Figure S1

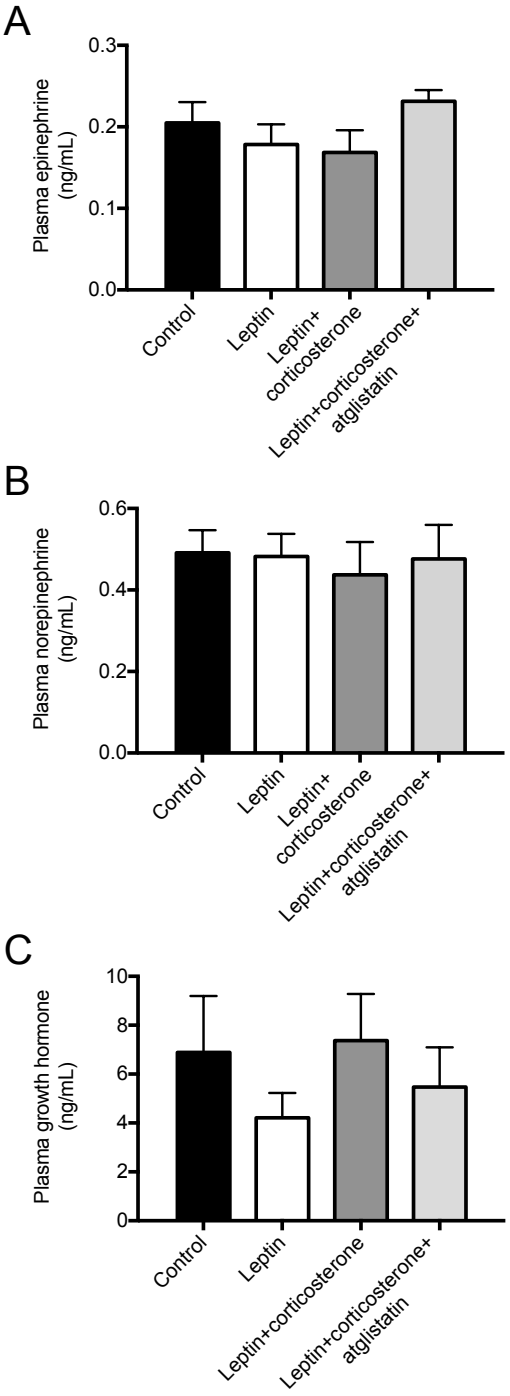

Fig. S1. Leptin's acute effect to reverse DKA results from suppression of hypercorticosteronemia. (A)-(C) Plasma epinephrine, norepinephrine, and growth hormone concentrations after a 6 hr infusion of leptin±corticosterone±atglistatin. There were no differences between groups by ANOVA with Bonferroni's multiple comparisons test. Data are the mean ± S.E.M. of n=7 (control), 7 (leptin), 10 (leptin+corticosterone), and 6 (leptin+corticosterone+atglistatin).

