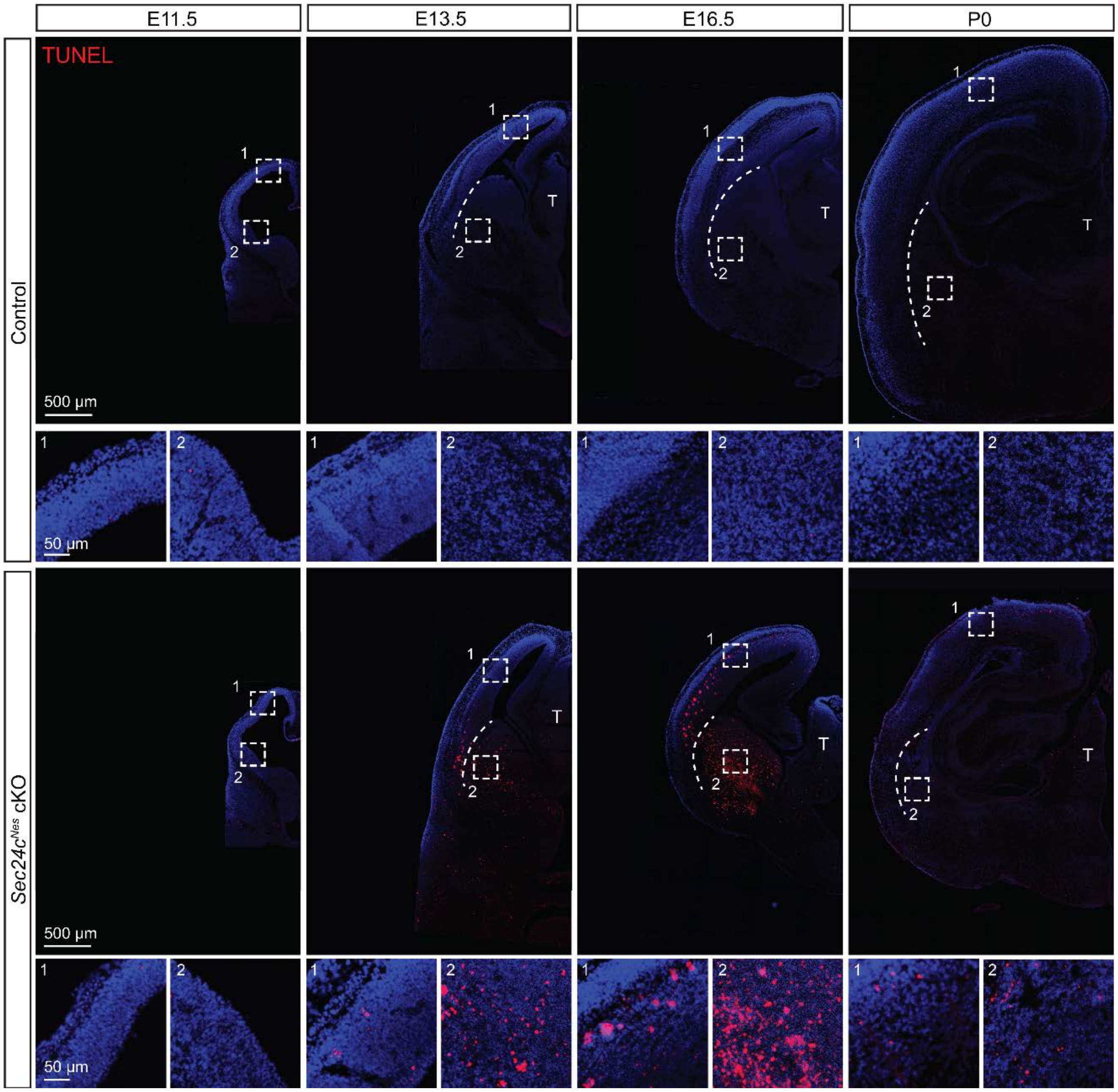
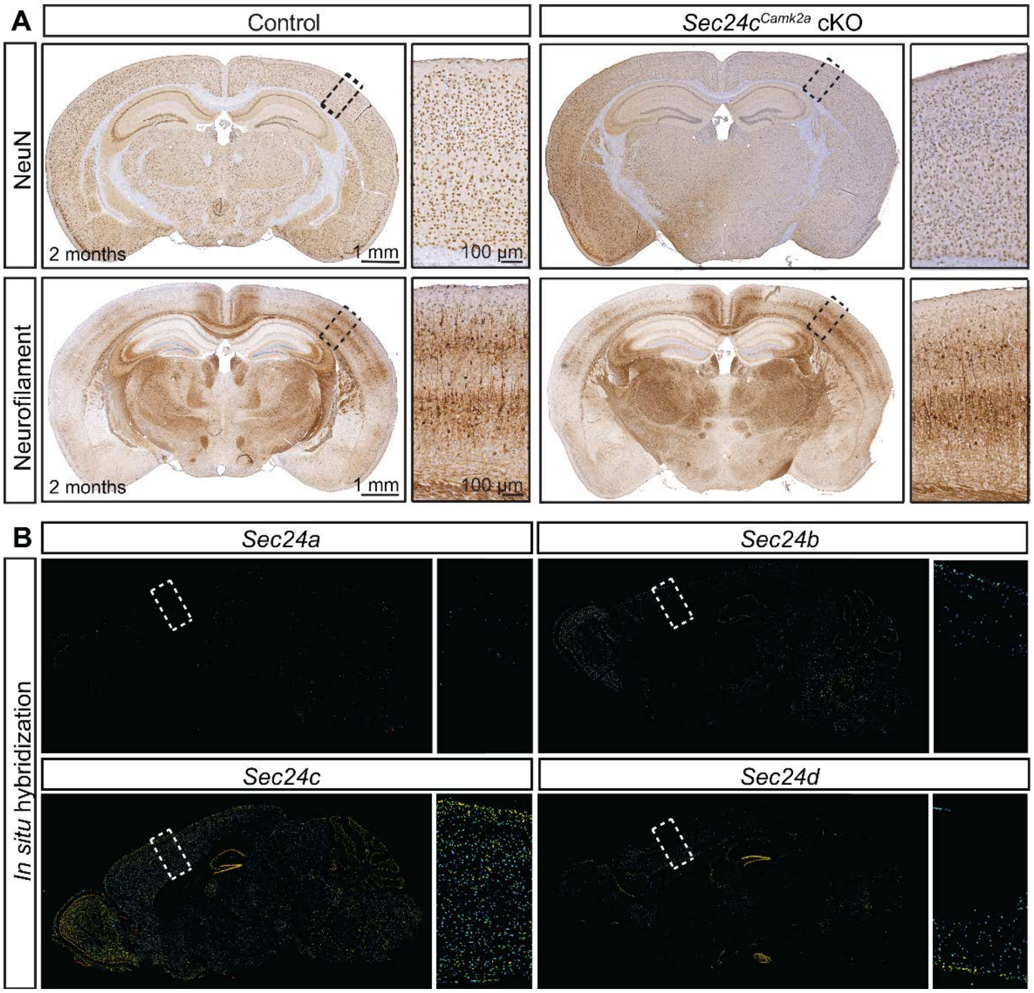


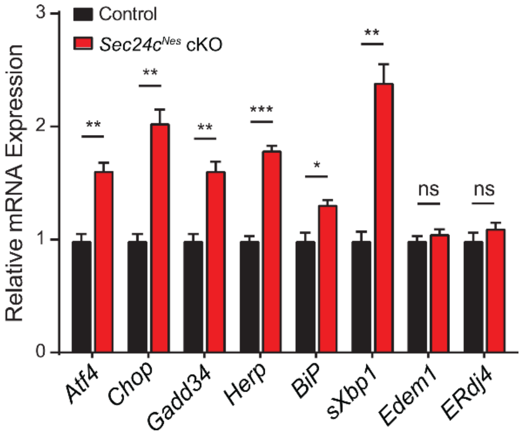
Supplemental Figure 1. Related to Figure 2. Expression patterns of SATB2, CTIP2, and TBR1 in cortices from control (n = 3) and *Sec24c*^{Nes}-cKO (n = 3) mice at P0.



