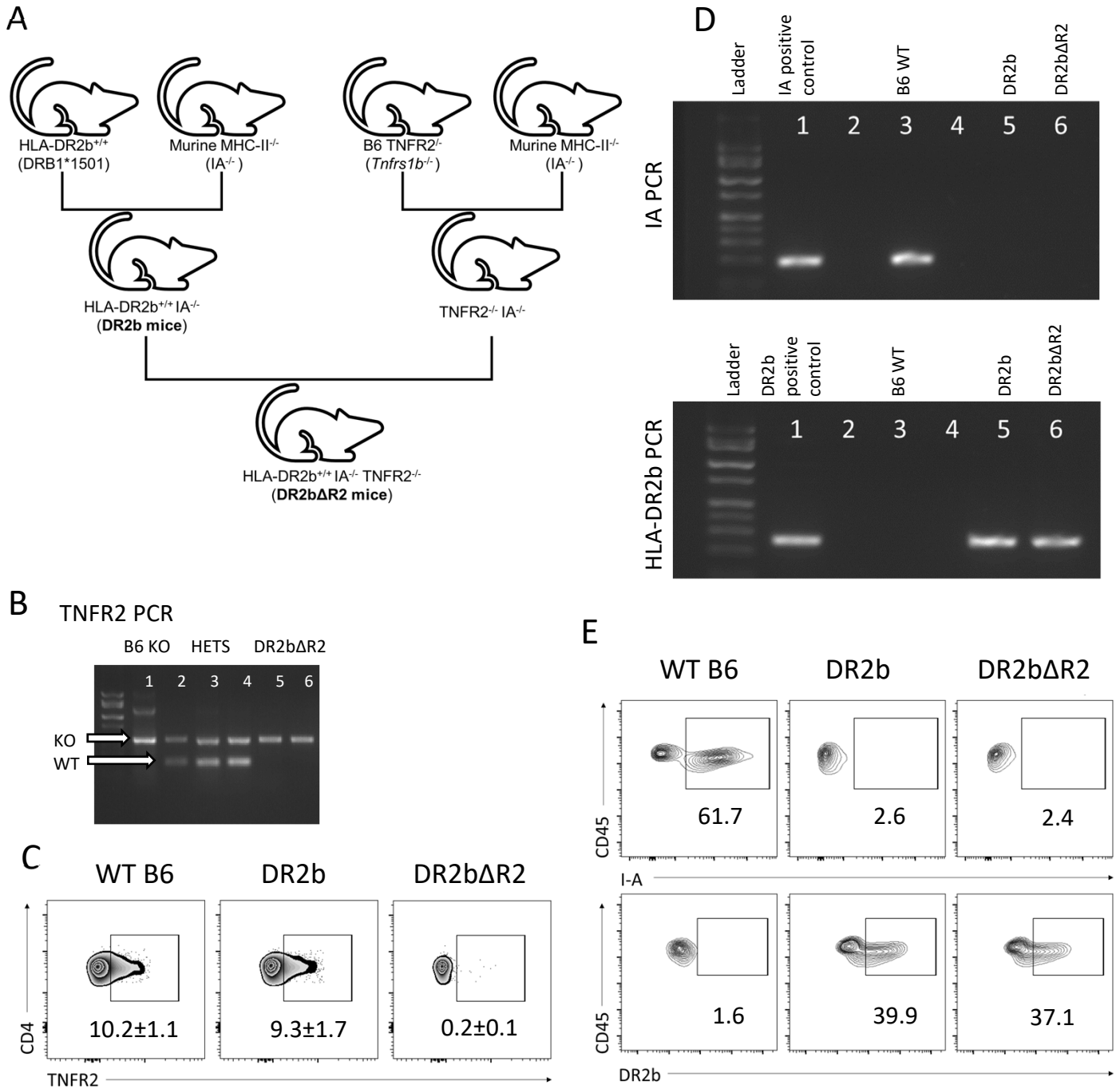
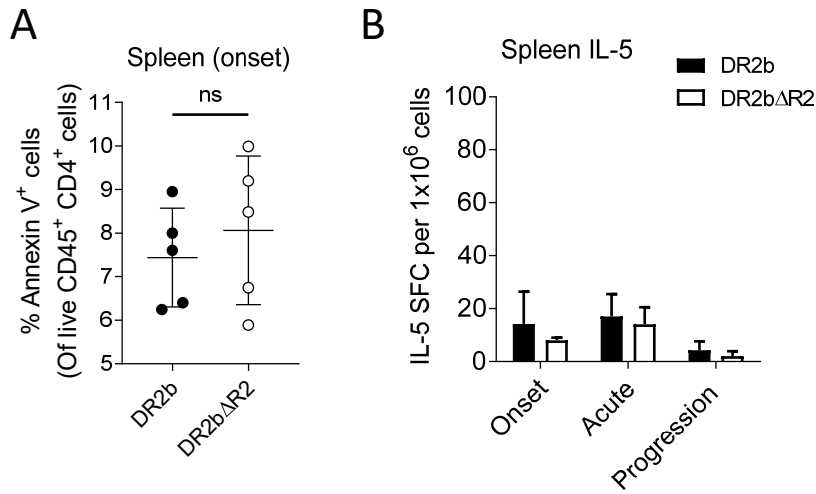


