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 splenocytes 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-γCNS+ mice or IFN-γCNS- 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.