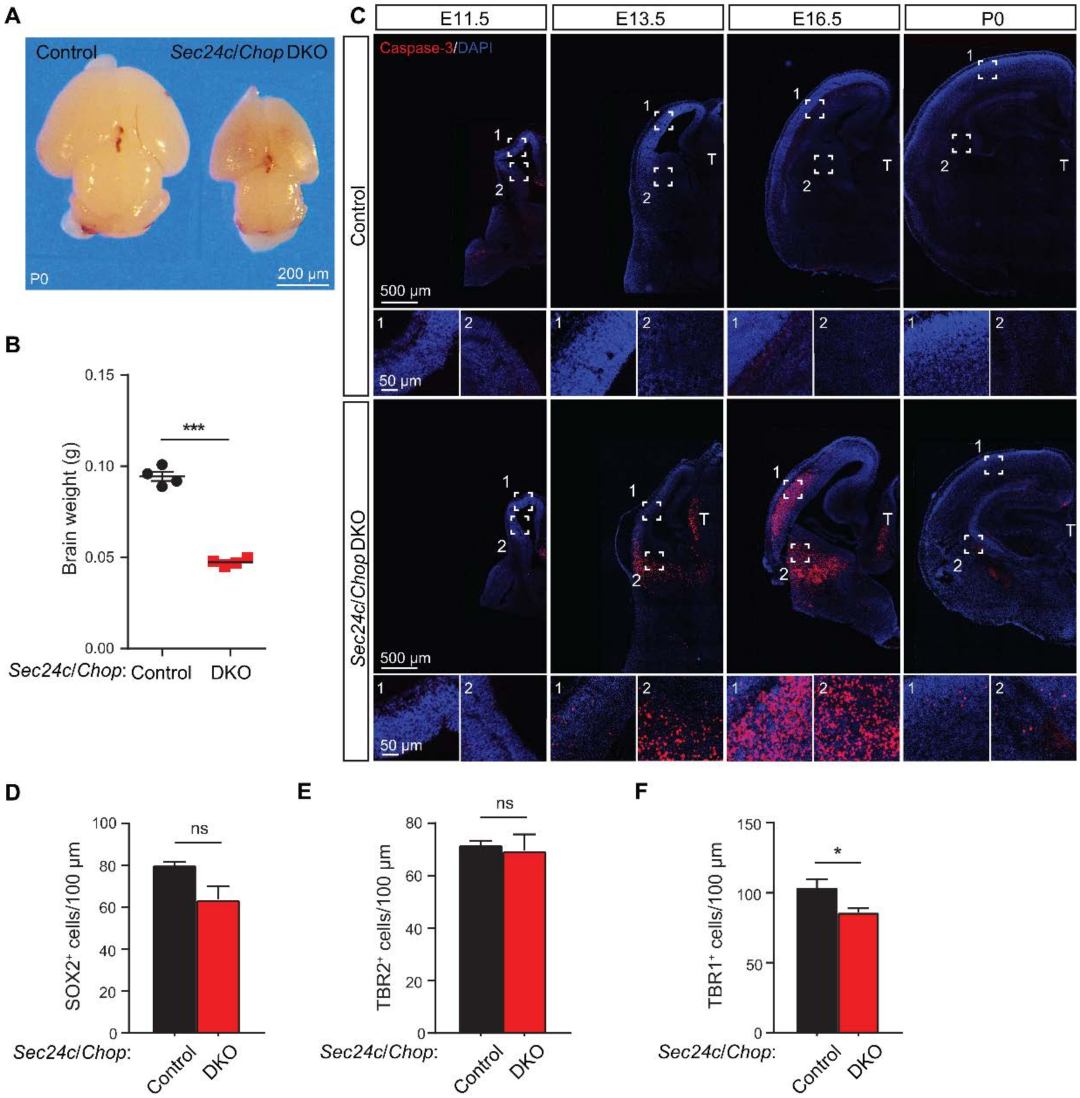
Supplemental Figure 2. Related to Figure 3. TUNEL assay on brain sections of control and *$Sec24c^{Nes}$*-cKO mice at E11.5, E13.5, E16.5, and P0. Magnified areas from cortex (1) and striatum (2) are also shown. 3 mice were used for each genotype at each age. Abbreviation: T, thalamus.



