Figure S1

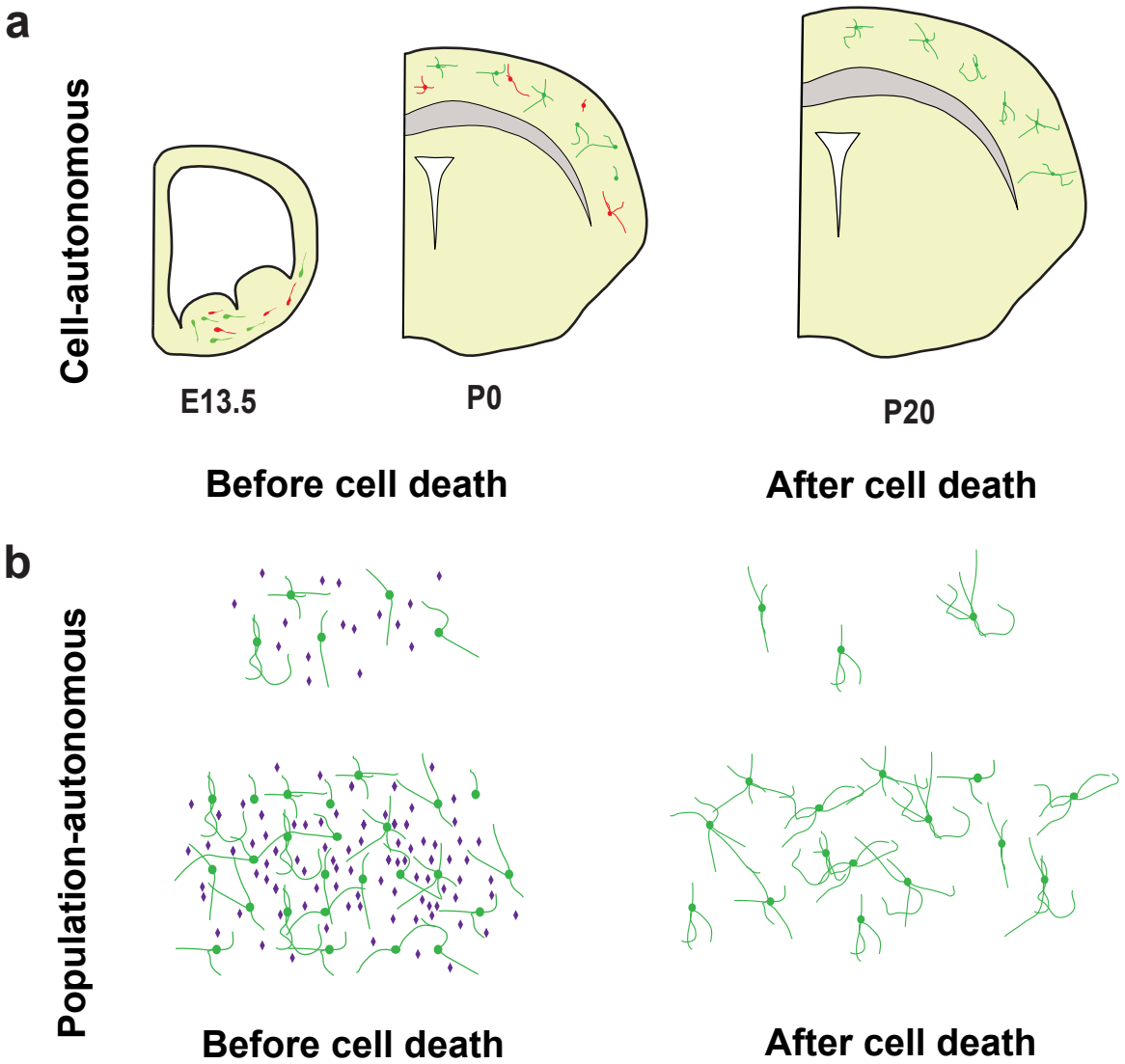

Figure S1 Proposed mechanisms of intrinsically determined cortical interneuron cell death. (a) A cell-autonomous mechanism, in which a fraction of interneuron precursors in the embryonic ventral forebrain (eg, embryonic day 13.5 (E13.5)) are individually destined to die later in development, regardless of the nature of their interactions with their environment. These cells, labeled in red, migrate into the cortex and eventually undergo cell death between postnatal days 0 and 20 (P0 and P20). In this scenario, these interneurons may die because they are produced defectively, or they may be programmed to die in a cell-autonomous fashion. **(b)** A population-autonomous mechanism, in which interneuron cell death is governed by competition for survival signals (purple) derived from other isochronic interneurons. Because these survival signals are produced by developing interneurons, their abundance scales to the number of developing interneurons present in the tissue. These interneuron-derived survival signals may be obtained via cell-cell contact, synaptic transmission, or neurotrophin receptors other than TrkB.

