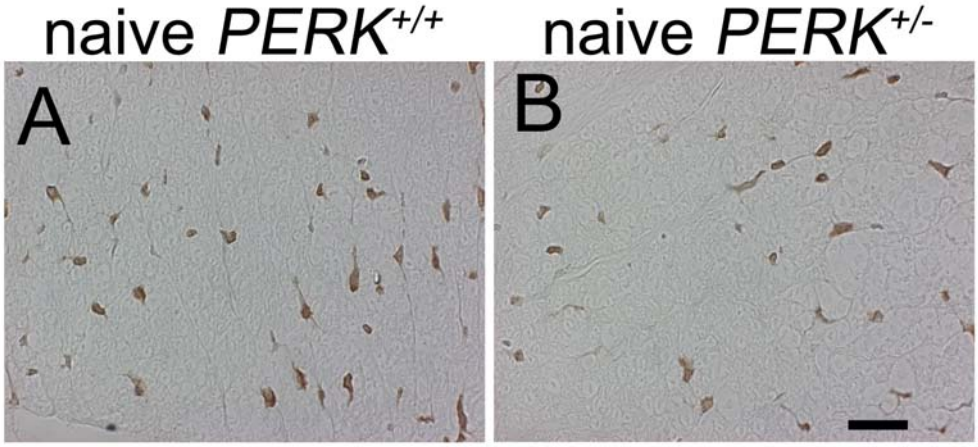
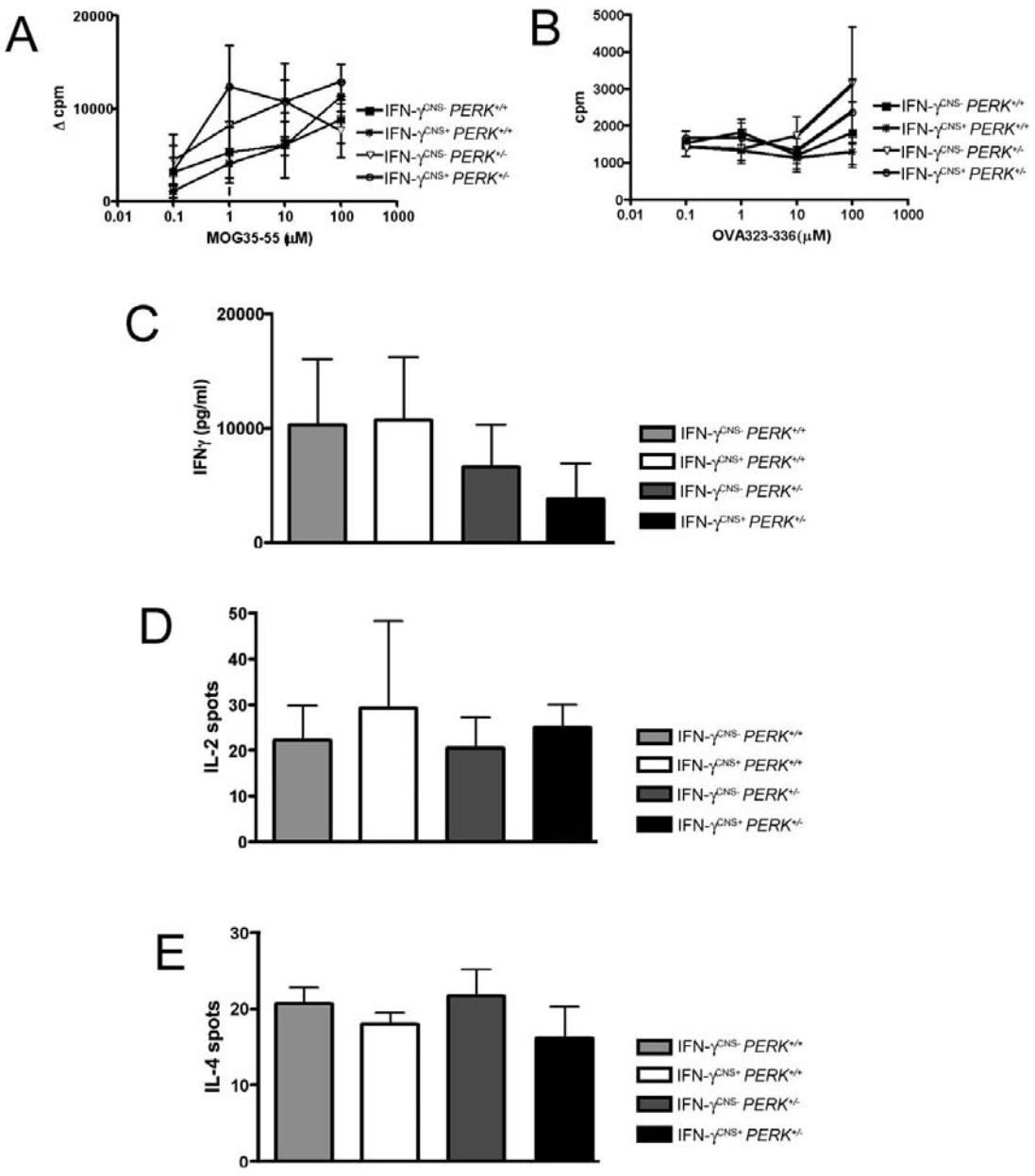
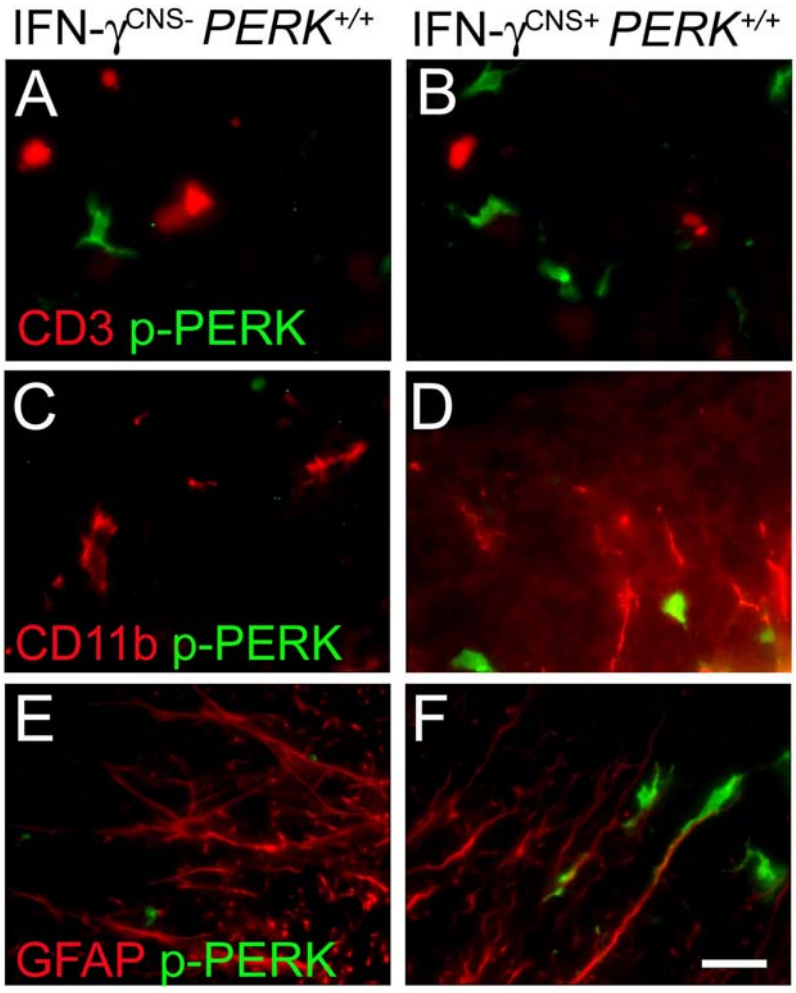