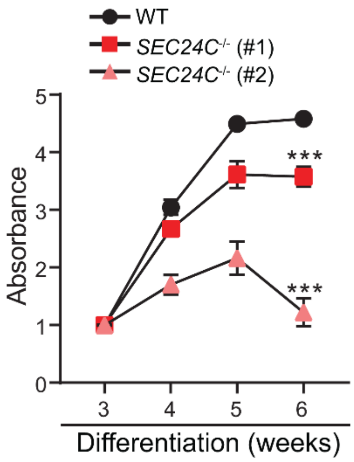
Supplemental Figure 3. Related to Figure 5. (**A**) Representative images of brain sections from 2-month-old controls (n = 2) and *Sec24c*^{Camk2a}-cKO (n = 2) mice immunostained with antibodies against NeuN or neurofilament. (**B**) Expression density maps of *Sec24a*, *Sec24b*, *Sec24c*, and *Sec24d* mRNA in the brains of 8-week-old WT C57BL/6 mice (from Allen Brain Atlas: http://www.brain-map.org/).



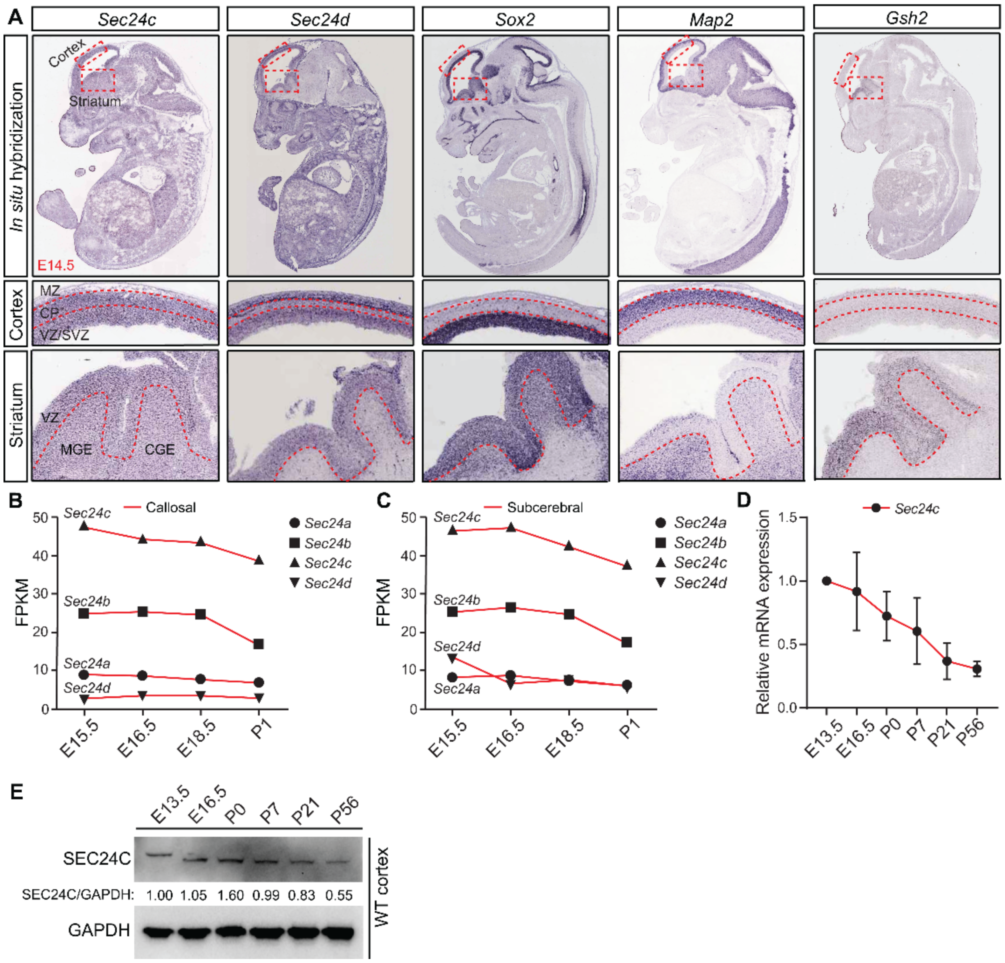
Supplemental Figure 4. Related to Figure 6. Relative levels (mean + SEM) of select UPR genes in the cortices of control (n = 3) and *Sec24c*^{Nes}-cKO (n = 3) mice at E13.5 by real-time RT-PCR. Abbreviations: ns, not significant. **P* < 0.05; ***P* < 0.01; ****P* < 0.001 (Student's *t*-test).



Supplemental Figure 5. Related to Figure 6. (**A**) Representative photograph of fixed brains dissected from control and *Sec24c*^{Nes}-cKO;*Chop*-KO mice at P0. (**B**) Mean weight (± SEM) of fixed brains from *Sec24c*^{Nes}-cKO;*Chop*-KO mice (n = 4 mice/genotype) at P0. (**C**) Immunostaining against cleaved caspase-3 in cortical sections of control and *Sec24c*^{Nes}-cKO;*Chop*-KO mice at E11.5, E13.5, E16.5, and P0. Areas from cortex (1) and striatum (2) are magnified. 3 mice were used for each genotype at each age. Average number (+ SEM) of SOX2$^+$ (**D**), TBR2$^+$ (**E**), and TBR1$^+$ (**F**) cells in cortices of control and *Sec24c*^{Nes}-cKO;*Chop*-KO mice at E16.5 show a specific reduction of TBR1$^+$ neurons in the brains from *Sec24c*^{Nes}-cKO;*Chop*-KO mice (n = 3 mice for each genotype). Abbreviations: DKO, double-knockout; ns, not significant; T, thalamus. *$P < 0.05$; ***$P < 0.001$ (Student's *t*-test).



