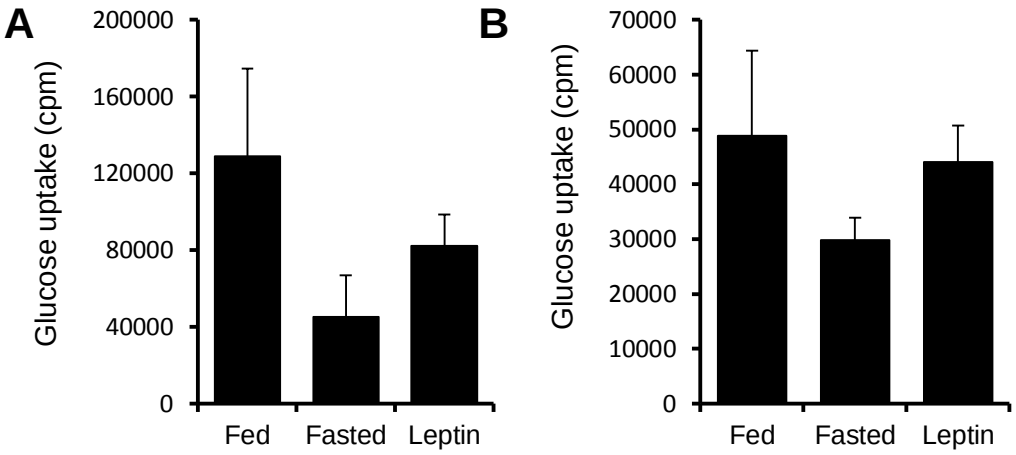
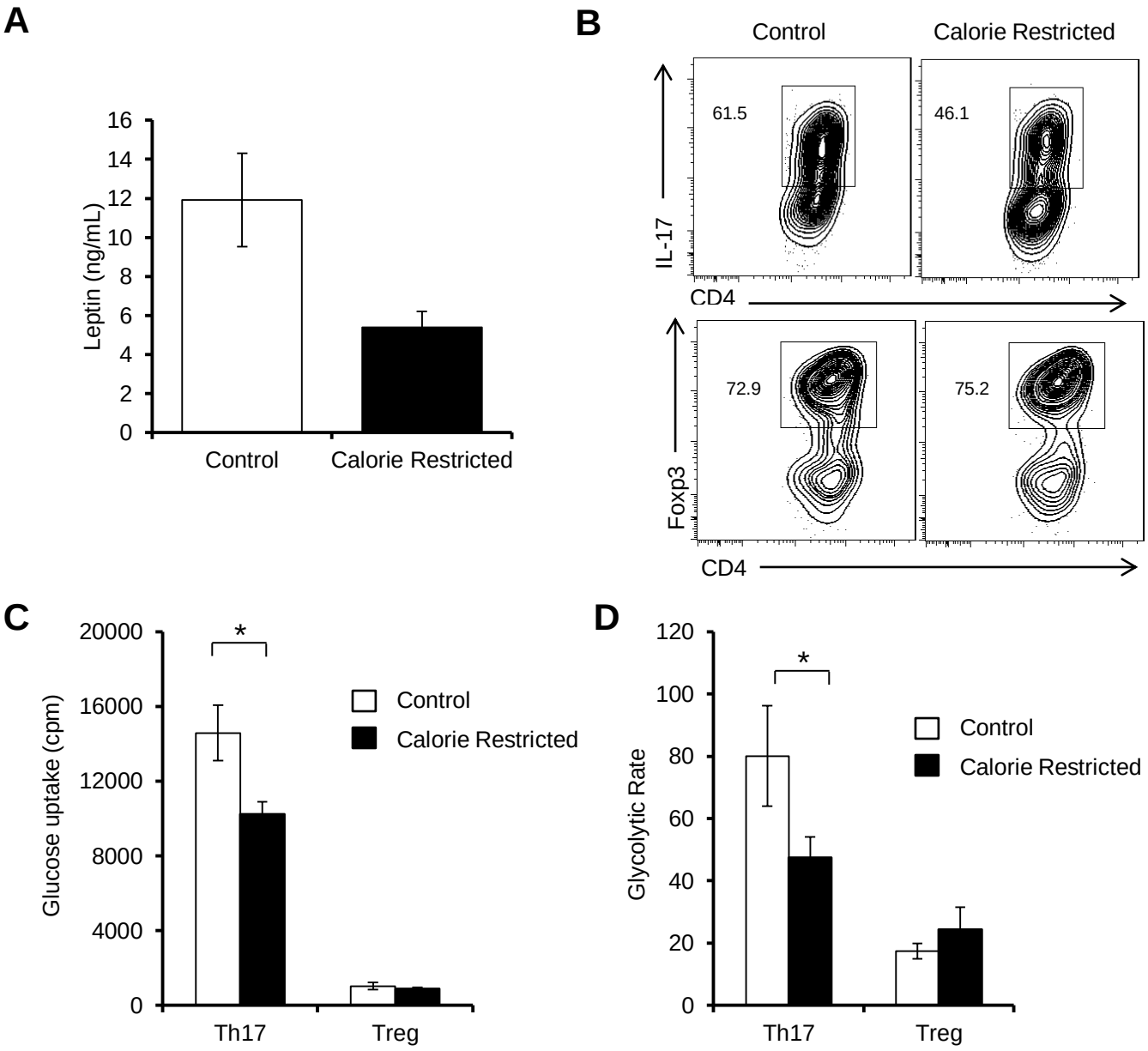
Supporting Information Figure 1



