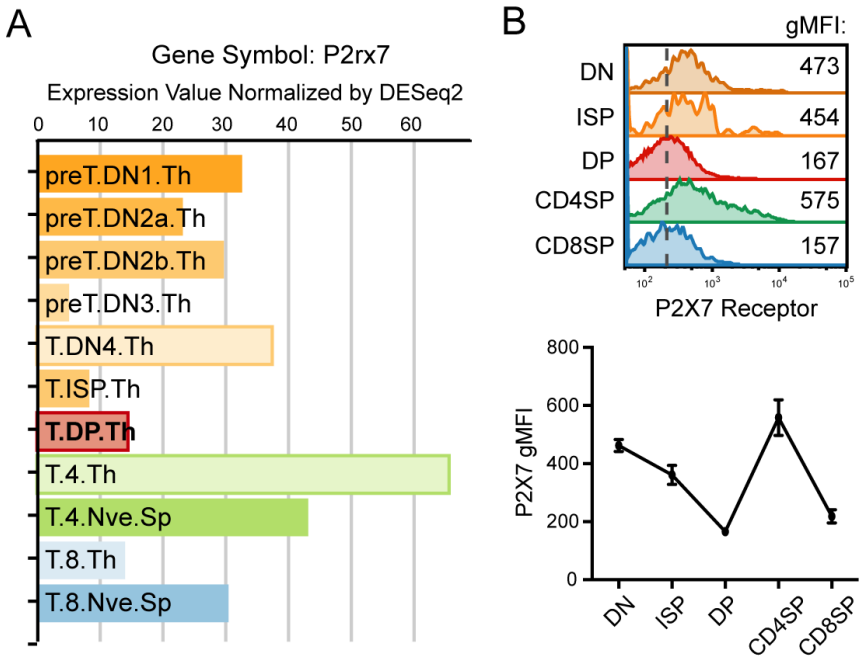
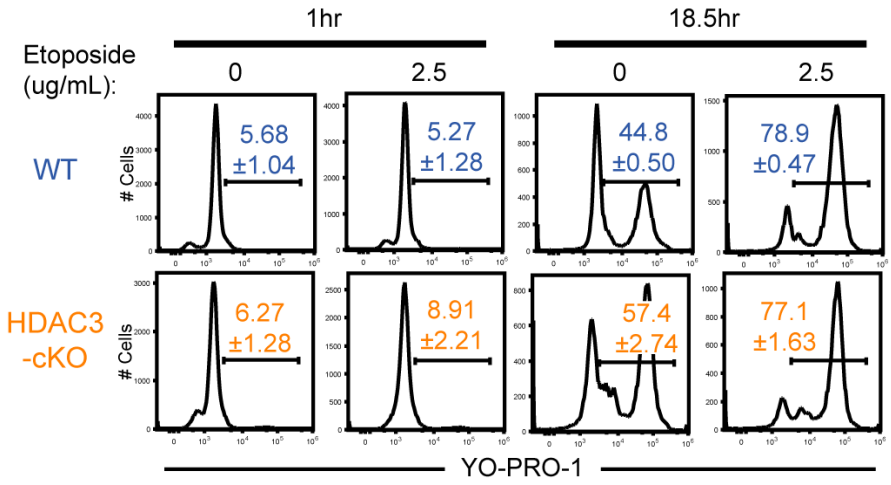
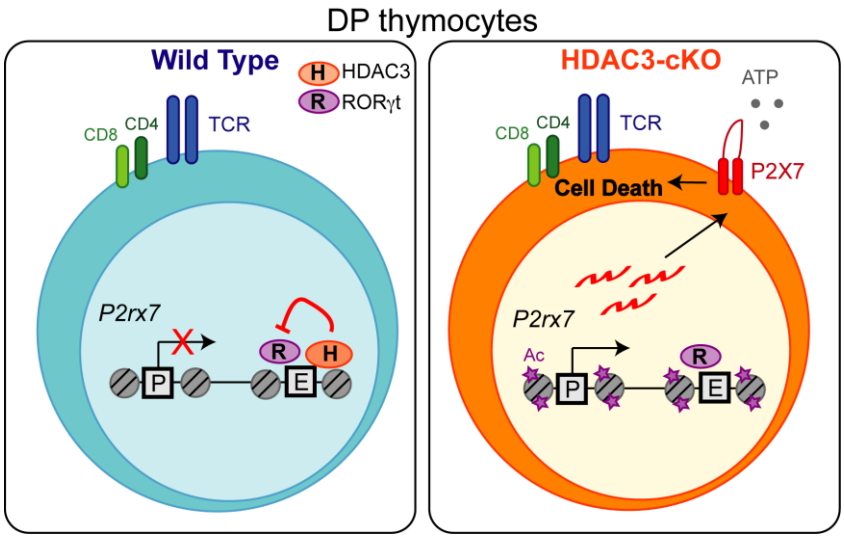
Supplementary Figures



Supplementary Figure 1. P2X7 receptor expression during T cell development. (**A**) Expression profile of *P2rx7* in thymic developmental stages (DN1-SP) and splenic naive CD4 and CD8 T cells. RNA-seq data was acquired from the Immunological Genome Consortium via the RNA-seq Gene Skyline (immgen.org). (**B**) P2X7 receptor protein expression in DN ($CD4^-$ $CD8^-$), ISP ($CD4^-CD8^+TCR\beta^-$), DP ($CD4^+CD8^+$), CD4SP ($CD4^+CD8^-TCR\beta^+$), and CD8SP ($CD4^-CD8^+TCR\beta^+$). FACS plot depict representative P2X7 receptor expression for each thymic stage and its corresponding gMFI. The plot below depicts mean ± SEM of gMFI of 4 mice from 3 independent experiments.



Supplementary Figure 2. Etoposide treatment of WT and HDAC3-deficient thymocytes. Thymocytes from WT and HDAC3-cKO mice were treated with or without 2.5ug/mL of etoposide for 1 hour or 18.5 hours. Plots show mean ± SEM of the frequency of YO-PRO-1^{+} DP thymocytes from 3-4 mice per group. Plots were gated from FVD^{-} (to remove necrotic cells) DP thymocytes. Etoposide treatment does not increase YO-PRO-1 staining after one hour, however after 18.5 hours etoposide treatment leads to a similar frequency of YO-PRO-1^{+} DP thymocytes between WT and HDAC3-cKO mice.



Supplementary Figure 3. Model. In WT DP thymocytes, HDAC3 associates with the *P2rx7* enhancer to repress its expression and reduce DP thymocyte sensitivity to extracellular ATP. However, when HDAC3 is absent, the *P2rx7* gene locus is hyperacetylated, RORγt promotes the expression of *P2rx7*, and HDAC3-deficient DP thymocytes show increased cell death via ATP. Hence, HDAC3 may function to repress RORγt transcriptional activity at the *P2rx7* enhancer to repress *P2rx7* expression in DP thymocytes.