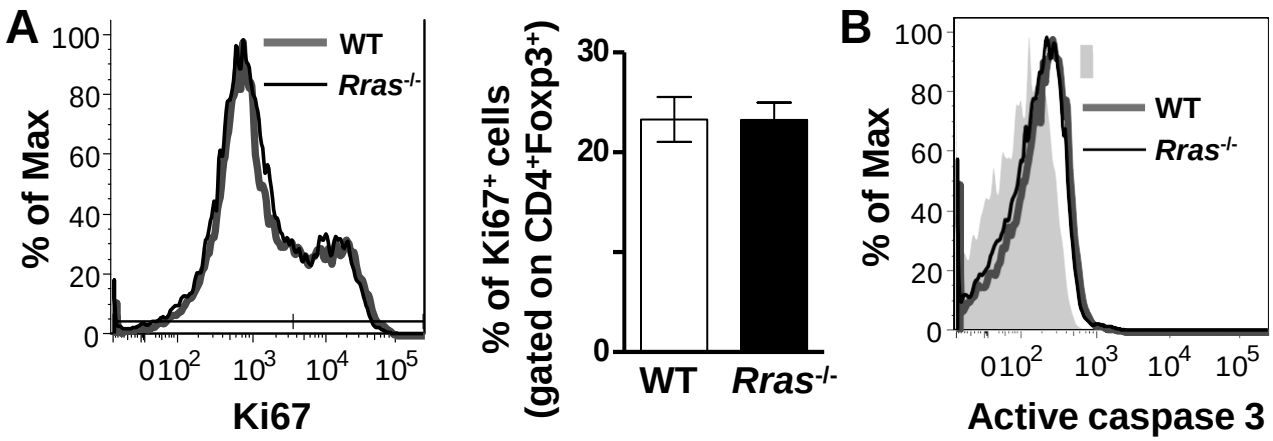

Figure S1. Proliferation and apoptosis of CNS-infiltrating CD4$^+$ T cells is unaltered in *Rras*$^{-/-}$ mice during EAE. A,B, EAE was induced in WT and *Rras*$^{-/-}$ mice at 6-8 wk of age by s.c. immunization with MOG_{35-55} peptide and CNS mononuclear cells were isolated 17 days later. Percentages of proliferating (Ki67$^+$) (A) and apoptotic (active caspase 3$^+$) (B) effector CD4 T cells (CD4$^+$Foxp3$^-$) were determined by flow cytometry. Representative histograms (A (left panel), B) and pooled data (A (right panel)) from one experiment with three mice in each group are shown.