Figure S2

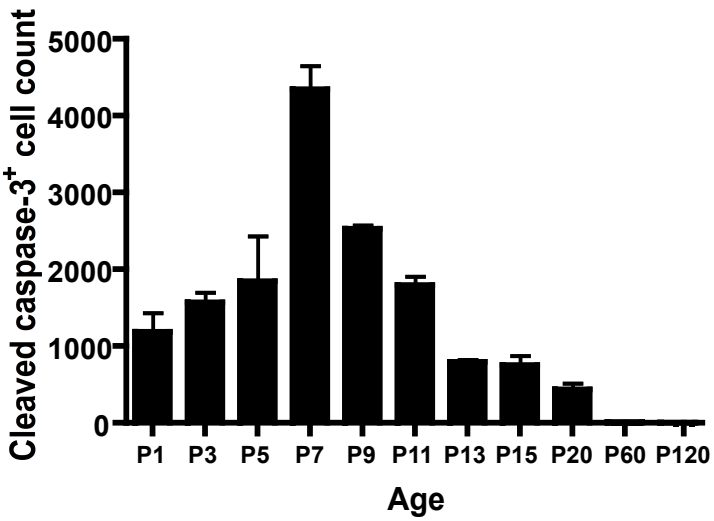

Figure S2 Temporal pattern of developmental cell death across the entire cellular population of the neocortex. Across the entire neocortical population of GAD67-GFP mice (GAD67-GFP+ and GAD67-GFP- cells), cleaved caspase-3 expression reaches a maximum at P7 and declines to undetectable levels between P20 and P60 (ANOVA, $F = 30.88$ and $P < 0.0001$; $n = 3$ per timepoint). Error bars represent the standard error of the mean.

Figure S3

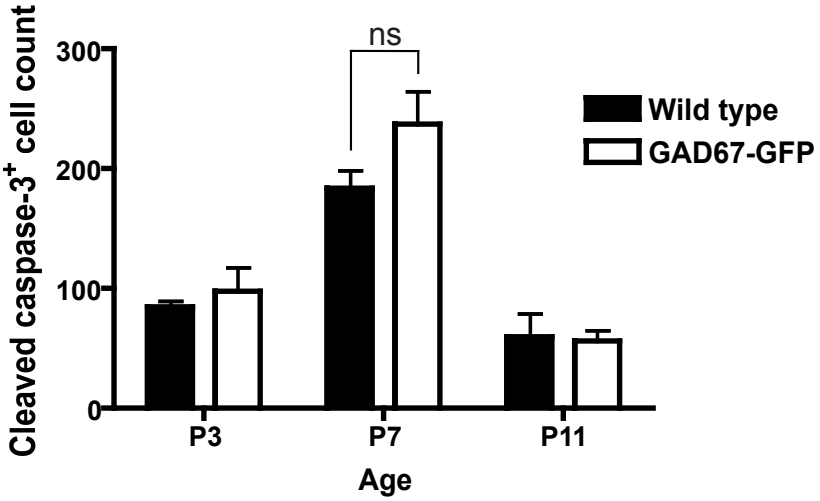

Figure S3 The disruption of the Gad67 allele by the Gad67-GFP knock-in does not affect developmental cell death. Across the entire cellular population of the cerebral cortex, the temporal profile of cleaved caspase-3 expression is similar in wild type (black) and GAD67-GFP mice (white; Student's t-test, P = 0.57 (P3); P = 0.16 (P7); P = 0.89 (P11); n = 3 per timepoint). Error bars represent the standard error of the mean.