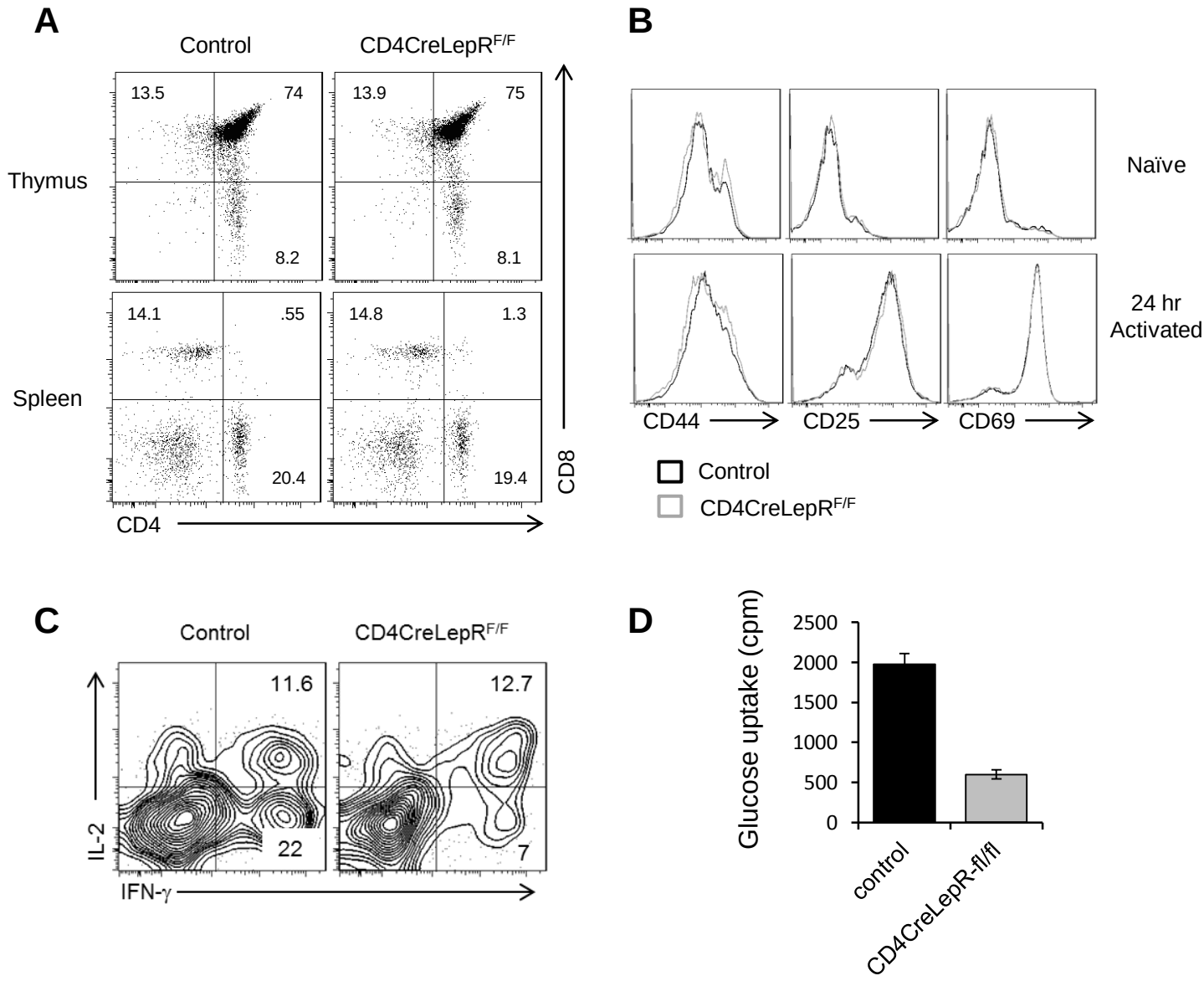
Supporting Information Figure 1. Examination of Th17 glucose metabolism in response to fasting and hypoleptinemia. Wildtype C57BL/6J mice were fed ad libitum (control) or fasted for 48 hours (fasted). Fasted mice received twice daily injections of leptin or PBS. Control fed mice also received PBS injections. $CD4^+$ T cells were isolated from spleen and polarized in vitro for 3 days to generate Th17 cells, followed by culture in (**A**) IL-2 containing media or (**B**) IL-23 containing media for 48 hours, after which glucose uptake was determined. Data are shown as mean ± SD of triplicate samples.