Figure S2

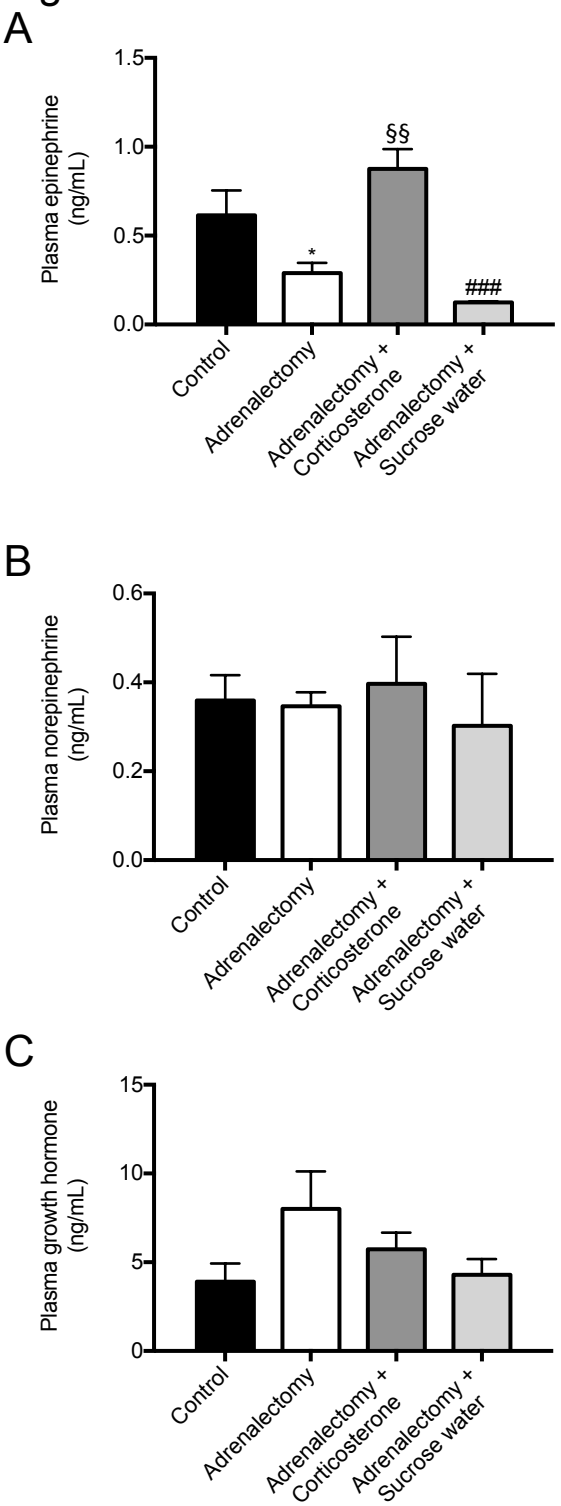

Fig. S2. Hypercorticosteronemia is necessary for DKA in fasted rats. (A)-(C) Plasma epinephrine, norepinephrine, and growth hormone concentrations. In all panels, data are the mean ± S.E.M. of n=8 (control), 11 (adrenalectomy), 8 (adrenalectomy+corticosterone), and 6 (adrenalectomy+sucrose water) per group. **P*<0.05, §§ *P*<0.01, ###*P*<0.001 vs. adrenalectomized rats by ANOVA with Bonferroni's multiple comparisons test.