Figure S4

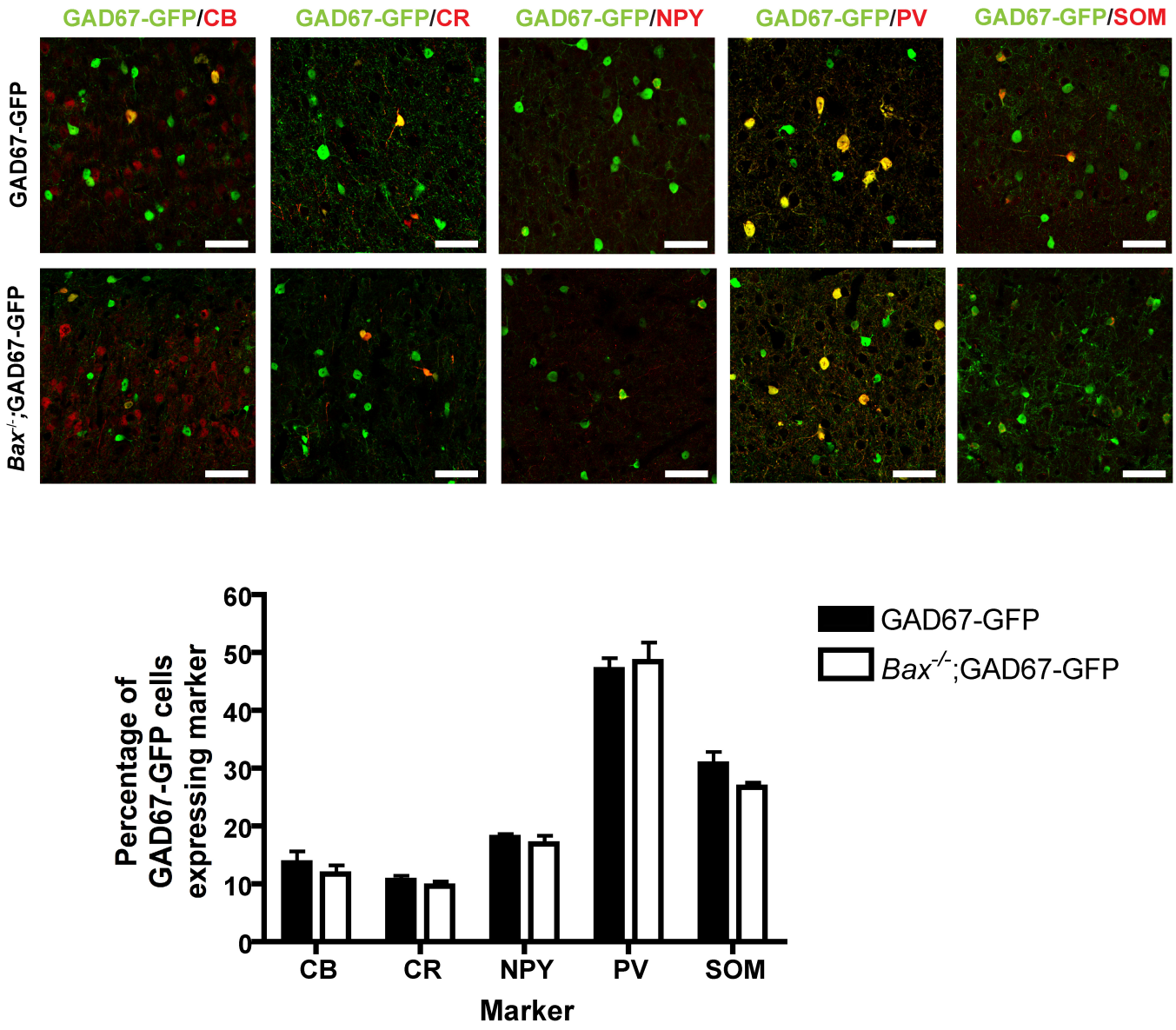

Figure S4 Bax-mediated cell death occurs in all neurochemically defined subtypes of cortical interneurons. Although the neocortical population is 49% larger in P120 Bax-/-; GAD67-GFP mice (Figure 1d), it is comprised of similar proportions of neurochemically defined interneuron subtypes, indicating that Bax-dependent cell death is not restricted to a particular subset of interneurons (CB = calbindin (Student's t-test, P = 0.51); CR = calretinin (P = 0.48); NPY = neuropeptide Y (P = 0.53); PV = parvalbumin (P = 0.74); SOM = somatostatin (P = 0.18); n = 3 per timepoint). Scale bar, 50 μm. Error bars represent the standard error of the mean.

