# Figure S1

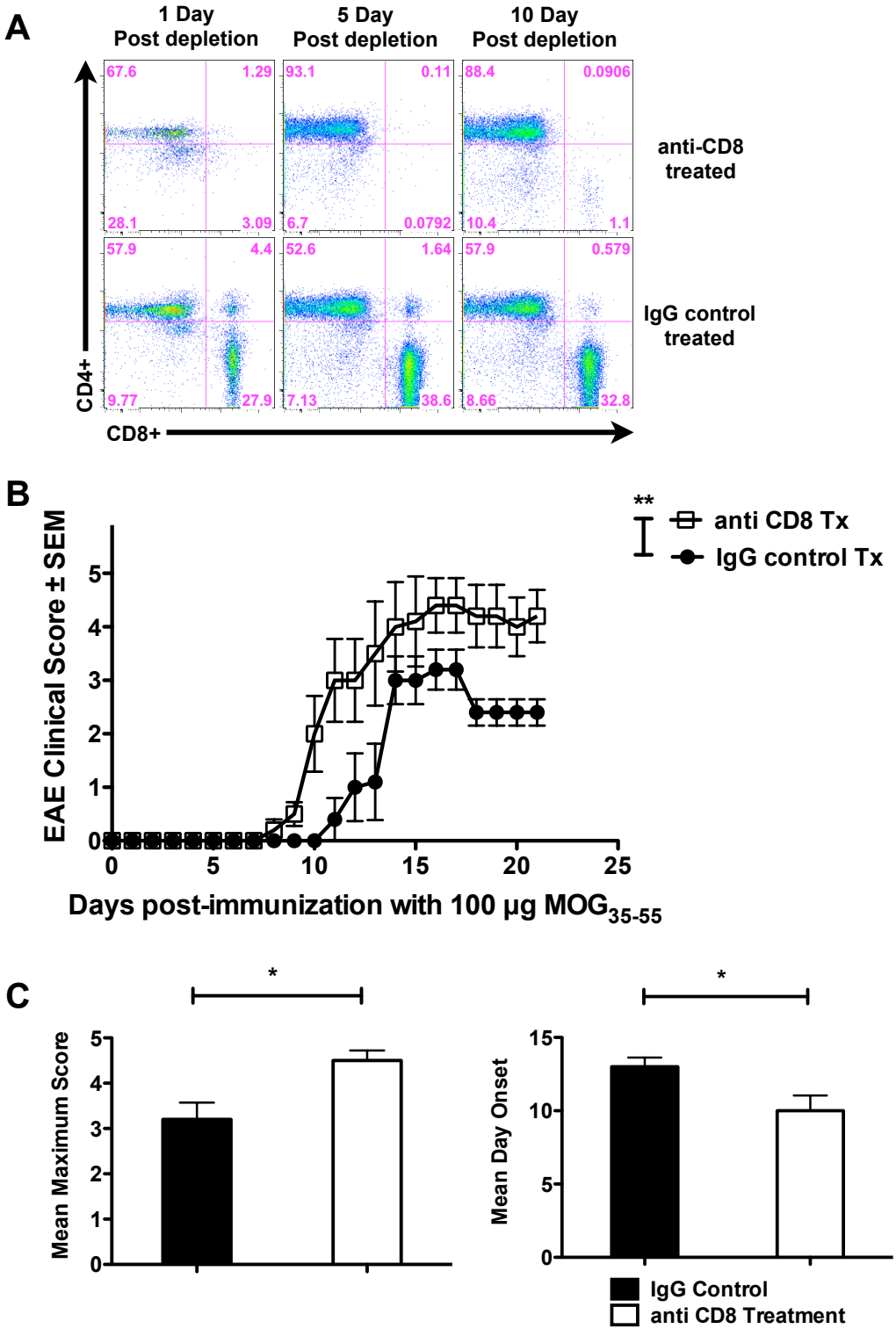



**Figure S1. Increase of EAE severity in antibody-mediated CD8 depleted mice.** (A) Flow cytometric data showing the successful depletion of CD8 T-cells from the peripheral immune compartment. (B) Clinical disease severity comparison between anti-CD8 depleted versus IgG control treated mice, post EAE induction. (C) Mean maximum EAE score and mean day of onset of CD8-depleted (vs. control) WT mice. *=p<0.05. Representative data from three independent experiments (5-7 mice per condition).