Figure S3

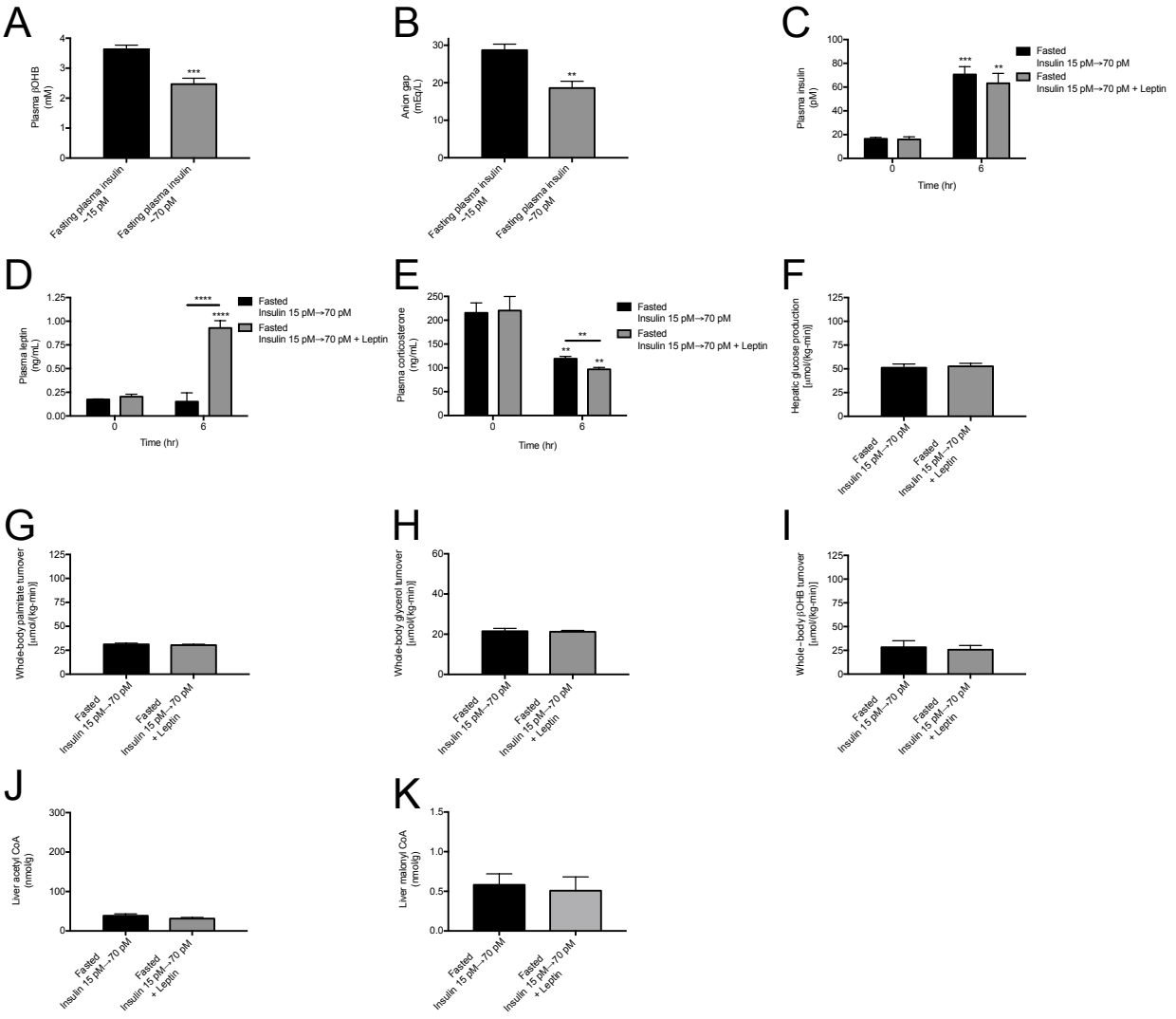

Fig. S3. Leptin has little to no acute effect in rats with plasma insulin ~70 pM. (A)-(B) Plasma βOHB concentrations and anion gap in rats with endogenous fasting plasma insulin concentrations ~15 pM and ~70 pM. (C)-(E) Plasma insulin, leptin, and corticosterone concentrations in T1D rats infused with insulin to achieve plasma insulin concentrations ~70 pM. (F)-(I) Hepatic glucose production, palmitate, glycerol, and βOHB turnover. (J)-(K) Liver acetyl and malonyl CoA concentrations. In all panels, data are the mean ± S.E.M. of n=6 per group. ***P*<0.01, ****P*<0.001, *****P*<0.0001, with asterisks directly over the bars representing comparisons to the same group at time zero by the 2-tailed paired Student's t-test, and asterisks spanning two bars representing comparisons of the two groups at the 6 hr time point by the 2-tailed unpaired Student's t-test.