Figure S5

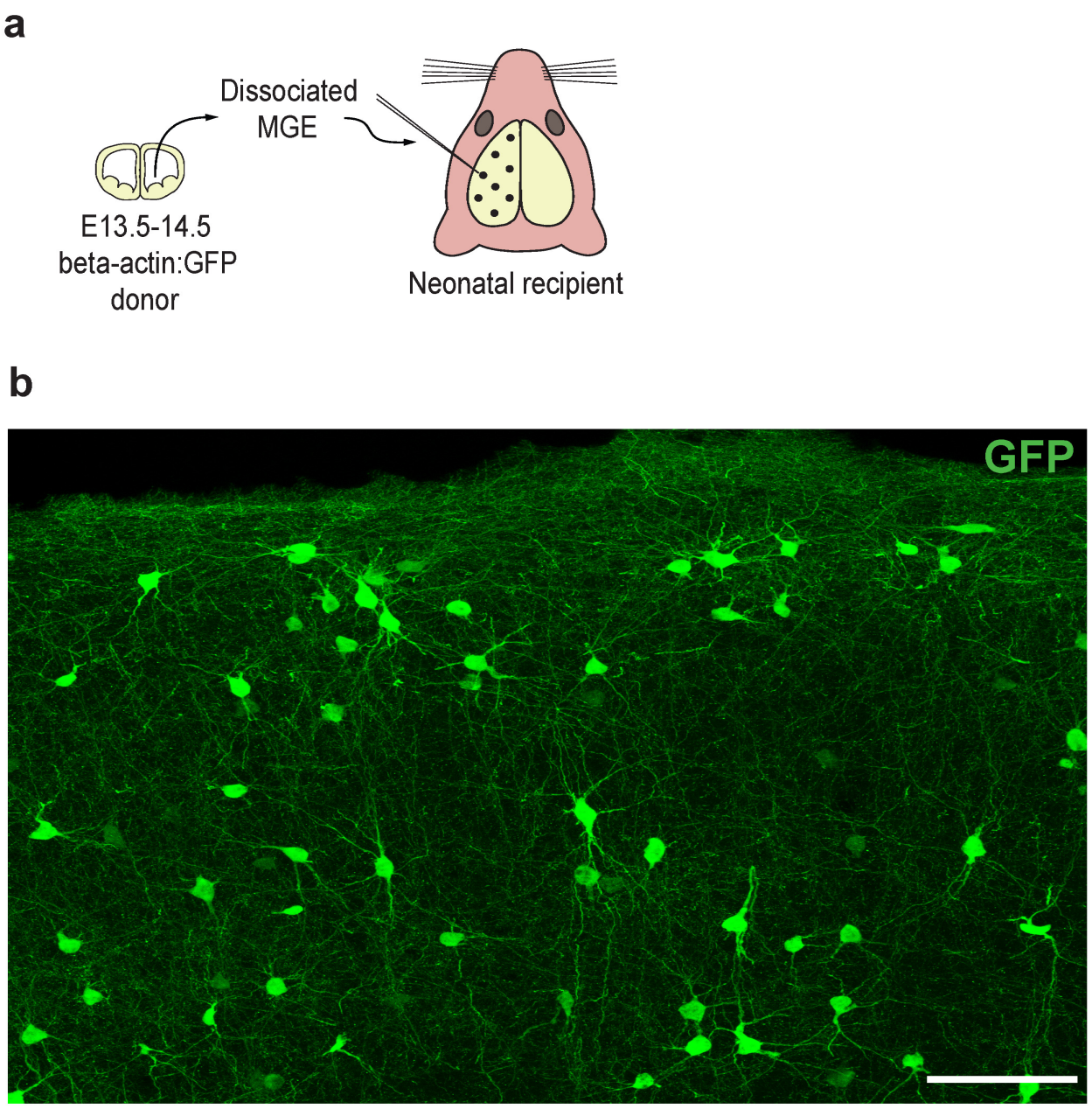

Figure S5 Heterochronic transplantation of embryonic interneuron precursors. **(a)** Cells were injected into eight sites in the recipient neocortex (black dots). **(b)** By 15 days after transplantation (DAT), GFP-labeled interneuron precursors have dispersed throughout the recipient neocortex and developed the anatomical properties of mature cortical interneurons. Scale bar, 80 μm.