# Figure S2

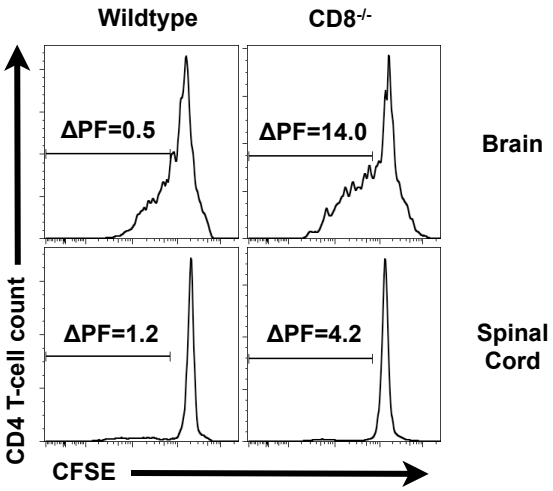
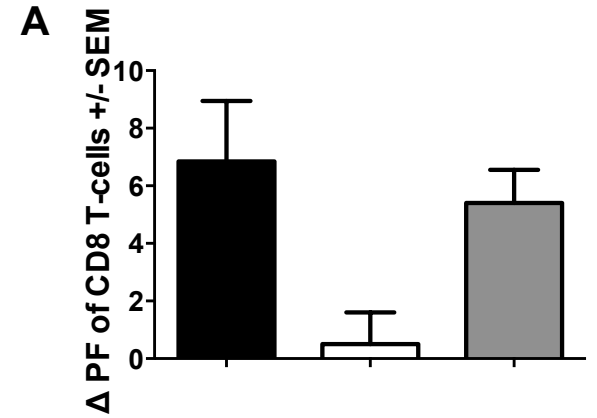



**Figure S2. Augmented CNS-specific CD4 T-cells autoreactivity within the CNS of CD8$^{-/-}$ mice.** CFSE-based proliferation assays were performed on cells isolated from brain and spinal cord of CD8$^{-/-}$ and WT mice at day 20 post-immunization. CFSE histograms are shown. ΔPF represents difference between proliferation in the presence of cognate antigen minus background. Representative of two independent experiments (n=10 per condition).

# Figure S3




| T-cell | MOG-CD8 | MOG-CD8 | MOG-CD8 |
|---|---|---|---|
| APC | WT | $KbDb^{-/-}$ | WT |
| Antibody | - | - | a-Qa-$1^{b}$ |

**Figure S3. Autoregulatory CD8 T-cell are ineffective in the absence of MHC Ia.** (A) Dependence of MHC I for CD8 T-cell activation was determined by performing an *in vitro* culture where MOG-specific CD8 T-cells were cultured with WT or MHC Ia deficient APC.