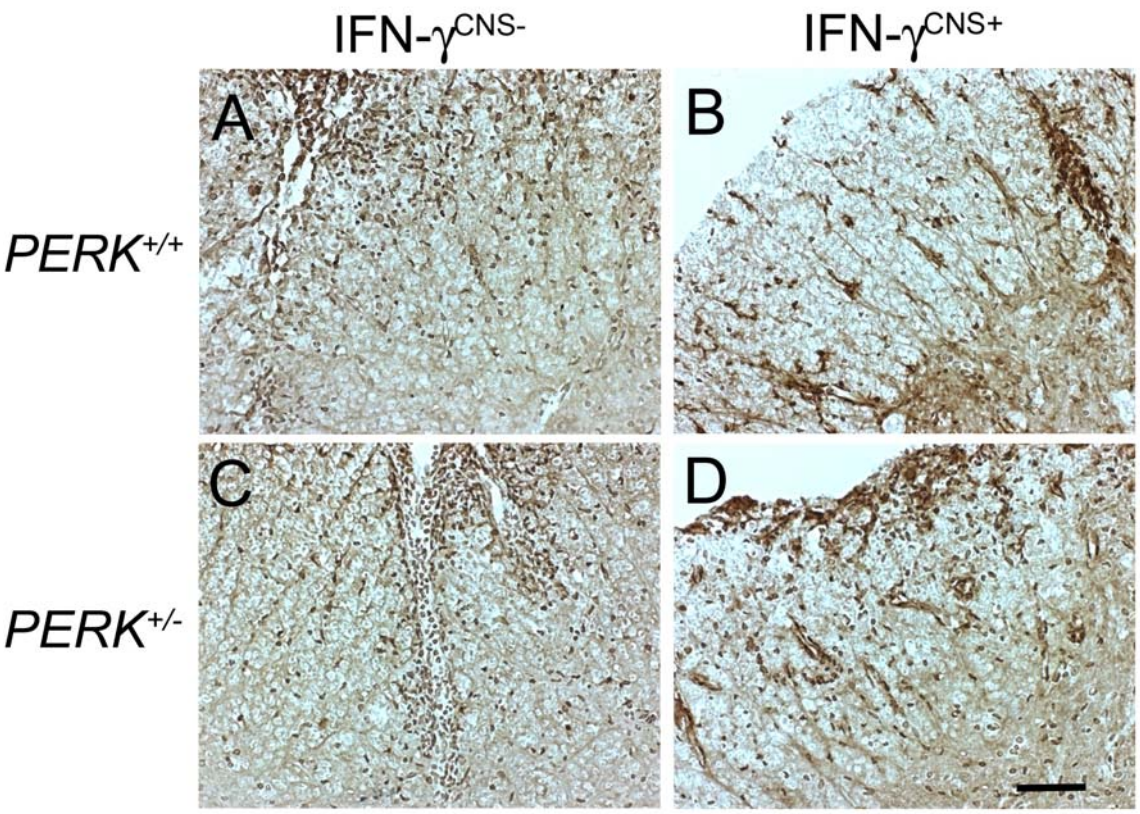
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4

