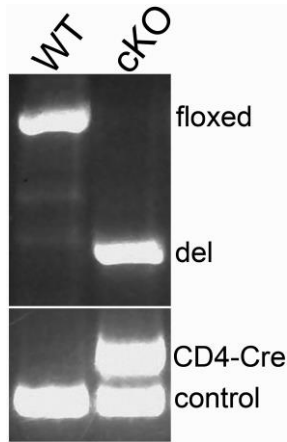
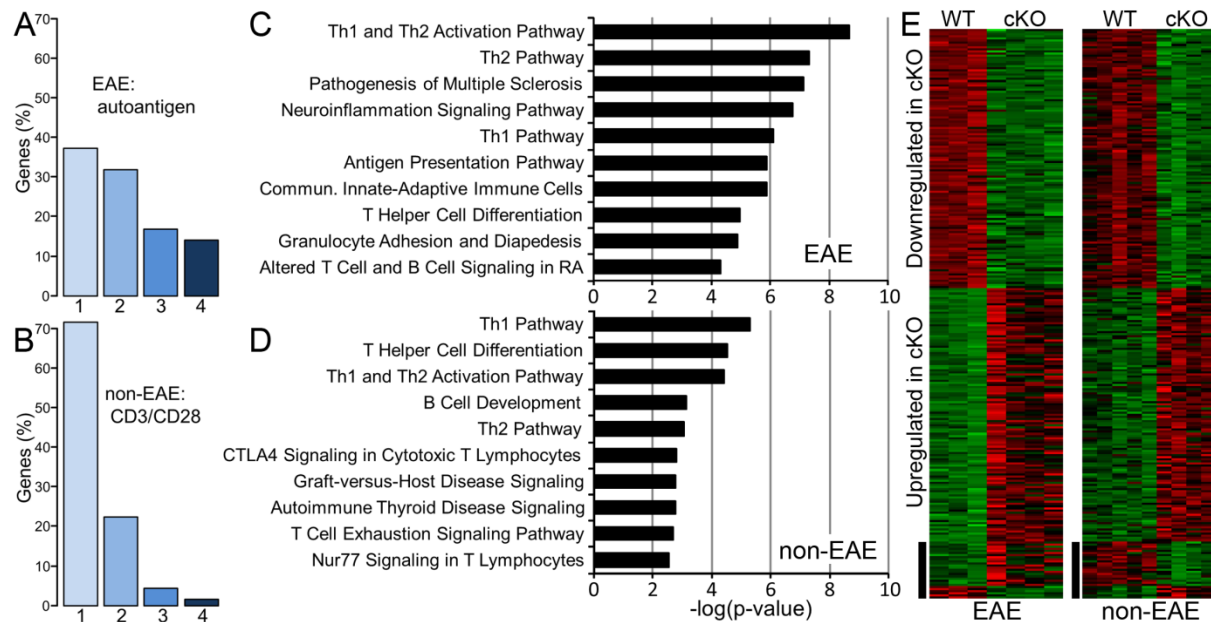


Supplemental Figure 1. Comparison of gene expression patterns of X escapees in CD4+ T cells in mice. (A) C57BL/6J naïve CD4+ T cells from spleen (GSE94671; 3 males and 3 females), (B) C57BL/6J stimulated CD4+ T cells from lymph nodes (GSE121292; Four Core Genotypes: 6 XX and 6 XY⁻), and (C) SJL stimulated CD4+ T cells from lymph nodes (GSE121705; Four Core Genotypes: 6 XX and 5 XY⁻) were analyzed for sexually dimorphic gene expression of five known X escapees, other than *Kdm6a*. In a box and whisker plot, the thick line inside the box represents the median of the data. The lower and upper ends of the box are quantiles (25% and 75%), and whiskers show the minimum and maximum values excluding outliers (dot). n.s.: not significant. Significance of differences between male and female (or XX and XY⁻) mice were determined using R package “edgeR”.



Supplemental Figure 2. Deletion of *Kdm6a* in CD8+ T cells. Genomic PCR for isolated CD8+ T cells showed deletion of *Kdm6a* in cKO mice. When the *Kdm6a* gene is developmentally knocked out in CD4-Cre cKO mice, it is deleted in both CD4+ T cells, as well as CD8+ T cells, in adults.



Supplemental Figure 3. CD4⁺ T cell transcriptomes from EAE mice and from healthy (non-EAE) mice. (A and B) Bar graph for the differentially expressed genes categorized by four different logFC degrees: (1) least stringent $-0.5 < \logFC < 0.5$, (2) $-1 < \logFC < -0.5$ and $0.5 < \logFC < 1$, (3) $-1.5 < \logFC < -1$ and $1 < \logFC < 1.5$, (4) most stringent $\logFC < -1.5$ and $1.5 < \logFC$. In the healthy group's naïve T cells stimulated with anti-CD3/CD28 antibodies, almost 70% of the differentially expressed genes showed small gene expression changes ($-0.5 < \logFC < 0.5$). In contrast, in the EAE group stimulated with autoantigen, many differentially expressed genes showed large fold changes. For significantly differentially expressed genes ($FDR < 0.1$, $\logCPM > 1$, $\logFC > 1$ or $\logFC < -1$), canonical pathway analysis was performed in (C) EAE and (D) healthy. Due to the small number of differentially expressed genes with more than 2 fold difference in healthy group, pathways in C and D consist of both up and down regulated genes. With this threshold ($FDR < 0.1$, $\logCPM > 1$, $\logFC > 1$ or $\logFC < -1$), 110 genes were differentially expressed in the healthy group, while 360 genes were significant in the EAE group. Th1 and Th2 related pathways remain the top enriched pathways in both healthy and EAE conditions. (E) Heatmap showing the pattern of 268 down (green) and up (red) regulated differentially expressed genes ($FDR < 0.1$, $\logFC > 0.5$ or $\logFC < -0.5$). While a majority of genes showed a common up- and down-regulated pattern, 27 genes at the bottom (indicated by thick black bar) changed in opposite directions. These 27 differentially regulated genes were enriched in the “inflammatory response” functional annotation group by gene ontology analysis (<https://david.ncifcrf.gov>).

Supplementary table 1. List of differentially expressed genes between WT and cKO.

(in separate Excel file)