Figure S6

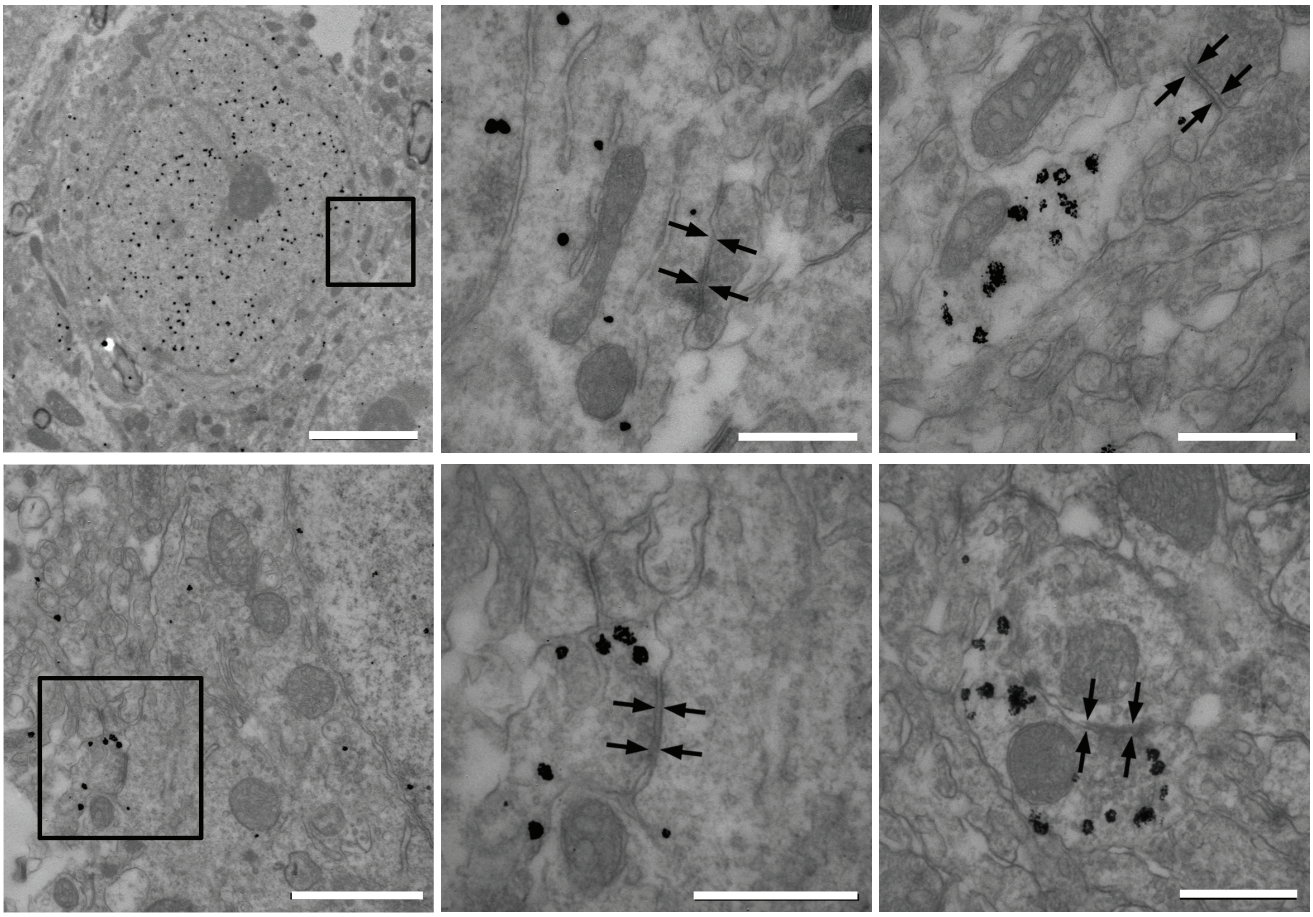

Figure S6 Transplanted interneurons establish synaptic contacts with recipient neurons. Upper left image: low magnification electron micrograph of beta-actin:GFP transplanted interneurons immunolabeled by silver-enhanced gold particles. Upper middle: boxed area from upper left image depicting axo-somatic synapses from an unlabeled cell onto the labeled cell body. Upper right: labeled dendrite receiving a synaptic contact from an unlabeled terminal. Lower left: low magnification electron micrograph of a labeled interneuron. Lower middle: boxed area from lower left image, depicting axo-somatic synapses from the labeled cell onto an unlabeled cell body. Lower right: labeled cell making a synaptic contact onto an unlabeled dendrite. Arrows indicate synaptic densities; Scale bars, 3μm (upper left), 1 μm (lower left), 500 μm (all others).