Figure S4

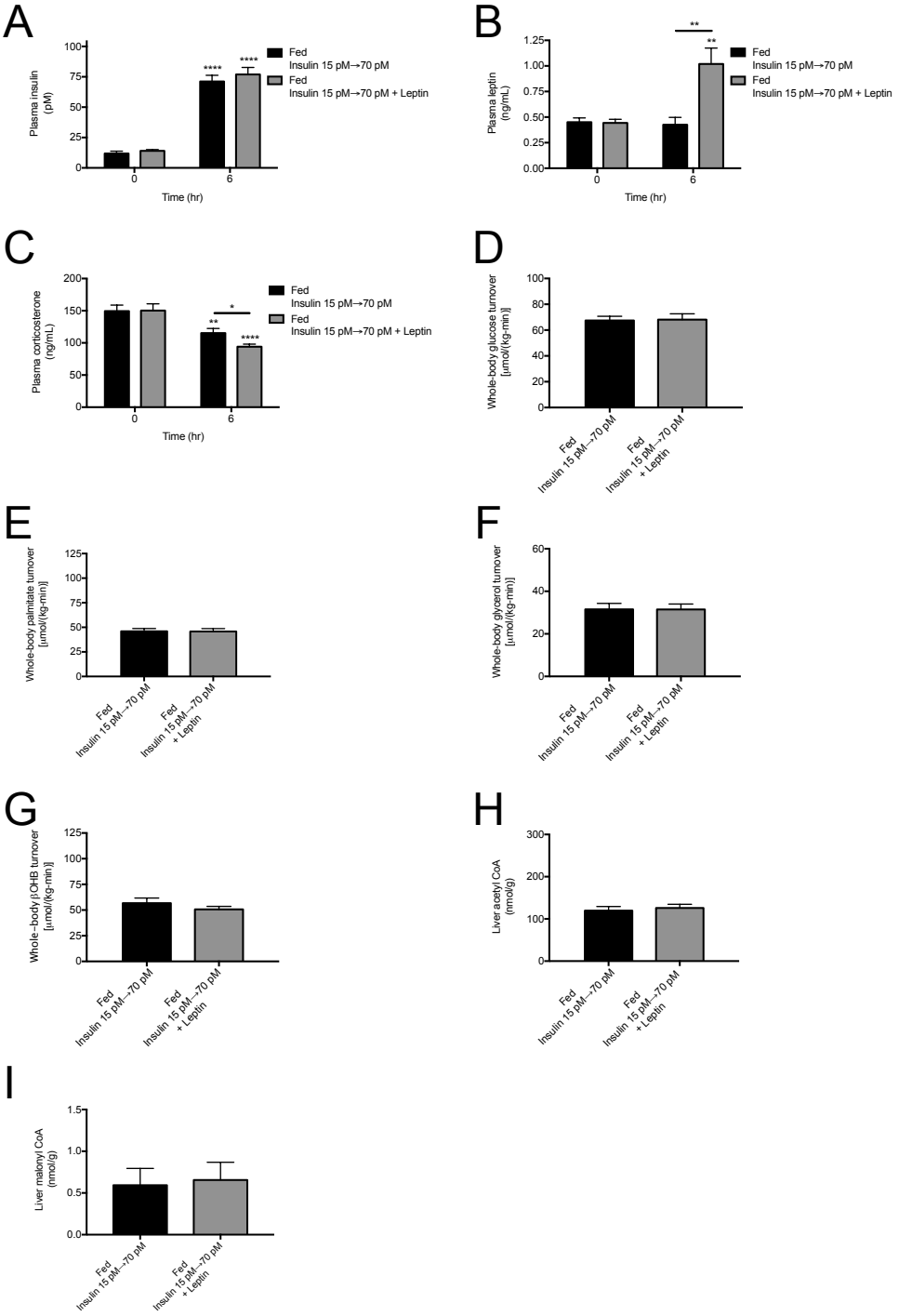

Figure S4. Leptin does not lower plasma glucose concentrations in fed rats with plasma insulin ~70 pM. (A)-(C) Plasma insulin, leptin, and corticosterone concentrations. (D)-(G) Whole-body glucose, palmitate, glycerol, and βOHB turnover. (H)-(I) Liver acetyl and malonyl CoA concentrations. In all panels, data are the mean ± S.E.M. of n=10-11 per group. **P*<0.05, ***P*<0.01, *****P*<0.0001, with asterisks directly over the bars representing comparisons to the same group at time zero by the 2-tailed paired Student's t-test, and asterisks spanning two bars representing comparisons of the two groups at the 6 hr time point by the 2-tailed unpaired Student's t-test.