Supplemental Figure 6. Related to Figure 7. XTT cell viability assays on WT and *SEC24C*-KO hiPSCs at 3, 4, 5, and 6 weeks of differentiation. Data collected from 3 independent experiments were presented as mean ± SEM. ***$P < 0.001$ (two-way ANOVA).



Supplemental Figure 7. Related to Figure 8. (**A**) Expression of *Sec24c*, *Sec24d*, *Sox2*, *Map2*, and *Gsh2* mRNA in the cortices of WT mice at E14.5 revealed by in situ hybridization (data from GenePaint: http://www.genepaint.org/). Areas from the cortex and striatum are magnified. (**B**, **C**) The mRNA levels of *Sec24a*, *Sec24b*, *Sec24c*, and *Sec24d* were determined by RNA-sequencing in callosal (Layer II-III) and subcerebral (Layer V) neurons at E15.5, E16.5, E18.5, and P1, respectively (data from DeCoN: http://decon.fas.harvard.edu/pyramidal/). (**D**, **E**) The mRNA and protein levels of SEC24C in the cortices of WT mice at different developmental stages, including E13.5, E16.5, P0, P7, P21, and P56, were analyzed by real-time RT-PCR (3 mice were used for each age) and immunoblotting (1 mouse were used for each age). Abbreviations: CGE, caudal ganglionic eminence; CP, cortical plate; FPKM, fragments per kilobase of transcript per million mapped reads; MGE, medial ganglionic eminence; MZ, marginal zone; VZ/SVZ, ventricular zone/subventricular zone.