Legend to Supplemental Figures.

Supplemental Figure 1. CC1 immunostaining revealed normal CC1 positive oligodendrocytes in the lumbar spinal cord of 9-weeks-old naïve mice. A. non-immunized *GFAP/ tTA; TRE/IFN-γ; PERK*$^{+/+}$ mice. B. non-immunized *GFAP/ tTA; TRE/IFN-γ; PERK*$^{+/-}$mice. N = 3, Scale bar = 25 μm.

Supplemental Figure 2. Both CNS delivery of IFN-γ and PERK mutation did not significantly affect peripheral T cell responses. Mice were immunized with MOG35-55 peptide, and 10 days later the spleenocytes were isolated and recall responses to MOG35-55 and OVA323-339 were analyzed. **A** and **B,** Thymidine incorporation of 5 x 10^5 splenocytes in response to increasing concentrations of MOG35-55 minus the expansion with comparable concentrations of OVA323-339 (Δ) after 4 days in culture. **C,** IFN-γ production by 5 x 10^5 splenocytes after 72 hours culture with 10 μM MOG35-55. **D** and **E**, The number of spots in an ELISPOT assay for IL-2 and IL-4 production by 2.5 x 10^5 spleen cells after 24 and 48 hours stimulation, respectively, with 10 μM MOG35-55. All panels: error bars represent SEM of three individual animals tested in two separate experiments.

Supplemental Figure 3. CNS delivery of IFN-γ did not activate PERK in T cells, microglia/macrophages and astrocytes. A and **B**, CD3 and p-PERK double immunostaining showed that the immunoreactivity of p-PERK was undetectable in CD3 positive T cells in lumber spinal cord of IFN-γ^{CNS+} mice or IFN-γ^{CNS-} mice at PID 14. **C**

and **D**, CD11b and p-PERK double immunostaining showed that the immunoreactivity of p-PERK was undetectable in CD11b positive microglia/macrophages in lumber spinal cord of IFN-γ^{CNS+} mice or IFN-γ^{CNS-} mice at PID 14. **E** and **F**, GFAP and p-PERK double immunostaining showed that the immunoreactivity of p-PERK was undetectable in GFAP positive astrocytes in lumber spinal cord of IFN-γ^{CNS+} mice or IFN-γ^{CNS-} mice at PID 14. N = 3, Scale bar = 10 μm.

Supplemental Figure 4. MHC-classII immunostaining revealed that CNS delivery of IFN-γ did not significantly change the numbers of MHC-classII positive cells in the lumbar spinal cord of mice on a *PERK* wild type or *PERK*$^{+/-}$ background at PID 17. N = 3, scale bar = 50 μm.