Figure S5

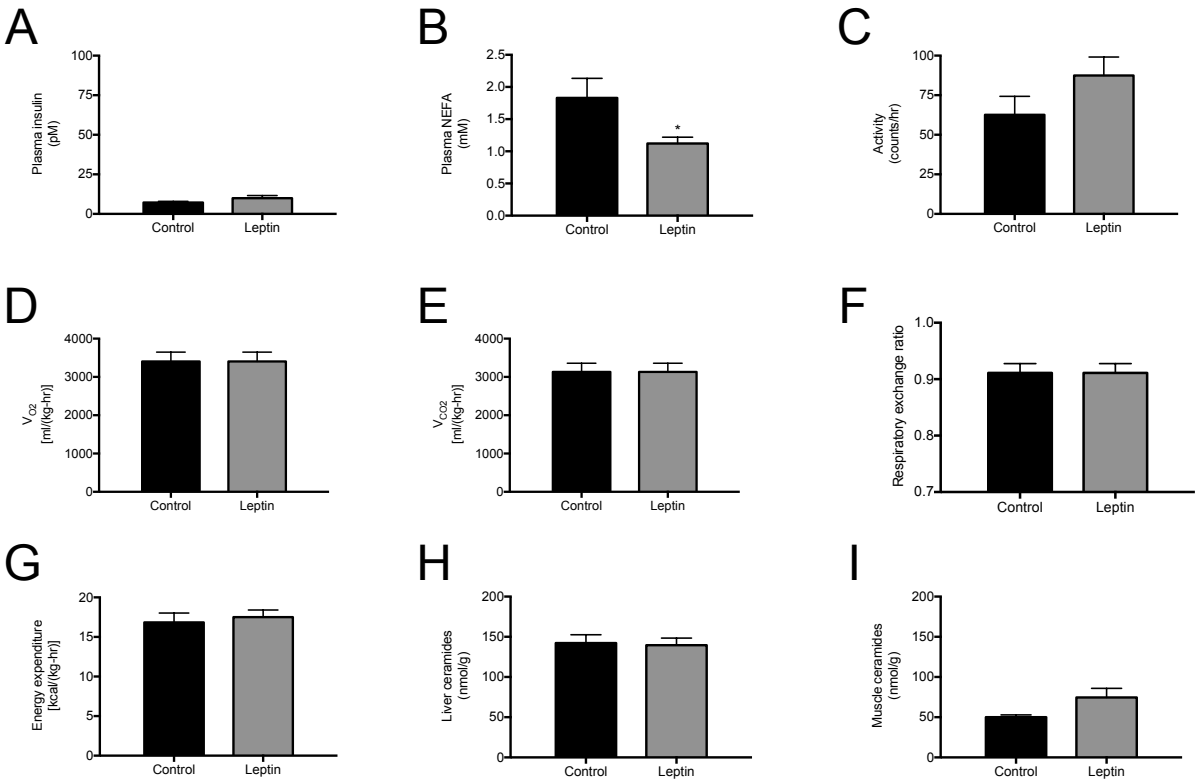

Fig. S5. The chronic effect of leptin to suppress hyperglycemia in T1D mice is pleotropic. (A)-(B) Plasma insulin and NEFA concentrations in chronic leptin-treated mice. **P*<0.05 by the 2-tailed unpaired Student's t-test. (C)-(E) Activity, VO_2, and VCO_2. (F) Respiratory exchange ratio. (G) Energy expenditure. (H)-(I) Liver and skeletal muscle ceramide concentrations. Data are the mean ± S.E.M. of n=8 (control) or 10 (leptin-treated) per group.