Figure S7

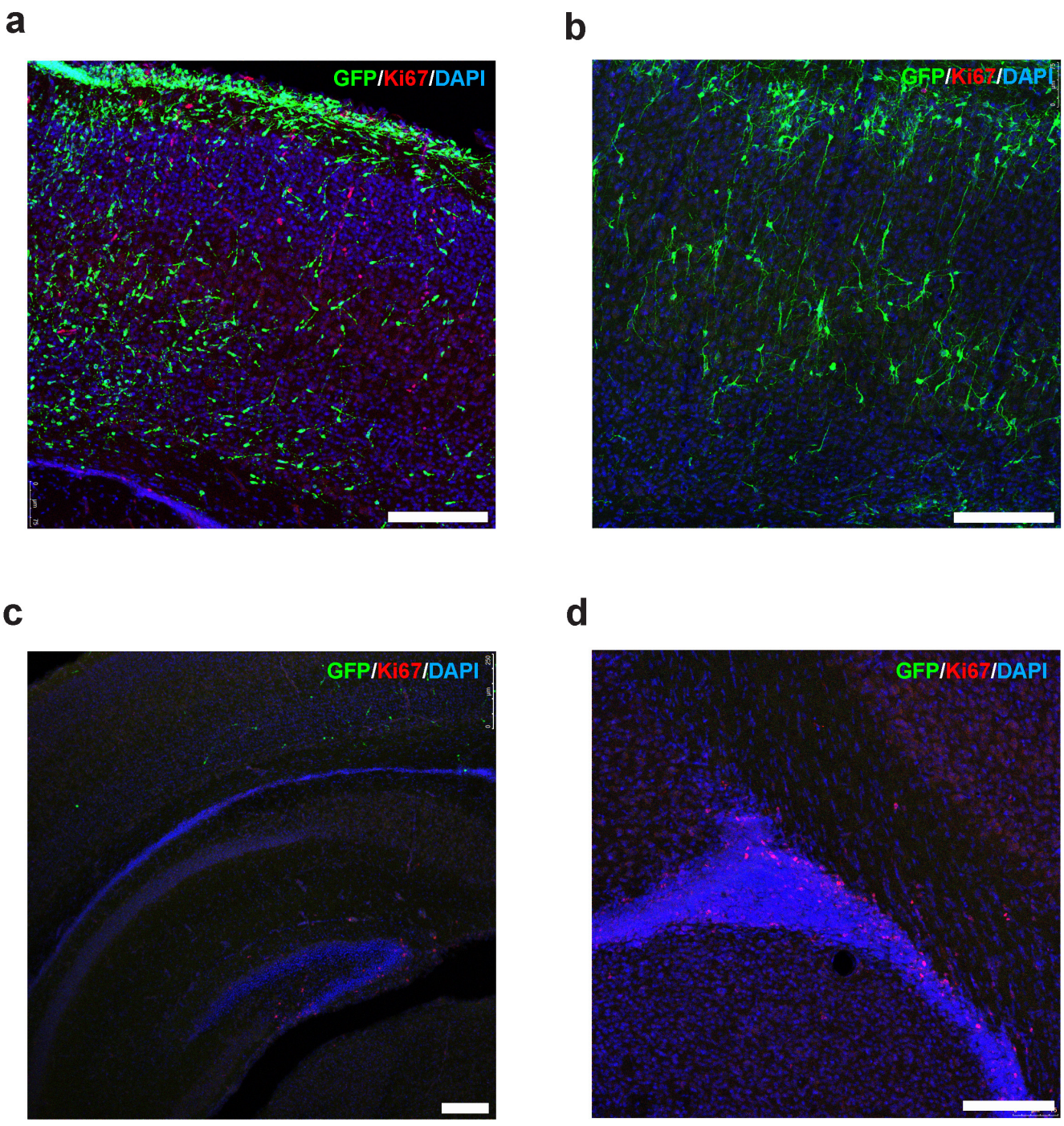

Figure S7 Trasplanted interneuron precursors do not proliferate in the recipient neocortex. At 3 DAT (**(a)** and **(c)**) and 7 DAT (**(b)** and **(d)**) transplanted interneurons (green) did not express Ki67 (red). Ki67 labeling was observed in other cells of the cortex **(a)**, the dentate gyrus of the hippocampus **(c)**, and the subventricular zone of the lateral ventricle **(d)**, sites where postnatal cell proliferation is known to occur. All cells are labeled by DAPI (blue). Scale bars = 150 µm.