# Figure S4

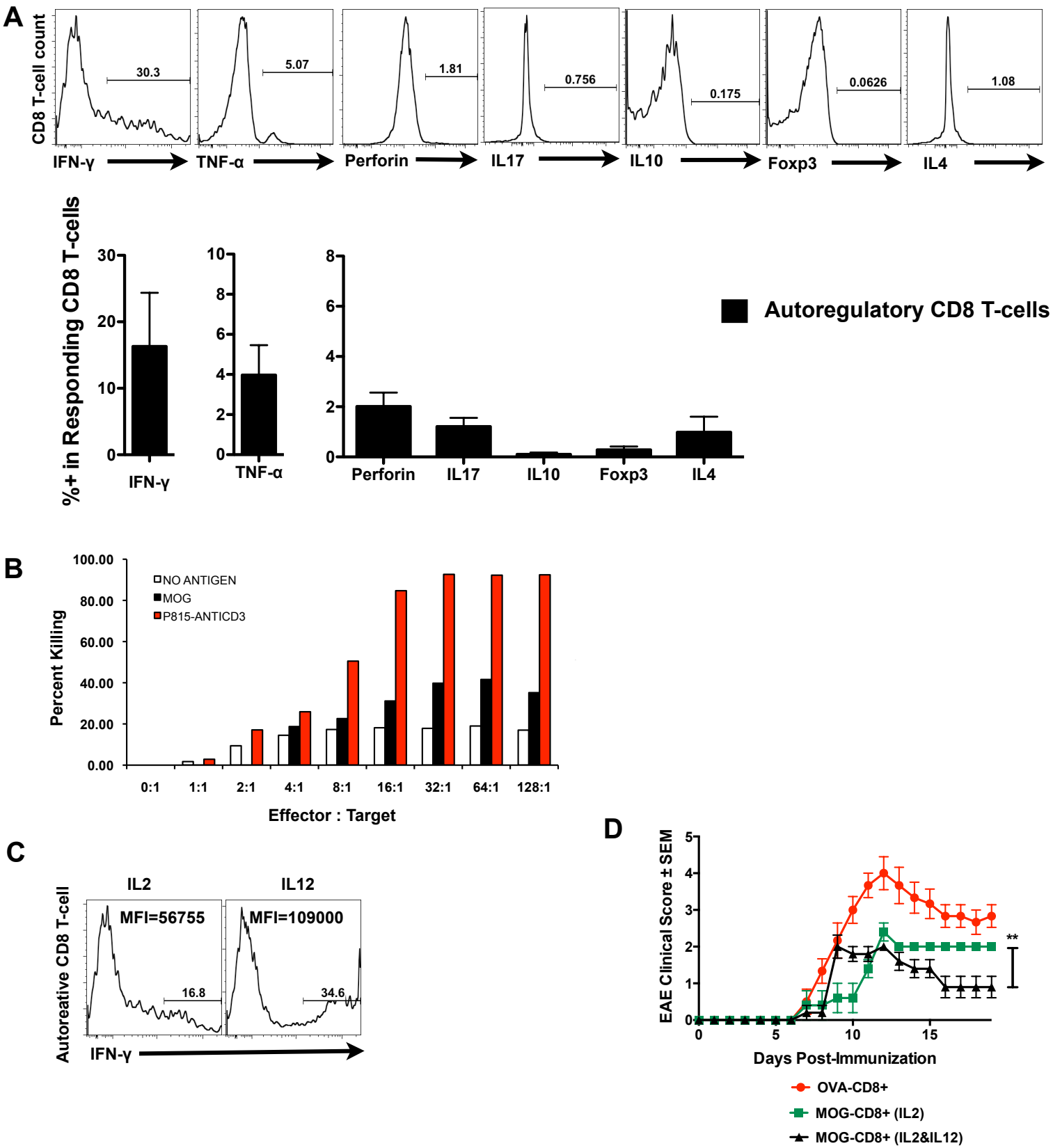



**Figure S4. Functional profile of autoregulatory CD8 T-cells.** (A) Intracellular cytokine stain of MOG-specific (i.e., proliferating/ CFSE Low) TCRβ+CD4-CD8+ T-cells. Representative histogram and cumulative graph of five independent experiments. (B) *In vitro* cytotoxicity assay is shown where MOG-loaded, splenic ConA blasts were co-cultured with increasing numbers of MOG-specific CD8 T-cells. Anti-CD3-decorated P815 target cells were used as positive controls. Percent killing was defined as live CFSE target cells for a particular ratio divided by live CFSE target cells in the no effector condition. (C) Intracellular cytokine stain of MOG-specific (i.e. proliferating /CFSE Low) TCRβ+CD4-CD8+ T-cells following IL12 modulation. Interval numbers indicate the percentage of IFN-γ+ CD8 T-cells within the responding population. Mean fluorescence intensity (MFI) within the IFN-γ+ population is shown. (D) Clinical disease severity comparison between control, standard and IL12 modulated MOG-specific CD8 T-cells is shown. Representative of three independent experiments (5-7 mice per condition).