Supporting Information Figure 2



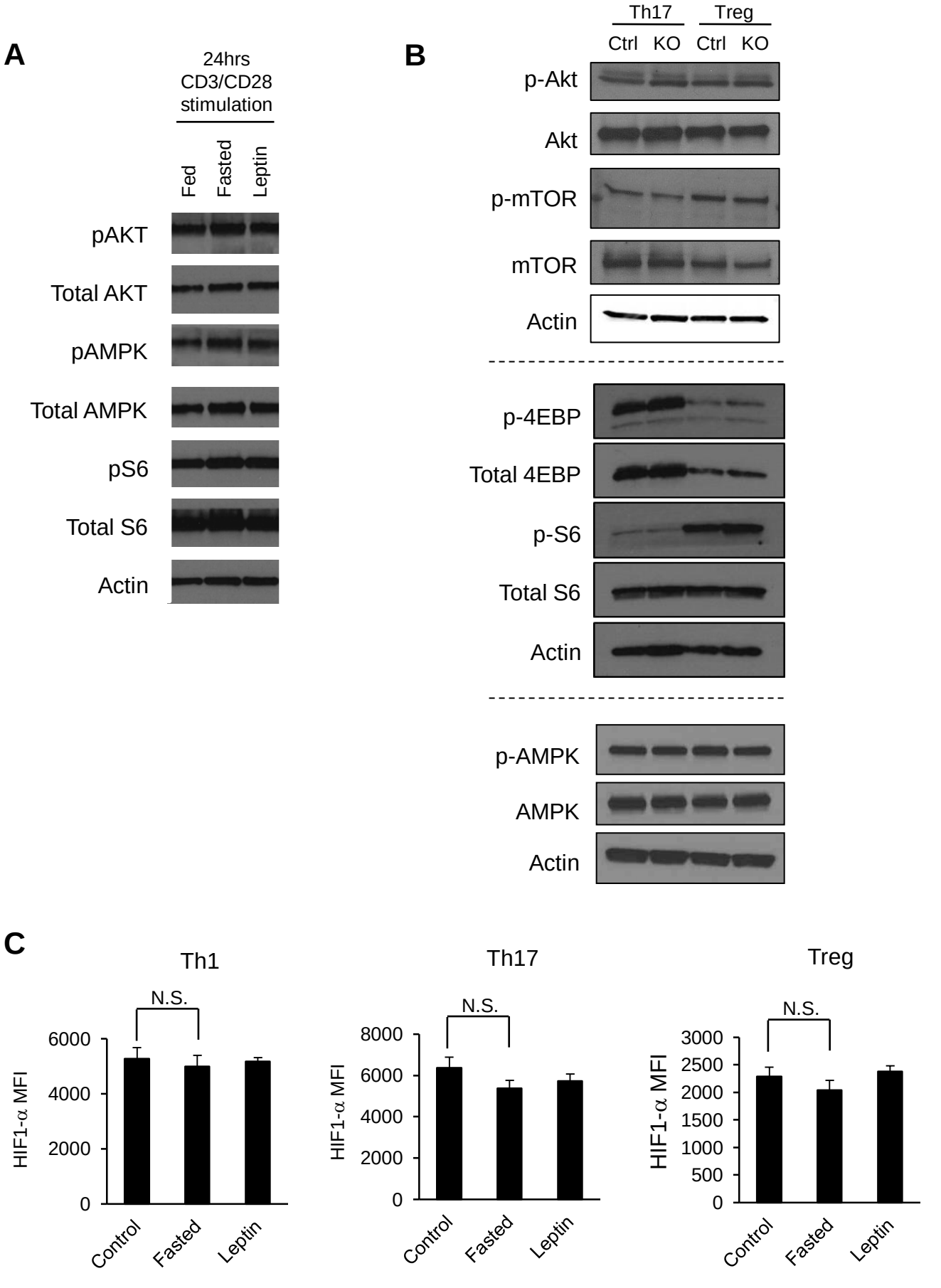
Supporting Information Figure 2. Chronic calorie restriction is associated with hypoleptinemia and inhibits Th17, but not Treg, metabolism and function. Wildtype C57BL/6J mice were fed ad libitum (control) or calorie-restricted to 50% of normal daily intake for 2 weeks. (**A**) Serum leptin levels were measured by ELISA. (**B-D**) $CD4^+$ T cells were isolated from spleen and polarized in vitro for 5 days to generate Th17 or Treg cells. (**B**) Th17 function was assessed by intracellular cytokine staining for IL-17 in live $CD4^+$ T cells, and Treg differentiation was measured by intracellular transcription factor staining for Foxp3. (**C**) Glucose uptake and (**D**) glycolytic rate were measured in Th17 and Treg from control or calorie-restricted mice. Data are representative of 2 independent experiments. (**C and D**) Data are shown as mean ± SD of triplicate samples. * indicates $p < 0.05$ by Student's *t*-test.