Figure S8

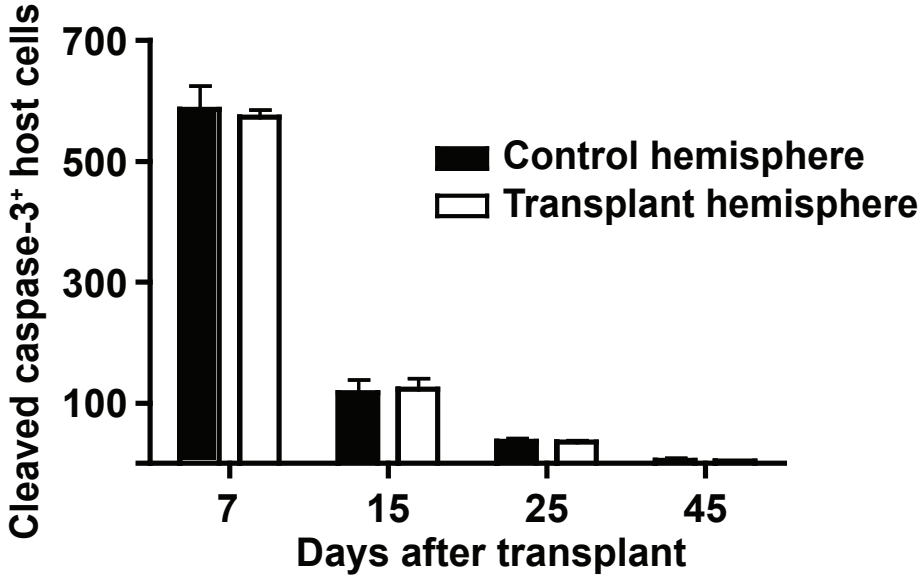

Figure S8 Temporal profile of cleaved caspase-3 expression across the total cellular population of the recipient neocortex. Transplantation does not alter the extent of cell death in the hemisphere that receives transplanted interneuron precursors (white), as compared to the contralateral, control hemisphere (black; Student's t-test, P = 0.76 (7 DAT), P = 0.83 (15 DAT), P = 0.89 (25 DAT), P = 0.67 (45 DAT); n = 5 per timepoint). In all figures, error bars represent the standard error of the mean.