Supplemental Figure 1



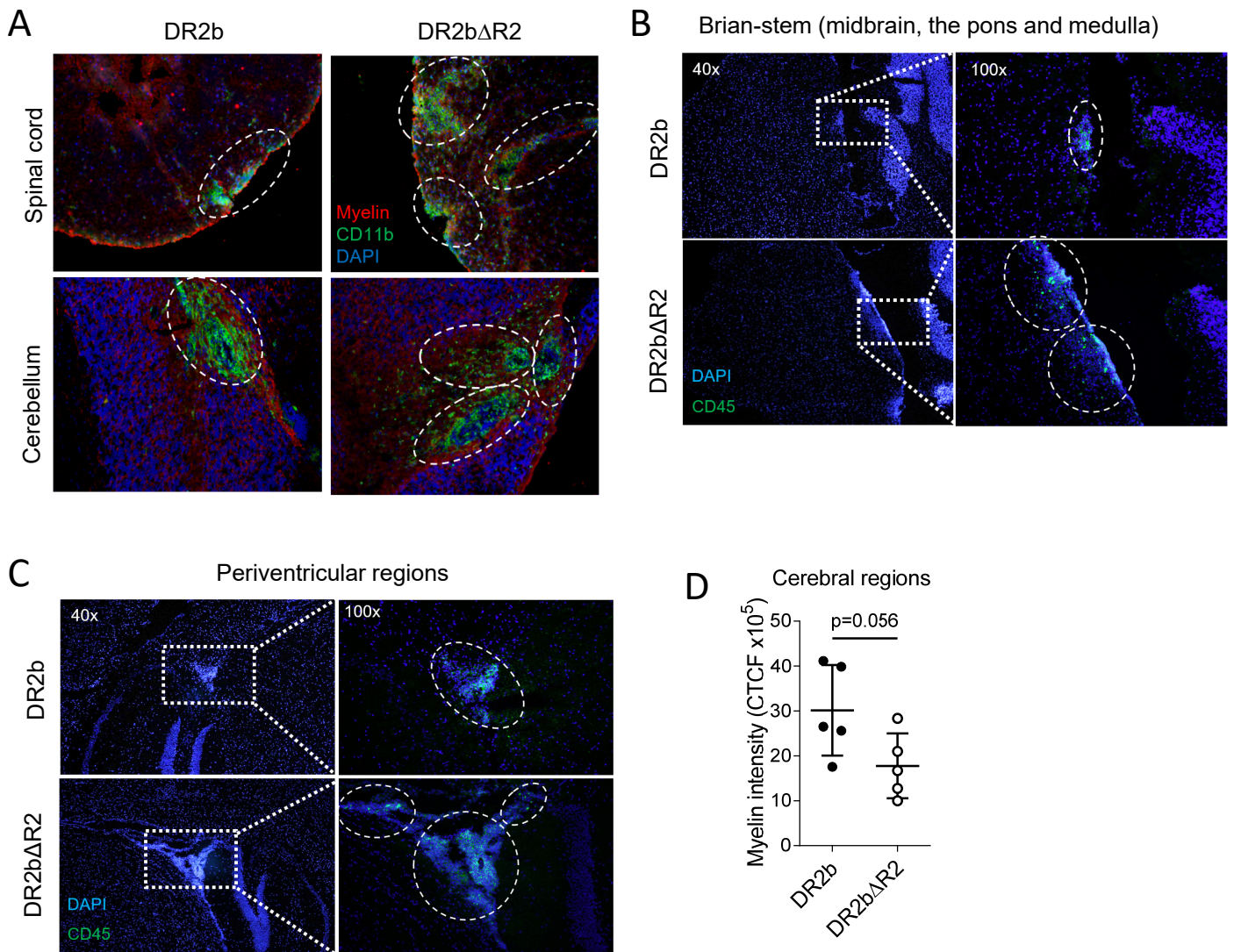
Supplemental Figure 1: Generation and validation of DR2b (DR2b^{+/+} I-A^{-/-} TNFR2^{+/+}) and DR2bΔR2 (DR2b^{+/+} I-A^{-/-} TNFR2^{-/-}) mice. (A) Breeding scheme for the generation of DR2bΔR2 mice from DR2b, I-A/E^{-/-}, and C57BL/6 TNFR2^{-/-} mice. (B) PCR analysis results of wildtype (WT; lower band) and knockout (KO; upper band) TNFR2 gene expression in B6 TNFR2^{-/-} mouse (KO; lane 1), DR2 TNFR2^{+/+} heterozygote mice (hets; lanes 2-4) and DR2bΔR2 mice (lanes 5 & 6). (C) Flow cytometry analysis for the expression of TNFR2 by CD4⁺ cells in spleens of B6, DR2b, and DR2bΔR2 mice. (D) PCR analysis results of I-A (top) and HLA-DR2b (bottom) expression in B6-WT mice (lane 3), DR2b mice (lane 5), and DR2bΔR2 (lanes 6), and a positive control DNA for I-A-expression or DR2b-expression (lane 1). (E) Flow cytometry analysis for the expression of I-A and DR2b on CD45⁺ cells from spleens of B6, DR2b, and DR2bΔR2 animals.