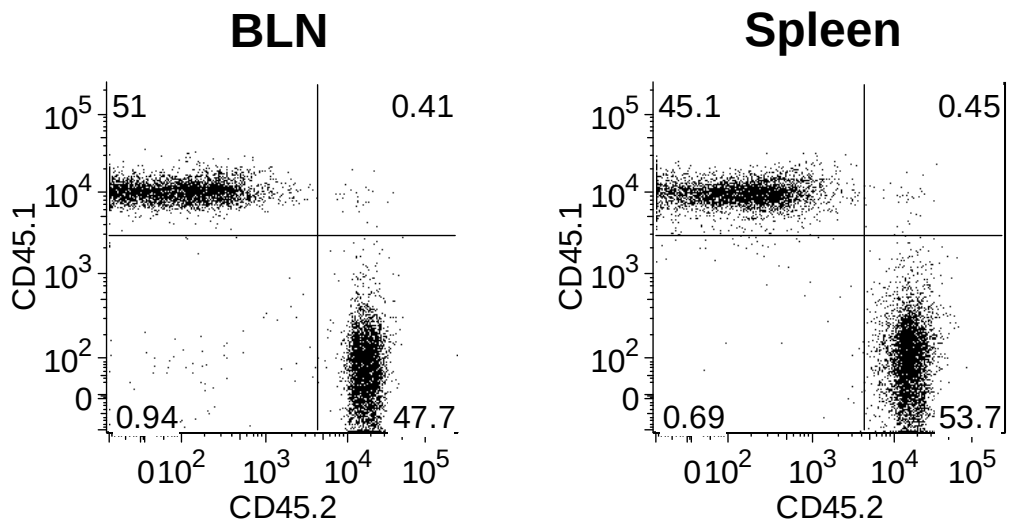

Figure S2. Proliferation and apoptosis of CNS-infiltrating CD4$^+$ T cells is unaltered in *Rras*$^{-/-}$ mice during EAE. Mixed BM chimera mice were generated as in Fig. 2. Ten weeks post BM transplantation the level of chimerism was determined in the BLN and spleen by flow cytometry. Percentages of WT (CD45.1$^+$) and *Rras*$^{-/-}$ (CD45.2$^+$) cells are shown. Representative data from two independent experiments each with two mice are shown.