Supporting Information Figure 3



Supporting Information Figure 3. T cell development and Th1 response in T cell-specific leptin receptor knockout mice. (**A and B**) T cells from CD4CreLepR$^{F/F}$ or littermate control mice were isolated from thymus and spleen and (**A**) the percentages of CD4^{+} and CD8^{+} T cells were assessed by surface staining. (**B**) T cells were activated for 24 hours with anti-CD3 and anti-CD28 and representative histograms of the expression of the activation markers CD44, CD25 and CD69 in live CD4^{+} T cells are shown. (**C and D**) CD4^{+} T cells from CD4CreLepR$^{F/F}$ or littermate control mice were isolated and polarized *in vitro* for 5 days to generate Th1 cells, and (**C**) Percentage of Th1 cells expressing cytokines IL-2 and IFN-γ and (**D**) Th1 cell glucose uptake were determined.

Supporting Information Figure 4



Supporting Information Figure 4. T cell signaling in response to malnutrition and leptin. (A) Wildtype C57BL/6J mice were fed ad libitum (column 1) or fasted for 48 hours (column 2). Fasted mice received twice daily injections of leptin (column 3) or PBS. Control fed mice also received PBS injections. $CD4^+$ T cells were isolated from spleen and lymph nodes and activated for 24 hours with plate-bound anti-CD3 and anti-CD28. Lysates were examined for phospho- and total protein levels of Akt, AMPK, and S6 by immunoblot. (**B**) $CD4^+$ T cells from $CD4CreLepR^{F/F}$ or littermate control mice were isolated and polarized *in vitro* for 5 days to generate Th17 or Treg cells. Phospho- and total protein levels for Akt, mTOR, 4EBP, S6, and AMPK were examined by immunoblot. (**C**) EAE was induced in wildtype C57BL/6J mice that were fed ad libitum (control), fasted for 48 hours, or fasted while receiving twice daily leptin injections (5 mice per group). Intracellular staining for HIF1-α in Th1 ($CD4^+IFN\text{-}\gamma^+$) (*left*), Th17 ($CD4^+IL\text{-}17A^+$) (*middle*), and Treg ($CD4^+Foxp3^+$) (*right*) from draining lymph nodes was performed. Data was analyzed by two-way ANOVA. Data are shown as mean ± SD of 5 mice.