Supplemental Figure 2



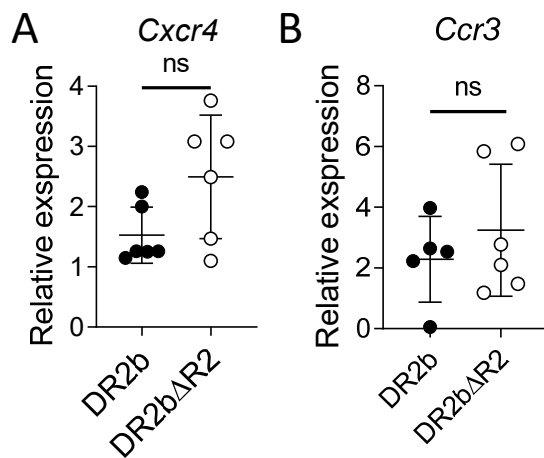
Supplemental Figure 2. (A) Annexin V expression in live (Ghost Dye⁻) CD4⁺ T cells from spleen of DR2b and DR2bΔR2 mice during EAE onset. Representative results from 2 independent experiments, n=5 mice per group. (B) Frequencies of MOG₃₅₋₅₅ specific IL-5 producing T cells in spleens of DR2b and DR2bΔR2 mice at onset, acute, and progression phases of EAE measured by cytokine ELISPOT assay. Data from 3 independent studies with n=5 mice per group. Student's *t*-test. ns = not significant. Error bars indicate mean ± SD.

Supplemental Figure 3



Supplemental Figure 3. (A-C) Representative immunofluorescence staining of lesions in (A) spinal cord (top) and cerebellum (bottom), (B) Brainstem, and (C) periventricular tissue sections analyzed at acute and progressive phase of disease of DR2b and DR2b Δ R2 mice immunized for EAE. Sections show nuclei stain (DAPI; blue) plus: myelin stain (FluoroMyelin; red) and CD11b⁺ cells (green) (A), or CD45⁺ cells (green) (B, C). Dashed circles represent active lesions with CD45⁺ or CD11b⁺ cell infiltrates. Representative data from n=3-6 mice per group. (D) Myelin fluorescence intensity measured by IF microscopy in the cerebral areas at EAE progression phase. Representative data from 2 experiments with n=5 per group. Student's *t*-test. Error bars indicate mean \pm SD.

Supplemental Figure 4



Supplemental Figure 4. Passive EAE induced by adoptive transfer of MOG₃₅₋₅₅-reactive T cells from DR2b donors into DR2b and DR2bΔR2 recipients. Expression of (A) *Cxcr4* and (B) *Ccr3* mRNA in the CNS of DR2b and DR2bΔR2 recipient mice at acute disease. Data from 3 independent experiments, n=3-5 mice per group. Statistical significance was determined by Student's *t*-test with Welch's correction. ns= not significant.