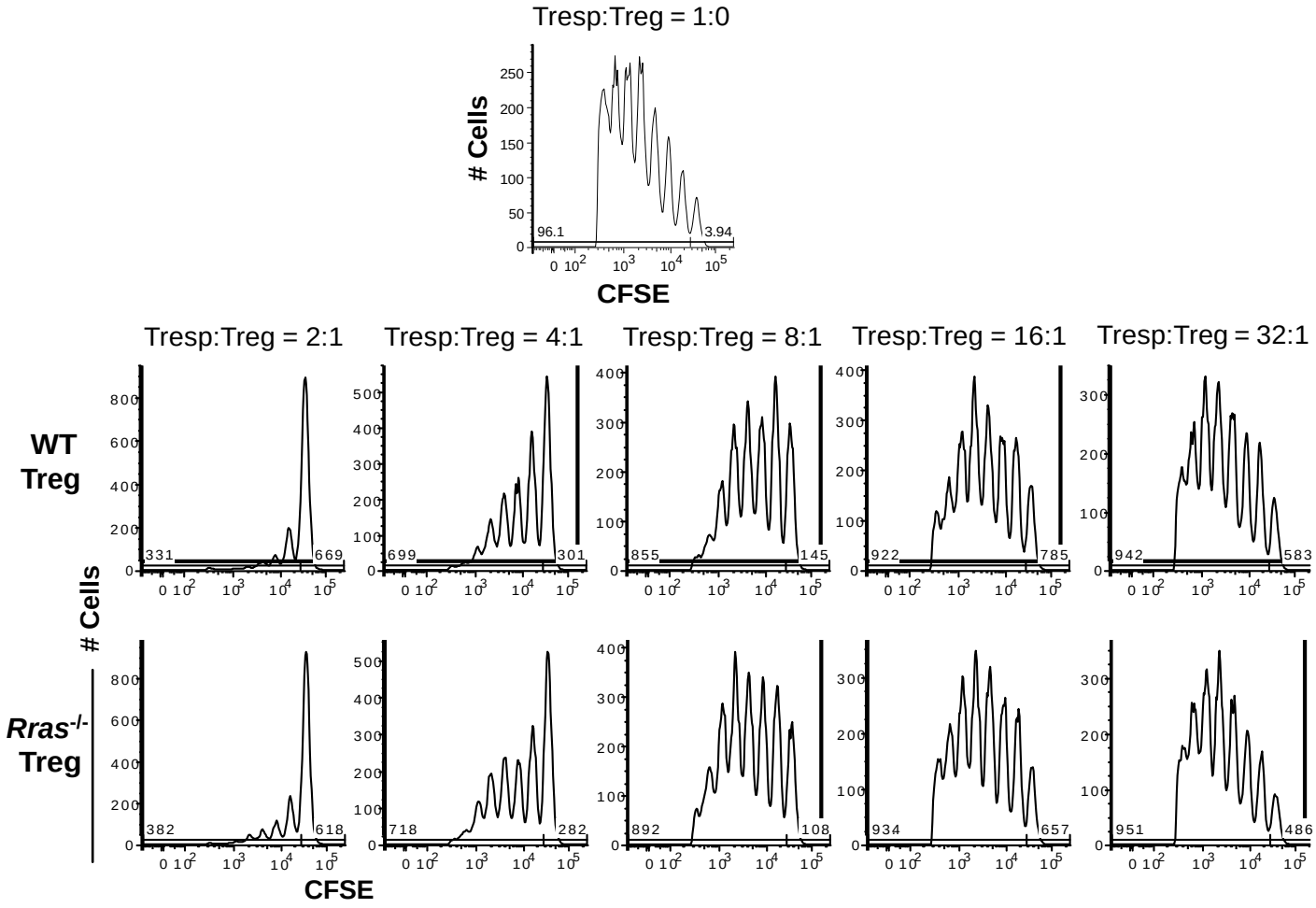

Figure S3. Equal in vitro suppressive ability of splenic Tregs isolated from WT and *Rras*$^{-/-}$ mice during EAE. CD4^{+}CD25^{-} responder cells (Tresp) from WT mice were labeled with CFSE and stimulated with anti-CD3 (3 mg/ml) and irradiated APCs (T cell-depleted syngeneic splenocytes) in the presence or absence of CD4^{+}CD25^{hi} Treg sorted from the spleens of WT and *Rras*$^{-/-}$ mice on day 17 after EAE induction. Four days later, proliferation of Tresp was determined by CFSE dye dilution by flow cytometry. Percentage of proliferating Tresp cells in the absence or presence of WT or *Rras*$^{-/-}$ Tregs at different Tresp/Treg ratios is shown. Representative data from two independent experiments are show

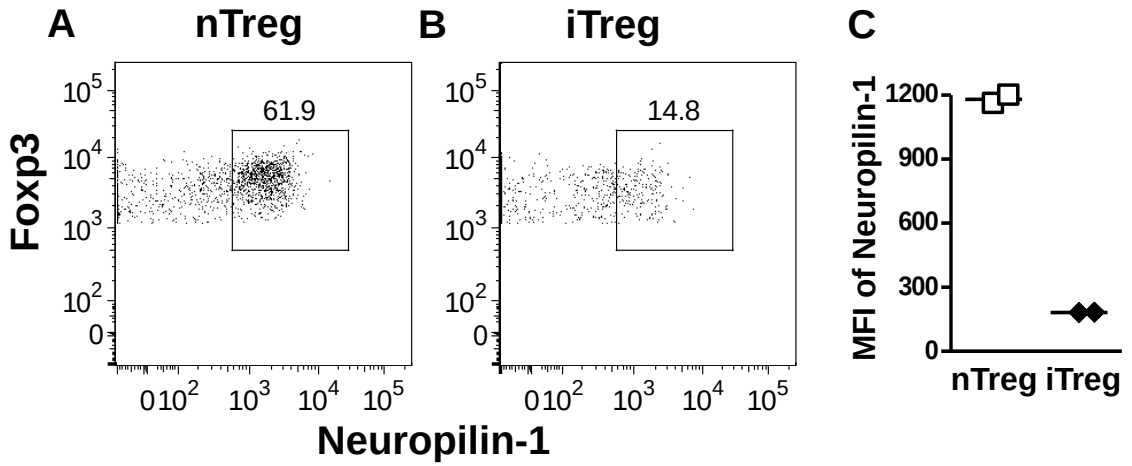

Figure S4. Neuropilin-1 is highly expressed on thymic nTregs, but not on in vitro-generated iTregs. A, Thymic nTreg (GFP^+) from $Foxp3^{EGFP}$ reporter mice were characterized for the expression of Neurophilin-1. A) $CD4^+EGFP^-$ cells from $Foxp3^{EGFP}$ reporter mice were FACS purified and were stimulated in vitro with plate-bound anti-CD3 (5 µg/ml) and soluble anti-CD28 (1 µg/ml) in the presence of purified TGF-β (5 ng/ml) for 72 h for the generation of $EGFP^+$ (Foxp3) iTreg cells. $CD4^+GFP^+$ cells were analyzed by flow cytometry for the expression of Neutrophilin-1. The percentage of Neuropilin-1^{hi} cells (A,B) and the MFI (C) of Neuropilin-1 gated on $CD4^+Foxp3^+$ is shown. Representative dot plots (A,B) and a scatter plot (C) from two independent experiments are shown.